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(54)发明名称

伊维菌素及其衍生物的用途

(57)摘要

伊维菌素及其衍生物的用途，涉及一种伊维菌素。所述伊维菌素是链霉菌产生的大环内酯阿维菌素的一种衍生物，所述伊维菌素及其衍生物在制备用于治疗哺乳动物高血糖、胰岛素抗性、高甘油三酯血症、高胆固醇血症、糖尿病、肥胖症等代谢相关疾病的药物，以及用于治疗法尼醇受体介导的胆汁阻塞、胆结石、非酒精性脂肪肝、动脉粥样硬化、炎症、癌症等疾病的药物中的应用。

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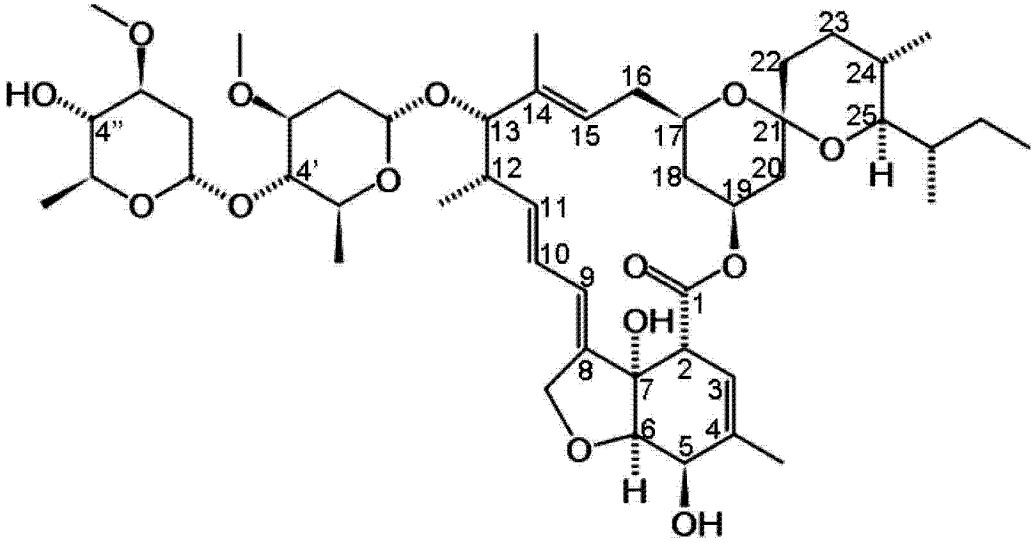
1. 伊维菌素及其衍生物在制备用于治疗哺乳动物代谢相关疾病的药物，以及用于治疗法尼醇受体介导的胆汁阻塞、胆结石、非酒精性脂肪肝、动脉粥样硬化、炎症、癌症的药物中的应用，所述伊维菌素的结构式为：



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2. 如权利要求 1 所述的应用，其特征在于所述代谢相关疾病包括高血糖、胰岛素抗性、高甘油三酯血症、高胆固醇血症、糖尿病或肥胖症。

3. 如权利要求 1 所述的应用，其特征在于所述衍生物包括阿维菌素或多拉克汀。

# 伊维菌素及其衍生物的用途

## 技术领域

[0001] 本发明涉及一种法尼醇受体 (Farnesoid X receptor,FXR) 的新型有效的配体伊维菌素 (ivermectin) 及其衍生物区别于抗寄生虫药物的新用途,以及用于新用途的伊维菌素的衍生物的设计、优化和合成的方法。

## 背景技术

[0002] 核受体是一种配体激活的转录因子。FXR 是人体 48 种核受体中非常重要的一员,在代谢、炎症、肿瘤等重大疾病及相关生理功能中起着重要的调控作用。FXR 的配体介导的药理作用原理是配体通过与 FXR 的配体结合域(LBD)结合,招募各类辅激活因子(或辅抑制因子)来调节下游靶基因。在体内,胆汁酸是 FXR 的内源性配体,FXR 的激活能够维持胆汁酸在肝脏和小肠中的正常循环和稳态,同时能够调节糖类、脂类和胆固醇的水平。FXR 牵涉到许多代谢相关的信号通路,成为治疗代谢疾病如胆汁阻塞、胆结石、非酒精性脂肪肝、动脉粥样硬化和糖尿病等出色的药物靶分子。最近,FXR 被发现能够调节肝脏的再生,小鼠 FXR 基因敲除会导致肝癌的形成。鹅去氧胆酸(英文名 chenodeoxycholic acid,缩写 CDCA)是一种能结合并激活 FXR 的胆酸,用于治疗胆结石。CDCA 是能结合 FXR 的配体中唯一用于临床的药物。但是 CDCA 对 FXR 的亲和性远远低于人工合成的 FXR 的配体 GW4064,而且 CDCA 还能结合胆酸结合蛋白(I-BABP)和胆酸转运蛋白(Bile Acid Transporter)等其它蛋白,因此,CDCA 也不是特异性以 FXR 为靶标的药物。目前,世界销售额前 100 名的药物中有高于 13% 的药物都是以核受体为靶标的,基于 FXR 参与调控的重要生理作用,筛选以 FXR 为靶标的新配体药物以及对配体药物进行优化、设计和开发具有重要的应用价值。

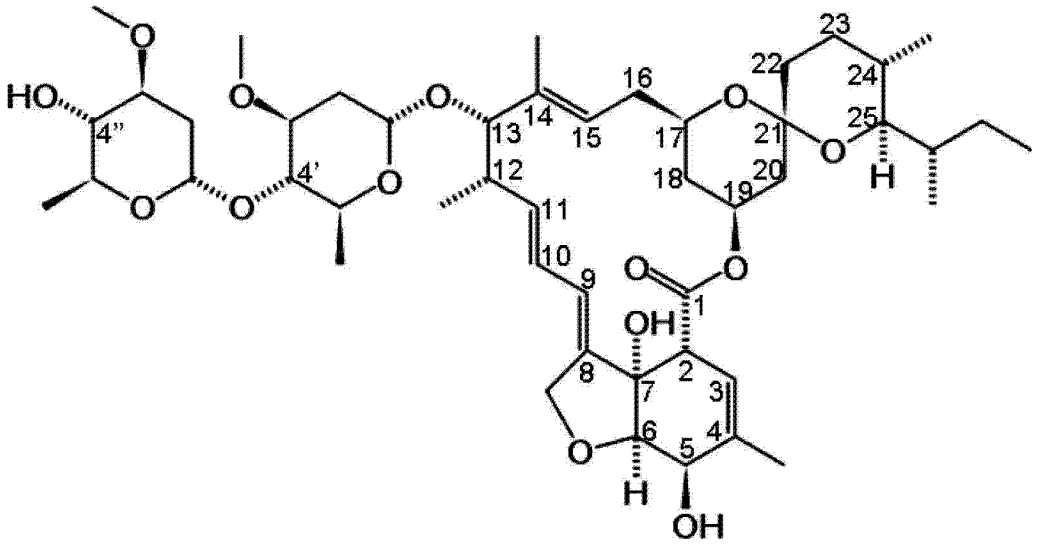
[0003] 伊维菌素 (ivermectin) 是链霉菌产生的大环内酯阿维菌素 (avermectin) 的一种衍生物,具有高效广谱的抗寄生虫作用,主要应用于家畜寄生虫控制和人丝虫感染的治疗。已有报道表明伊维菌素在无脊椎动物中的靶标是 GABA 和 GluClR 等离子通道受体。Hibbs 研究组首先解析了 GluClR/ivermectin 复合物的结构,揭示了 ivermectin 抗寄生虫的作用机制,但这些无脊椎动物中的离子通道受体不存在于脊椎动物。多拉克汀(Doramectin)也是阿维菌素的衍生物。也广泛用于家畜寄生虫控制和人丝虫感染的治疗。迄今为止尚未报道在哺乳动物中存在伊维菌素的靶标。

## 发明内容

[0004] 本发明的目的在于提供伊维菌素及其衍生物的用途。

[0005] 所述伊维菌素 (ivermectin) 是链霉菌产生的大环内酯阿维菌素 (avermectin) 的一种衍生物,具有高效广谱的抗寄生虫作用,主要应用于家畜寄生虫控制和人丝虫感染的治疗,其结构式(记为结构式Ⅰ)为 :

[0006]



[0007] 结构式Ⅰ

[0008] 所述伊维菌素具有完全不同于抗寄生虫作用的新功能。该功能的特征在于，首次提出伊维菌素在哺乳动物体内存在特异性靶标蛋白法尼醇受体，伊维菌素通过高亲和力并特异性结合法尼醇受体 (FXR)，调节哺乳动物血清中糖、脂和胆固醇的代谢，有效降低糖尿病动物模型血清中糖、脂和胆固醇的水平，改善相应的症状。伊维菌素还能通过法尼醇受体介导抑制炎症反应。因此，所述伊维菌素及其衍生物在制备用于治疗哺乳动物高血糖、胰岛素抗性、高甘油三酯血症、高胆固醇血症、糖尿病、肥胖症等代谢相关疾病的药物，以及用于治疗法尼醇受体介导的胆汁阻塞、胆结石、非酒精性脂肪肝、动脉粥样硬化、炎症、癌症等疾病的药物中的应用。

[0009] 所述伊维菌素衍生物，例如阿维菌素（avermectin）、多拉克汀（Doramectin）等。

[0010] 阿维菌素（avermectin）是在伊维菌素结构式中 C22-C23 位为双键。我们发现阿维菌素能高亲和力特异性结合 FXR，也是 FXR 的配体。因此，阿维菌素具有用于治疗哺乳动物高血糖、胰岛素抗性、高甘油三酯血症、高胆固醇血症、糖尿病、肥胖症等代谢相关疾病，以及用于治疗法尼醇受体介导的胆汁阻塞、胆结石、非酒精性脂肪肝、动脉粥样硬化、炎症、癌症等疾病的新用途。

[0011] 多拉克汀（Doramectin），是在伊维菌素结构式中 C22-C23 位为双键，C25 位是苯环侧链取代。我们发现多拉克汀能高亲和力特异性结合 FXR，也是 FXR 的配体。因此，多拉克汀具有用于治疗哺乳动物高血糖、胰岛素抗性、高甘油三酯血症、高胆固醇血症、糖尿病、肥胖症等代谢相关疾病，以及用于治疗法尼醇受体介导的胆汁阻塞、胆结石、非酒精性脂肪肝、动脉粥样硬化、炎症、癌症等疾病的新用途。

[0012] 伊维菌素作为抗寄生虫药物用于家畜和人体，其使用的安全性已经在全世界得到认证。因此，本发明通过 X 射线晶体衍射，从原子水平上提供了伊维菌素与法尼醇受体结合的独特结构模式，为以法尼醇受体为靶标的配体药物设计提供了安全的先导药物小分子以及药物优化结构模板和设计方法。

[0013] 以法尼醇受体与伊维菌素结合的结构模式为根据（附录 1），以伊维菌素结构式（如结构式Ⅰ）为结构基础，进行药物设计、药物合成和药物筛选的方法，具体步骤为：以结构式Ⅰ为结构基础，对该结构式中 C3-C4，C8-C9，C10-C11，C14-C15 碳碳双键进行改造；对 C5、C7、C4”位羟基进行改造；对 C4、C12、C14、C24、C25 位的侧链进行改造；对 C13 位的糖基进

行水解以及其他基团进行取代等改造方法。特征在于以上任何单一改造和不同方式改造的组合在制备治疗哺乳动物高血糖、胰岛素抗性、高甘油三酯血症、高胆固醇血症、糖尿病、肥胖症等代谢相关疾病，以及用于治疗法尼醇受体介导的胆汁阻塞、胆结石、非酒精性脂肪肝、动脉粥样硬化、炎症、癌症等疾病中的应用。

[0014] 本发明的技术方案是：

[0015] 通过高通量筛选得到抗寄生虫药物伊维菌素 (ivermectin) 是FXR的特异性配体。根据对伊维菌素的结构优化设计方案，发现多拉克汀和阿维菌素也是FXR的特异性配体。

[0016] 基于体外转染实验中荧光素酶报告基因活性分析及分子结构水平阐述这种受体与配体间的特异的选择性识别；通过体外的细胞培养和小鼠模型检测 ivermectin 处理后相关靶基因的表达及相关信号通路的调节状态，阐述对下游信号通路功能的影响；检测 ivermectin 处理的小鼠模型中各项生化指标的变化并结合相应的信号通路的功能变化阐述致病的分子机理；用糖尿病肥胖症模型小鼠经伊维菌素药物处理，确定伊维菌素在用于治疗哺乳动物高血糖、胰岛素抗性、高甘油三酯血症、高胆固醇血症、糖尿病、肥胖症等疾病，以及代谢相关的法尼醇受体介导的胆汁阻塞、胆结石、非酒精性脂肪肝、动脉粥样硬化等疾病中的用途，确定伊维菌素在治疗炎症反应中的用途。并根据FXR在癌症细胞中具有调节作用衍生出 ivermectin 在癌症中的治疗作用。

[0017] 将FXR/ivermectin制备复合物，通过结晶学手段，对该复合物进行结晶、X射线晶体衍射以及结构解析，从原子水平阐明了FXR与伊维菌素相互结合的独特结合模式，为以FXR为靶标的哺乳动物的上述疾病的治疗药物的设计提供了安全的先导药物小分子以及药物设计的结构模板和设计方法。

## 附图说明

[0018] 图1为GW4064与ivermectin分别和FXR结合促进了FXR募集辅调节因子。在图1中，横坐标表示生物素标记的几种辅调节因子与FXR结合序列的多肽。

[0019] 图2为0.5μM ivermectin对FXR受体的特异性转录激活。用FXR等不同核受体的全长表达质粒和不同核受体相应的内源结合元件构建的报告基因共同转染COS-7细胞。转染后，用DMSO或0.5μM ivermectin处理细胞。

[0020] 图3为ivermectin对FXR受体转录活性的激活是受配体浓度影响的。在图3中，横坐标表示配体浓度的对数值。

[0021] 图4为FXR/ivermectin蛋白复合体的结构图。结合在FXR LBD配体口袋的ivermectin用棒状结构式表示。在图4中，NcoR2表示与FXR和ivermectin形成复合体的辅调节因子NcoR中与FXR结合序列的多肽。

[0022] 图5为结合在FXR上的ivermectin电子云图谱。

[0023] 图6为Ivermectin和FXR结合的关键位点及其对FXR转录活性的影响与ivermectin相互作用的关键氨基酸的突变对ivermectin和GW4064激活FXR转录活性的影响。全长表达FXR(wt)或相应点突变的表达质粒与EcRE报告基因公转染于COS-7细胞后用ivermectin和GW4064处理细胞后检测转录活性。在图6中，横坐标表示野生型的FXR(WT)和4个氨基酸位点的突变体。

[0024] 图7为Ivermectin通过FXR下调血清中糖的水平。

[0025] 图 8 为 Ivermectin 通过 FXR 下调血清中胰岛素的水平。

[0026] 图 9 为 Ivermectin 通过 FXR 下调血清中胆固醇的水平。

[0027] 图 10 为 Ivermectin 能下调血清中甘油三酯的水平。

[0028] 图 11 为 Ivermectin 处理对小鼠摄食量无影响。

[0029] 图 12 为 Ivermectin 处理后小鼠的体重没有变化。

[0030] 图 13 为利用实时荧光定量 PCR 方法检测 Ivermectin 处理后小鼠肝脏内 FXR 靶基因及和糖类、甘油三酯和胆固醇代谢相关的基因表达。10~12 周龄野生型小鼠和 FXR 基因敲除型小鼠通过腹腔注射 40%HBC(2-hydroxypropyl-β-cyclodextrin) 或由 40%HBC 稀释的 ivermectin 14 天，摄食量每隔一天称一次，Kcal，kilocalories ;BW，body weight。处理 14 天后饥饿 6h，称体重(F)。眼球取血收集血清用于糖脂水平检测。取肝脏冻存用于提取 RNA 检测基因表达水平。

[0031] 在图 7~13 中，WT 表示野生型小鼠，KO 表示 FXR 基因敲除型小鼠。白色柱子表示用 HBC 溶剂处理的对照组小鼠，黑色柱子表示 ivermectin 处理的实验组小鼠。每组 6 只小鼠。* 表示相对对照组的数据具有显著差异性，* 为 $p<0.05$ ;** 为 $p<0.01$，*** 为 $p<0.001$。

[0032] 图 14 为 Ivermectin 处理对 KK-Ay 糖尿病模型小鼠摄食量无影响。

[0033] 图 15 为 Ivermectin 处理后降低了 KK-Ay 糖尿病模型小鼠体重。

[0034] 图 16 为 Ivermectin 处理后降低了 KK-Ay 小鼠中血糖水平。

[0035] 图 17 为 Ivermectin 处理后降低了 KK-Ay 小鼠中胰岛素水平。

[0036] 图 18 为 Ivermectin 处理后降低了 KK-Ay 小鼠中胆固醇水平。

[0037] 图 19 为 Ivermectin 处理后降低了 KK-Ay 小鼠中甘油三酯水平。

[0038] 图 20 为 Ivermectin 处理后降低了 KK-Ay 小鼠中自由脂肪酸水平。

[0039] 图 21 为 Ivermectin 处理后检测和血糖、胆固醇、甘油三酯和脂肪酸代谢的相关基因表达。10~12 周龄 KK-Ay 小鼠分别腹腔注射 HBC 对照、GW4064(30mg/kg) 和 ivermectin(1.3mg/kg) 14 天，摄食量每隔一天称一次，Kcal，kilocalories ;BW，body weight。处理 14 天后饥饿 6h，称体重(B)。眼球取血收集血清用于糖脂水平检测。取肝脏冻存用于提取 RNA 检测基因表达水平。

[0040] 在图 14~21 中，白色柱子表示 HBC 溶剂处理的对照组小鼠，斜纹柱子表示用用 GW4064 处理的实验组小鼠，黑色柱子表示 ivermectin 处理的实验组小鼠。每组 6 只小鼠。* 表示相对对照组的数据具有显著差异性，* 为 $p<0.05$ ;** 为 $p<0.01$。

[0041] 图 22 为 Ivermectin 通过 FXR 介导抑制 LPS 诱导的炎症反应相关基因表达(iNOS)。

[0042] 图 23 为 Ivermectin 通过 FXR 介导抑制 LPS 诱导的炎症反应相关基因表达(TNFa)。

[0043] 图 24 为 Ivermectin 通过 FXR 介导抑制 LPS 诱导的炎症反应相关基因表达(IL-6)。

[0044] 图 25 为 Ivermectin 通过 FXR 介导抑制 LPS 诱导的炎症反应相关基因表达(MIP-1a)。

[0045] 在图 22~25 中，WT 表示野生型小鼠，KO 表示 FXR 基因敲除型小鼠。白色柱子表示用 HBC 溶剂处理的对照组小鼠，斜纹柱子表示用用 GW4064 处理的实验组小鼠，黑色柱子表示 ivermectin 处理的实验组小鼠。每组 6 只小鼠。* 表示相对对照组的数据具有显著差异性，* 为 $p<0.05$ ;** 为 $p<0.01$。

[0046] 图 26 为 Ivermectin 通过 FXR 介导抑制 NF-κB(p65) 的转录活性。

[0047] 图 27 为 Ivermectin 通过 RXR 介导抑制 NF-κB(p65) 的转录活性。

[0048] 图 28 为阿维菌素和多拉克汀具有与伊维菌素相似的 FXR 高亲和力。在图 28 中，横坐标表示配体浓度的对数值。

[0049] 图 29 为阿维菌素与多拉克汀具有与伊维菌素类似的诱导 FXR 募集各种辅调节因子的能力。

## 具体实施方式

[0050] 蛋白纯化

[0051] 1. 克隆

[0052] (1) 以 pcDNA-FXR 质粒为模板，0.5μL 50mM 前向引物 5′GATATGGATCCAATCCAGAGTCCGCTGACCTC，0.5μL 50mM 反向引物 3′GATATCTCGAGCTAGTACAAGT CCTTGTAGATC 为引物，4μL 10×PCR buffer，1μL 10mM dNTP 及 5U pfu 酶（Invitrogen）加水（Milli-Q）补足至 50μL 体系进行 PCR 反应以获得含有双酶切位点 BamH Ⅰ和 Xho Ⅰ的人源 FXR LBD（配体结合域）（氨基酸残基数 243-472）的 PCR 产物。PCR 反应程序为：

[0053] 94℃ 2min

[0054]

94℃ 30s
58℃ 1min
72℃ 1min
} 30 个循环

[0055] 72℃ 10min

[0056] (2) 酶切克隆插入 DNA 片段和 pET24a（Novagen）载体用 BamH Ⅰ和 Xho Ⅰ对 PCR 产物及 pET24a 载体进行酶切。

[0057] 酶切体系为：

[0058]

| | |
|---|---|
| FXR LBD PCR 产物或 pET24a 载体 | 1 ug (10μL) |
| BamHⅠ（Thermo） | 0.5 μL |
| XhoⅠ （Thermo） | 0.5 μL |
| 4× Digestion Buffer （Thermo） | 4 μL |

[0059]

| | |
|---|---|
| $ddH_2O$ （Milli-Q） | 25 μL |

[0060] 37℃ 1.5h。

[0061] (4) 酶切后的 PCR 产物和 pET24a 载体通过加有 SYBR DNA 染料的 1% 琼脂糖凝胶分离并通过 Promega 胶回收试剂盒进行片段回收处理。

[0062] (5) 将回收片段和载体以摩尔比 3 ： 1 连接。

[0063] 连接体系为：

[0064]

| | |
|---|---|
| FXR LBD PCR 产物 | 2 μL |
| pET24a（Novagen）载体 | 2 μL |
| 5×Ligation Buffer 连接缓冲液（Invitrogen） | 2 μL |
| T4 DNA Ligase（T4 DNA 连接酶-Invitrogen） | 0.5 μL |
| 加 $ddH_2O$ 至 | 10μL |

[0065] 室温反应 30min。

[0066] (6) 取 2μL 连接产物转化入 50μL Trans109 感受态细胞，冰浴 30min 后 42℃热激 30s。加入无抗生素的 LB 液体培养基 250μL，于 225rpm 37℃预摇 40min 后，取 150μL 转化产物涂于添加有 50μg/ml 卡那霉素的 LB 固体培养基平板，37℃过夜培养。

[0067] (7) 次日，挑取单克隆于 2ml 含 50μg/ml 卡那霉素的 LB 液体培养基，37℃摇床培养 10h。

[0068] (8) 采用 Qiagen MiniPrep 质粒小提试剂盒对所摇菌液进行质粒提取。

[0069] (9) 对提取的质粒进行酶切鉴定。酶切鉴定体系：

[0070]

| | |
|---|---|
| 质粒 | 2 μL |
| BamH Ⅰ（Thermo） | 0.5 μL |
| Xho Ⅰ （Thermo） | 0.5 μL |
| 4×Digestion Buffer （Thermo） | 2 μL |
| $ddH_2O$ （Milli-Q） | 15 μL |

[0071] 37℃恒温箱酶切反应 30min 后用 1% 琼脂糖凝胶进行检测以确定目的片段成功插入表达载体。最后将获得的质粒进行测序鉴定。得到六聚组氨酸标记的人类核受体FXR LBD的表达质粒，表示为 pET24a-His6-FXR LBD。

[0072] 2. 目的蛋白表达和纯化

[0073] (1) 转化

[0074] 将 pET24a-His6-FXR LBD 转化进 BL21（DE3）感受态细胞，取 1μL 质粒转化入 50μL BL21 感受态细胞，冰浴 30min 后放入 42℃水浴锅中热激 30s。加入无抗生素的 LB 液体培养基 250μL 于 225rpm 37℃预摇 40min 后取 15μL 涂于添加有 50μg/ml 卡那霉素的 LB 固体培养基平板，37℃过夜培养。

[0075] (2) 摇菌

[0076] 次日挑单克隆于 50ml 含 50μg/ml 卡那霉素的 LB 液体培养基中 37℃预摇 8h 后转入含 50μg/ml 卡那霉素的 1.5L LB 液体培养基中，当 OD600 达到 1.0 左右时，加入 0.1mM 的 IPTG 在 16℃下低温诱导表达。

[0077] (3) 收集含有诱导目的蛋白的菌体细胞

[0078] 诱导表达过夜的 1.5L 菌液于 4℃ 3,000rpm 离心 10min 收集细菌，用纯化缓冲液 100ml（20mM Tris pH8.0,150mM NaCl,10%glycerol,25mM imidazole）重悬菌液，冻存于 -80℃。

[0079] (4) 蛋白质提取

[0080] 采用 Fisher Scientific Sonic Dismembrator 超声破碎仪以振幅 60%,5s 工作 10s 休息的频率超声波处理 8min。

[0081] BECKMAN 离心机以 20,000rpm 4℃离心 30min 后取上清。

[0082] (5) 蛋白质纯化

[0083] 将上清过 5ml 的镍离子交换柱(NiSO4-loaded HisTrap HP column,GE Healthcare),使目的蛋白质充分富集到镍柱上。

[0084] 采用 GE 公司 AKTA 蛋白质纯化系统及 UNICORN 软件操作。

[0085] 洗泵:先用水洗,再用缓冲液洗。操作步骤为:在 System Control 窗口中,依次选择:Manual → Pump → Pumpwashbasic → PumpA,PumpB → On → Excute。

[0086] 层析柱连接:先启动系统泵,待有溶液流出时,将层析柱动态接入系统,使流出的蛋白质可以经过 UV 检测到峰值,打开 UNICORN 软件,编辑蛋白洗脱的程序:

[0087] 20ml 洗脱缓冲液进行柱平衡

[0088] 25-500mM 咪唑进行梯度竞争性结合柱子以洗脱目的蛋白质

[0089] 15ml 缓冲液进行柱平衡。

[0090] 蛋白质洗脱:用洗脱缓冲液 A、B 梯度洗脱该柱子上的蛋白(洗脱缓冲液 A 成分:25mMTris,150mM NaCl,25mM Imidazole 和 10% 甘油,pH 7.5;洗脱缓冲液 B 成分:25mM Tris,150mM Imidazole 和 10% 甘油,pH7.5),通过控制咪唑浓度梯度变化在 25~500mM,以在合适浓度竞争下洗脱含相似结构的组氨酸标签的目的蛋白质。

[0091] 采用 Q 阴离子交换柱利用目的蛋白质所带负电荷进一步分离纯化过镍柱后的蛋白质,方法同上。蛋白洗脱缓冲液换为洗脱缓冲液 C、D (洗脱缓冲液 C:25mM Tris,pH7.5;洗脱缓冲液 D:25mM Tris,1.0M NaCl,pH7.5)。

[0092] 采用 Hiload26 分子筛层析柱(GE Healthcare)利用分子量不同进一步纯化目的蛋白质,步骤如下:

[0093] 将 Q 柱收集的蛋白质盛入 Millipore 10kD 的浓缩管,4℃ 4,000g,20min 离心到终体积 10ml 后,经注射器注入 AKTA 端口后开始程序运行,方法同上。蛋白洗脱缓冲液换为含有 10mM NaCl 的洗脱缓冲液 C(洗脱缓冲液 C:25mM Tris,pH7.5)。

[0094] (6) 制备蛋白质复合体

[0095] 采用从金斯瑞定制合成的 NcoR2 多肽 (PASNLGLEDIIRKALMGS) 与 FXR LBD 蛋白复合体:分子筛柱层析得到的 20ml 蛋白质与 NcoR2 多肽及 ivermectin 按摩尔比 1 : 1 : 1 混合加入 10kD MILLIPORE 15ml 浓缩管中浓缩,4℃ 4,000 离心浓缩,将蛋白浓缩到 10mg/ml 的终浓度。

[0096] 蛋白结晶,晶体数据收集与结构解析

[0097] 采用悬滴法进行结晶筛选,FXR/ivermectin/NcoR2 复合物在室温条件下,悬滴液成分为 1.0μl 上述蛋白多肽配体复合体溶液混合上 1.0μl 结晶缓冲液(50mM HEPES pH7.0,3.5Msodium formate)。生长成熟的蛋白晶体用液氮进行急速冷冻保存。在上海光源的 BL17U1 线站进行数据采集。经 X 光照射处理后,所得衍射数据通过 HKL2000 软件处理确定每个不对称单元含有两个分子,晶体空间基团为 I 212121 (a=53.01, b=161.76, c=169.02, α=90°, β=90°, γ=90°),具体结构解析使用由 CCP4 程序包(http://www.ccp4.ac.uk)中的 Molrep、Phaser 等通过分子置换确定出大致结构模型,通过 Coot 的人工

模型精细构建及 REFMAC 和 phenix.refine 深入修饰的多次循环，得到最终蛋白复合物结构，这一结构模型的 Rwork 和 Rfree 分别为 25.4% 和 28.2%，分辨率为2.81Å。具体的三维晶体结构空间元素见附录 1。

[0098] 辅因子结合实验

[0099] 通过 Alphascreen 分析方法，用 Alpha Screen nickel chelate detection kit 试剂盒（Perkins-Elmer）检测配体诱导核受体募集各种辅调节因子的结合能力（Li et al. 2005）。该实验的反应体系是 20nM 的融合组氨酸标签的受体 LBD 蛋白，20nM 生物素化标记的辅因子多肽，5μg/ml 的供体和受体珠子，缓冲液（50mM MOPS, 50mM NaF, 0.05mM CHAPS, and 0.1mg/ml bovine serum albumin, pH7.4），反应体系 50μL 于 384 孔板中室温反应 1h 后用 AlphaScreen 检测仪读取 680nm 激发光下 520-620nm 的发射光信号。用于 Alphascreen 分析的生物素标记的多肽序列如下：

[0100] SRC1-2, SPSSHSSLTERHKILHRLLQEGSP;

[0101] SRC2-3, QEPVSPKKKENALLRYLLDKDDTKD;

[0102] SRC3-3, PDAASKHKQLSELLRGGSG;

[0103] NCOR-2, GHSFADPASNLGLEDIIRKALMGSF.

[0104] 瞬时转染实验

[0105] 1. 质粒：

[0106] (1)FXR 全长质粒：将人类 FXR 全长 cDNA 表达序列采用经典克隆方法克隆到 pCMX 表达载体。

[0107] (2) 获得关键结合位点的 FXR 点突变表达载体。使用 Quick-Change site-directed mutagenesis 试剂盒（Stratagene）进行突变，突变反应体系如下：

[0108]

| | |
|---|---|
| 野生型质粒 pCMX-FXR (50 ng) | 0.5 μL |
| 突变引物 (100 μM stock) | 0.2 μL |
| pfu DNA 聚合酶（Invitrogen） (2 U) | 1 μL |
| 10 mM dNTPs | 1 μL |
| 10×PCR buffer | 5 μL |
| ddH20 | 43 μL |

[0109] 94℃ 2min

[0110]

94℃ 30s
55℃ 1min
72℃ 7min
} 15 个循环

[0111] 4℃ forever

[0112] 20μL PCR 产物用 Dpn Ⅰ甲基化酶消化后取 2μL 消化产物转化入大肠杆菌 Trans109 感受态细胞，冰浴 30min 后 42℃热激 30s。加入无抗生素的 LB 液体培养基 250μL 于 225rpm37℃预摇 40min 后取 150μL 涂于添加有 100μg/ml 氨苄青霉素的 LB 固体培养基

平板，37℃过夜培养。

[0113] 次日，挑取单克隆于 2ml 含 100μg/ml 氨苄青霉素的 LB 液体培养基，37℃过夜培养。采用 Qiagen MiniPrep 质粒小提试剂盒对所摇菌液进行质粒提取。对质粒进行测定鉴定。

[0114] (3) 各内源结合元件的报告基因直接商业购买。

[0115] 2. 转染：

[0116] 使用含有 10% 胎牛血清的 DMEM 培养基进行猴肾上皮细胞 COS-7 细胞培养，转染前一天在 24 孔板进行 COS-7 细胞接种，接种密度为 $5\times10^4$ 细胞 / 每孔，第二天进行转染。转染使用 Lipofectamine 2000(Invitrogen)进行瞬时转染(Li et al.2005)。在报告基因分析实验中，使用 200ng 的核受体全长表达质粒或其突变体表达质粒与 200ng 的内源启动子报告基因以及 30ng 的 Renilla 荧光素酶表达质粒进行共转染。每孔添加 500μLOpti-MEM 培养 5h 后，添加稀释在 Opti-MEM 的配体药物至相应浓度，处理 18h。各种核受体及相应的报告基因使用如下：人 FXR，EcRE-Luc；人 PPARs(α，δ，and γ)，PPRE-Luc；人 RORs(α，β和 γ)，Pcp2/RORE-Luc；人 GR 和 PR，MMTV-Luc；人 RARα 和 RARβ，βRE-Luc。用于检测炎症反应相关的报告基因分析中，转染 p65 使用的是含 NF-κB(p65) 的靶基因启动子结合元件的两种报告基因 (IL6)×3-luc 和 NF-κB-luc。

[0117] 3. 报告基因分析：

[0118] 配体药物处理 18h 后，用 Promega 公司的双荧光素梅报告基因分析试剂盒进行报告基因活性分析。裂解细胞用于荧光素酶检测实验，取 10μL 细胞裂解细胞转移到 96 孔板，加入 50μL 荧光素酶反应液后使用 EnSpire™2300 多功能酶标仪 (Perkin Elmer) 检测在 560nm 下的发射光信号，后加入 Stop&Glo® 反应液终止荧光素酶反应并检测 renilla 荧光素酶活力。报告基因的活性以 renilla 活性为内参。

[0119] 小鼠试验

[0120] 使用 10-12 周的野生型 C57BL/6J 小鼠和同样背景的 FXR 基因缺失纯合子小鼠 ($FXR^{-/-}$) 以及糖尿病肥胖症模型小鼠(KK-Ay)，在厦门大学实验动物中心 SPF 级别动物房，用高脂饲料 (Research Diets,D12492) 喂养，自由饮水。按对照组、伊维菌素处理组和 / 或 GW4064 处理组分，每组 6 只，分别通过腹腔注射对照(40% 的 HBC(2-hydroxypropyl-β-cyclodextrin)) 溶液、用对照溶液稀释的 ivermectin (按药物质量 / 小鼠体重来算，注射量为 1.3mg/kg)，和 / 或用对照溶液稀释的 GW4064 (30mg/kg)。每天早上 9 点腹腔注射一次，连续注射 14 天，每隔一天称小鼠体重和小鼠摄食量。14 天结束后，给小鼠饥饿 6h，自由进水。禁食 6h 后，称小鼠体重，用最后体重相对注射试验处理前的初始体重百分比表示小鼠体重的变化(附图 4F 和 5B)。然后从眼球取血，分离得到血清。血清中成分分别是由以下试剂盒测得：糖 - 氧化酶法(北京普利莱)；胰岛素(Crystal Chem.Inc.,USA)；胆固醇(Bioassay Systems,USA)；甘油三酯(北京普利莱和 WAKO Chemicals Inc.,Japan)；自由脂肪酸(Bioassay Systems,USA)。取下小鼠肝脏，液氮冻存，供提取 RNA 进行荧光定量 PCR 检测基因表达使用。

[0121] 荧光定量 PCR 检测基因表达

[0122] 从对照 (40%HBC) 或 ivermectin 处理的野生型和 FXR 敲除的小鼠模型中获得肝脏组织；从对照、GW4064 或 ivermectin 处理过的 KK-Ay 小鼠模型中获得肝脏组织，冻存于 -80

度冰箱。用 RNA 提取试剂盒 (Omega Bio-Tek,GA) 从组织中提取总 RNA。采用 TAKARA 反转录试剂盒进行反转录,采用 SYBR 绿色荧光染料在 CFX™96 系统 (BIO-RAD) 实时监测系统下进行荧光定量 PCR 分析基因表达水平。

[0123] 反应体系如下 :

[0124]

| | | |
|---|---|---|
| SYBR Premix Ex Taq (2×) | 12.5 μL | 总计 25 μL |
| PCR 前引物 (10 μM) | 1 μL | |
| PCR 后引物 (10 μM) | 1 μL | |
| cDNA 模版 | 2 μL | |
| 灭菌蒸馏水 | 8.5 μL | |

[0125] 两步法扩增 PCR 程序 :

[0126] 预变性

[0127] 95℃ 30s

[0128] PCR 反应

[0129]

| | | |
|---|---|---|
| 95℃ | 5s | 40 个循环。 |
| 60℃ | 40s | |

[0130] 以下给出具体实施例 :

[0131] 实施例 1,证明 ivermectin 是一种高亲和力和高特异性的新型 FXR 配体。

[0132] 通过 AlphaScreen 来筛选 FXR 的特异性配体,并检测 FXR 与辅激活因子或辅抑制因子的作用。检测发现 ivermectin 能够诱导 FXR 募集辅激活因子,如 :SRC1,SRC2 和 SRC3,该能力略低于配体 GW4064 ;相对于 GW4064 而言,FXR 对于辅抑制因子也有一定的募集能力 (图 1)。因此,ivermectin 作为 FXR 部分激活剂以一种独特方式发挥其调节功能。

[0133] 为了证明 ivermectin 能够特异性的结合 FXR,我们用 FXR 的内源报告基因 EcRE 和表达全长 FXR 的质粒共转染 COS-7 细胞。结果发现,在检测的不同核受体中,ivermectin 只特异性激活了 FXR 的转录活性(图 2)。这体现了 ivermectin 作为 FXR 配体的高特异性。

[0134] 为了证明 ivermectin 激活 FXR 的转录活性的工作浓度,我们用表达全长 FXR 的质粒和 EcRE 报告基因共转染 COS-7 细胞,用不同浓度梯度的 ivermectin 处理转染后的细胞,检测 FXR 的转录活性。结果显示 FXR 的转录活性是和 ivermectin 的浓度成正相关的,当 ivermectin 浓度达到 1uM 时,FXR 的转录活性达到饱和(图 3)。而且从该结果可以看出,ivermectin 对激活 FXR 转录活性的半数有效浓度与 GW4064 很接近,激活饱和浓度与 GW4064 相同,进一步表明了 ivermectin 对 FXR 的高亲和力。

[0135] 实施例 2,FXR/ivermectin 复合物的晶体结构解析

[0136] 为了从分子水平揭示 ivermectin 和 FXR 相互识别和结合的分子机制,我们解析了分辨率达2.8Å的 FXR/ivermectin 与辅抑制因子 NcoR 核受体结合基序形成复合物的晶体结构(附录 1,图 4)。结构显示 ivermectin 与 FXR 配体结合域的结合符合经典的“三明治”构象。从电子云图看,ivermectin 清晰的存在与 FXR 的配体结合口袋(图 5)。在复合物结构中,电子密度图不能清晰的看出 FXR 羧基末端 AF-2 的螺旋结构,是因为 ivermectin 的结合

导致AF-2螺旋的不稳定性造成的(图4)。这从分子机制方面解释了ivermectin在诱导FXR转录活性和辅激活因子的能力方面要比合成的FXR的配体GW4064弱,同时ivermectin对辅抑制因子NcoR也有一定的募集能力的现象(图1),进一步说明ivermectin以一种的独特结合方式调节FXR的功能。FXR与ivermectin结合模式的具体信息见附录1。

[0137] 实施例3,Ivermectin在FXR配体结合口袋中独特的结合位点

[0138] 为了验证FXR配体结合口袋中与ivermectin直接结合的氨基酸位点,我们根据FXR与ivermectin复合体的结构对两者相互结合的关键位点进行了点突变,检测这些突变后的FXR收配体调节的转录活性以确定这些结合位点对于ivermectin结合的重要性。

[0139] A291对于FXR配体结合域大小的调节有着重要的作用。当把291位的丙氨酸(A)突变为色氨酸(W)时,由于色氨酸比丙氨酸大得多的侧链基团占据了配体结合口袋的空间,会导致FXR的配体结合口袋会变小,从而影响FXR配体的结合。与我们所期望的一致,报告基因分析实验结果表明,A291W的突变导致GW4064和ivermectin都不能激活FXR的转录活性(图6)。表明FXR的291位丙氨酸残疾对GW4064或ivermectin结合并激活FXR转录活性是极其关键的。

[0140] 在疏水链上的284位苯丙氨酸(F)分别能够与GW4064和ivermectin形成疏水相互作用,从而稳定配体和受体的结合。当F284突变为组氨酸(H)时,这两种疏水相互作用就会消失。但是另一方面,对于GW4064而言,突变成组氨酸后可能形成氢键相互作用,因此,疏水相互作用的消失导致ivermectin不能激活FXR的转录活性,但GW4064的激活能力却没有受到影响(图6)。这说明ivermectin与FXR配体结合口袋的结合具有区别与GW4064的独特的结合方式。

[0141] 另外,L287T和H447F的突变明显降低了GW4064介导的FXR的转录活性,但却显著地增加了ivermectin对FXR转录活性的激活(图6)。这也说明GW4064和ivermectin与FXR的结合方式有着很大的区别,说明对于FXR功能的调节也有明显的不同。

[0142] 实施例4,Ivermectin通过FXR介导来调节糖类和脂类的代谢

[0143] FXR作为一种重要的核受体,它首先被作为胆酸的受体调节肝脏和小肠内胆汁酸的循环和平衡。近来发现,FXR能够调节生物体内糖类和脂类的代谢。合成的FXR配体GW4064能够通过FXR降低血糖、血脂和胆固醇的水平,能够缓解高血糖症和肥胖的症状,但由于GW4064的细胞毒性和药效限制性导致其不能临床使用;同时一些文章也提到GW4064对于机体的血糖没有明显的效果。因此,GW4064对血糖的调节尚存在争议。发现新的FXR的配体药物显得更加重要和有意义。

[0144] 为了检测ivermectin对小鼠模型生理功能,我们采用野生型和FXR基因敲除小鼠进行试验。高脂饲料喂养的小鼠,两周腹腔注射对照和ivermectin后发现,ivermectin对小鼠的进食和体重没有影响(图11、12)。在野生型小鼠的肝脏中,ivermectin处理显著降低了血清中糖类和胆固醇水平,但在FXR敲除的小鼠中没有明显变化(图7和9)。在野生型小鼠的血清中,ivermectin处理显著降低了胰岛素的水平(图8),说明ivermectin可能通过增加胰岛素的敏感性达到了降血糖的效果。但是在FXR基因敲除小鼠中药物处理对胰岛素的水平没有显著变化,说明ivermectin调节血清中血糖、胰岛素和胆固醇是通过FXR进行的。另外,ivermectin也显著降低了野生型小鼠血清中甘油三酯(Tg)水平,虽然在FXR敲除小鼠中,ivermectin也明显降低了甘油三酯的水平,但在野生型小鼠中,这种程度降低幅

度更大，显著性更强(图 10)，这说明 ivermectin 对于小鼠血清中甘油三酯水平的降低在一定的程度上部分依赖于 FXR 受体。通过荧光定量实时 PCR 检测配体药物处理过的小鼠肝脏糖、脂、胆固醇代谢相关基因的表达结果表明，ivermectin 达到降血糖、血脂和胆固醇的生理功能与糖、脂、胆固醇代谢相关基因的表达调控一致（图 13)，说明 ivermectin 通过 FXR 调节代谢相关基因的表达从而实现生理功能的调节。这些结果表明，ivermectin 是 FXR 的特异性配体，同时证明 ivermectin 在体内生理功能的调节是通过 FXR 实现的。

[0145] 实施例 5，Ivermectin 在糖尿病小鼠模型中的作用

[0146] 既然 ivermectin 作为 FXR 的配体能够在正常小鼠的体内发挥重要的代谢调节功能，那么 ivermectin 是否能够对病理小鼠具有改善疗效？为了检测 ivermectin 在糖尿病肥胖症模型小鼠体内的药效，我们选择了 KK-Ay 小鼠作为实验对象。这种小鼠在 8-10 周左右表现出明显的高血糖和肥胖的症状。在实验中，我们用 GW4064 作为阳性对照。高脂饲料喂养下，十四天的腹腔注射后，ivermectin 和 GW4064 都显著地降低了血清中胆固醇、甘油三酯和自由脂肪酸的含量(图 18~20)；但在血糖方面，ivermectin 显著降低了血清中糖和胰岛素的水平，表明 ivermectin 可能通过增加胰岛素的敏感性达到了降低血糖的效果，在这方面 ivermectin 作为 FXR 的配体的功能要显著优越于 GW4064（图 16~17)。另一方面，ivermectin 处理的小鼠肝脏中糖、脂和胆固醇合成相关基因的表达显著下调，GW4064 处理后大多数检测基因也达到了类似的效果，但是在很多基因尤其是胆固醇合成相关基因的表达调控中，GW4064 的调控功能明显差于 ivermectin（图 21)。这些结果表明，ivermectin 对糖尿病、肥胖症模型小鼠具有很好的平衡血糖、血脂和胆固醇的效果，而且相比合成的配体 GW4064 具有更优的功能和疗效。

[0147] 实施例 6，Ivermectin 通过 FXR 介导抑制 LPS 诱导的炎症反应

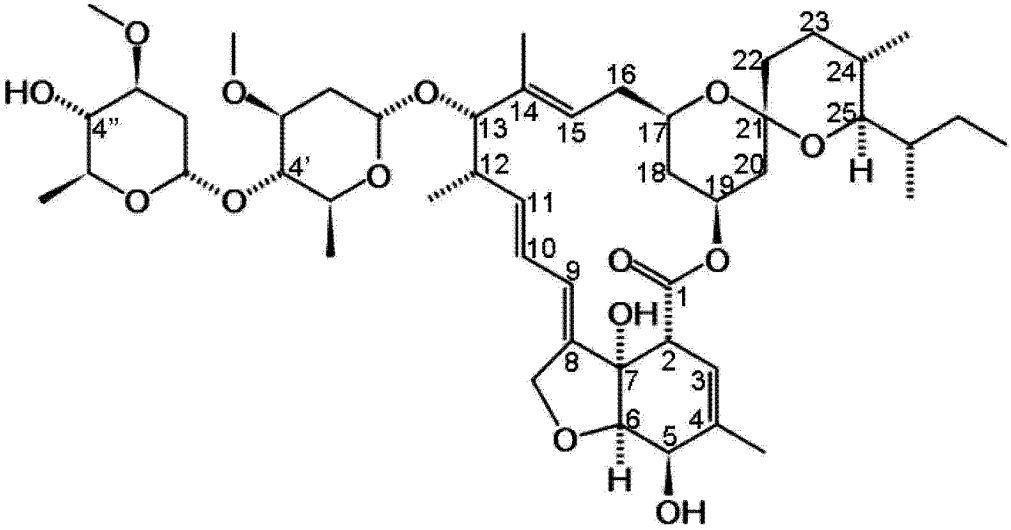
[0148] 近来一些报道证明，ivermectin 能够抑制 LPS 诱导的炎症发应，并减少由于过量 LPS 诱导的小鼠的死亡。同时，ivermectin 对于过敏性哮喘的治疗有明显的疗效，但其具体的作用机制还不清楚。为了证明 ivermectin 对于 LPS 诱导的炎症反应的抑制是否与 FXR 相关，我们用 ivermectin 和 LPS 处理野生型和 FXR 敲除的小鼠肝脏细胞。在野生型小鼠肝脏细胞中，ivermectin 能够明显的抑制炎症因子的表达，例如 :iNOS，TNFa，IL-6 和 MIP-1a(图 22~25)；但在 FXR 敲除的小鼠肝脏细胞中没有明显的变化。同时，为了检测由 ivermectin 激活的 FXR 受体对于促进炎症基因表达的转录因子 NF-κB 的转录活性的影响，我们共转表达全长 FXR 和 RXR 的质粒、p65 的质粒和 NF-κB 的两种内源报告基因。结果证明 :在 FXR/RXR 存在的条件下，ivermectin 能够明显地抑制 p65 的转录活性(图 26 和图 27)，进一步证明了 ivermectin 在抑制炎症反应功能方面是依赖于 FXR 进行的。

[0149] 实施例 7，基于 FXR/ivermectin 复合物结构的 ivermectin 衍生物药物设计

[0150] 通过上述实施例发现，伊维菌素具有区别与抗寄生虫药物作用的完全不同的功能，可用于治疗哺乳动物高血糖、胰岛素抗性、高甘油三酯血症、高胆固醇血症、糖尿病、肥胖症等代谢相关疾病，以及用于治疗法尼醇受体介导的胆汁阻塞、胆结石、非酒精性脂肪肝、动脉粥样硬化、炎症、癌症等疾病的新用途。再根据对 FXR 与 ivermectin 相互结合的结构模式，以 ivermectin 作为一个安全的先导化合物，以 ivermectin 的分子结构为药物设计模板，以 ivermectin 和 FXR 受体的结合位点及其构效关系为依据，对 ivermectin 的某些基团进行适当的修饰，可能提高配体与受体结合的亲和力和特异性，而达到最佳的药物疗

效，从而以最少的配体药物量，达到最佳的药物治疗效果，减少药物对细胞和机体的毒性。Ivermectin 结构式如下：

[0151]



[0152] 以该结构式为结构基础，对该结构式中 C3-C4，C8-C9，C10-C11，C14-C15 碳碳双键进行改造；对 C5、C7、C4”位羟基进行改造；对 C4、C12、C14、C24、C25 位的侧链进行改造；对 C13 位的糖基进行水解以及其他基团进行取代等改造方法。以上任何单一改造和不同方式改造的组合在制备治疗哺乳动物高血糖、胰岛素抗性、高甘油三酯血症、高胆固醇血症、糖尿病、肥胖症等代谢相关疾病，以及用于治疗法尼醇受体介导的胆汁阻塞、胆结石、非酒精性脂肪肝、动脉粥样硬化、炎症、癌症等疾病中的应用。根据上述设计原则，阿维菌素和多拉克汀也是符合该原则的伊维菌素衍生物，发现阿维菌素和多拉克汀也是 FXR 的高亲和力特异性配体(图 28)，能诱导 FXR 特异性地募集多种辅调节因子(图 29)。

[0153] 附录 1

[0154]

```
HEADER    ----                                        XX-XXX-9-    XXXX
COMPND    ---
REMARK    3
REMARK    3 REFINEMENT.
REMARK    3   PROGRAM     : REFMAC 5.6.0117
REMARK    3   AUTHORS     : MURSHUDOV,VAGIN,DODSON
REMARK    3
REMARK    3    REFINEMENT TARGET : MAXIMUM LIKELIHOOD
REMARK    3
REMARK    3  DATA USED IN REFINEMENT.
REMARK    3   RESOLUTION RANGE HIGH (ANGSTROMS) :   2.90
REMARK    3   RESOLUTION RANGE LOW  (ANGSTROMS) : 116.86
REMARK    3   DATA CUTOFF            (SIGMA(F)) : NONE
REMARK    3   COMPLETENESS FOR RANGE        (%) :  98.21
REMARK    3   NUMBER OF REFLECTIONS             :   15531
REMARK    3
REMARK    3  FIT TO DATA USED IN REFINEMENT.
```

[0171]

```
REMARK   3   CROSS-VALIDATION METHOD          : THROUGHOUT
REMARK   3   FREE R VALUE TEST SET SELECTION  : RANDOM
REMARK   3   R VALUE      (WORKING + TEST SET) : 0.25558
REMARK   3   R VALUE            (WORKING SET) :  0.25331
REMARK   3   FREE R VALUE                      :  0.29623
REMARK   3   FREE R VALUE TEST SET SIZE   (%) :  5.0
REMARK   3   FREE R VALUE TEST SET COUNT      :   819
REMARK   3
REMARK   3  FIT IN THE HIGHEST RESOLUTION BIN.
REMARK   3   TOTAL NUMBER OF BINS USED           :      20
REMARK   3   BIN RESOLUTION RANGE HIGH           :    2.900
REMARK   3   BIN RESOLUTION RANGE LOW            :    2.975
REMARK   3   REFLECTION IN BIN     (WORKING SET) :      971
REMARK   3   BIN COMPLETENESS (WORKING+TEST) (%) :    89.92
REMARK   3   BIN R VALUE           (WORKING SET) :    0.303
REMARK   3   BIN FREE R VALUE SET COUNT          :       46
REMARK   3   BIN FREE R VALUE                    :    0.395
REMARK   3
REMARK   3  NUMBER OF NON-HYDROGEN ATOMS USED IN REFINEMENT.
REMARK   3   ALL ATOMS                 :     3654
REMARK   3
REMARK   3  B VALUES.
REMARK   3   FROM WILSON PLOT           (A**2) : NULL
REMARK   3   MEAN B VALUE      (OVERALL, A**2) :  77.305
REMARK   3   OVERALL ANISOTROPIC B VALUE.
REMARK   3    B11 (A**2) :    -0.37
REMARK   3    B22 (A**2) :     0.35
REMARK   3    B33 (A**2) :     0.01
REMARK   3    B12 (A**2) :     0.00
REMARK   3    B13 (A**2) :     0.00
REMARK   3    B23 (A**2) :     0.00
REMARK   3
REMARK   3  ESTIMATED OVERALL COORDINATE ERROR.
REMARK   3   ESU BASED ON R VALUE                            (A):   1.502
REMARK   3   ESU BASED ON FREE R VALUE                       (A):   0.426
REMARK   3   ESU BASED ON MAXIMUM LIKELIHOOD                 (A):   0.327
REMARK   3   ESU FOR B VALUES BASED ON MAXIMUM LIKELIHOOD (A**2):  16.480
REMARK   3
REMARK   3 CORRELATION COEFFICIENTS.
REMARK   3   CORRELATION COEFFICIENT FO-FC      :   0.906
REMARK   3   CORRELATION COEFFICIENT FO-FC FREE :   0.886
REMARK   3
REMARK   3  RMS DEVIATIONS FROM IDEAL VALUES        COUNT    RMS    WEIGHT
REMARK   3   BOND LENGTHS REFINED ATOMS        (A):  3700 ; 0.012 ; 0.020
REMARK   3   BOND ANGLES REFINED ATOMS   (DEGREES):  5025 ; 2.370 ; 2.011
REMARK   3   TORSION ANGLES, PERIOD 1    (DEGREES):   445 ; 7.096 ; 5.000
```

[0217]

```
REMARK   3   TORSION ANGLES, PERIOD 2     (DEGREES):   162 ;41.571 ;25.247
REMARK   3   TORSION ANGLES, PERIOD 3     (DEGREES):   607 ;23.325 ;15.000
REMARK   3   TORSION ANGLES, PERIOD 4     (DEGREES):    14 ;18.993 ;15.000
REMARK   3   CHIRAL-CENTER RESTRAINTS        (A**3):   596 ; 0.178 ; 0.200
REMARK   3   GENERAL PLANES REFINED ATOMS      (A):  2699 ; 0.007 ; 0.021
REMARK   3
REMARK   3  ISOTROPIC THERMAL FACTOR RESTRAINTS.      COUNT   RMS    WEIGHT
REMARK   3
REMARK   3  NCS RESTRAINTS STATISTICS
REMARK   3   NUMBER OF NCS GROUPS : NULL
REMARK   3
REMARK   3  TWIN DETAILS
REMARK   3   NUMBER OF TWIN DOMAINS  : NULL
REMARK   3
REMARK   3
REMARK   3  TLS DETAILS
REMARK   3   NUMBER OF TLS GROUPS  : NULL
REMARK   3
REMARK   3
REMARK   3  BULK SOLVENT MODELLING.
REMARK   3   METHOD USED :  MASK
REMARK   3   PARAMETERS FOR MASK CALCULATION
REMARK   3   VDW PROBE RADIUS   :   1.20
REMARK   3   ION PROBE RADIUS   :   0.80
REMARK   3   SHRINKAGE RADIUS   :   0.80
REMARK   3
REMARK   3  OTHER REFINEMENT REMARKS:
REMARK   3  HYDROGENS HAVE BEEN USED IF PRESENT IN THE INPUT
REMARK   3  U VALUES       : REFINED INDIVIDUALLY
REMARK   3
CRYST1   53.008  161.759  169.018  90.00  90.00  90.00 I 21 21 21
SCALE1      0.018865  0.000000  0.000000        0.00000
SCALE2      0.000000  0.006182  0.000000        0.00000
SCALE3      0.000000  0.000000  0.005917        0.00000
ATOM      1  N   ASN C 742      29.535 -19.999 -42.932  1.00146.14           N
ATOM      2  CA  ASN C 742      29.694 -20.610 -41.573  1.00131.37           C
ATOM      3  CB  ASN C 742      31.189 -20.765 -41.193  1.00140.09           C
ATOM      4  CG  ASN C 742      32.012 -19.494 -41.424  1.00148.16           C
ATOM      5  OD1 ASN C 742      32.283 -18.739 -40.488  1.00148.99           O
ATOM      6  ND2 ASN C 742      32.433  19.268  42.670  1.00148.21           N
ATOM      7  C   ASN C 742      28.901 -19.879 -40.479  1.00128.91           C
ATOM      8  O   ASN C 742      29.420 -19.630 -39.383  1.00124.17           O
ATOM      9  N   LEU C 743      27.641 -19.544 -40.780  1.00127.89           N
ATOM     10  CA  LEU C 743      26.788 -18.788 -39.840  1.00119.00           C
ATOM     11  CB  LEU C 743      25.670 -17.989 -40.541  1.00104.27           C
ATOM     12  CG  LEU C 743      26.017 -16.532 -40.868  1.00 92.01           C
```

[0263]

```
ATOM     13  CD1 LEU C 743      26.731 -16.448 -42.215  1.00 81.21           C
ATOM     14  CD2 LEU C 743      24.780 -15.644 -40.831  1.00 77.51           C
ATOM     15  C   LEU C 743      26.291 -19.566 -38.605  1.00122.75           C
ATOM     16  O   LEU C 743      26.863 -19.369 -37.533  1.00136.39           O
ATOM     17  N   GLY C 744      25.261  20.424  38.691  1.00109.40           N
ATOM     18  CA  GLY C 744      24.417 -20.677 -39.861  1.00 97.04           C
ATOM     19  C   GLY C 744      22.997 -20.248 -39.534  1.00 96.15           C
ATOM     20  O   GLY C 744      22.715 -19.052 -39.532  1.00106.23           O
ATOM     21  N   LEU C 745      22.101 -21.197 -39.236  1.00 87.05           N
ATOM     22  CA  LEU C 745      20.731 -20.836 -38.840  1.00 75.33           C
ATOM     23  CB  LEU C 745      19.778 -22.012 -38.889  1.00 72.34           C
ATOM     24  CG  LEU C 745      18.316 -21.608 -39.152  1.00 78.31           C
ATOM     25  CD1 LEU C 745      17.380 -22.815 -39.181  1.00 76.85           C
ATOM     26  CD2 LEU C 745      17.787 -20.571 -38.168  1.00 77.61           C
ATOM     27  C   LEU C 745      20.600 -20.175 -37.472  1.00 87.57           C
ATOM     28  O   LEU C 745      20.215  19.010  37.409  1.00 99.57           O
ATOM     29  N   GLU C 746      20.901 -20.899 -36.385  1.00 82.18           N
ATOM     30  CA  GLU C 746      20.643 -20.390 -35.010  1.00 72.64           C
ATOM     31  CB  GLU C 746      21.361 -21.234 -33.948  1.00 66.27           C
ATOM     32  C   GLU C 746      20.909 -18.885 -34.765  1.00 71.89           C
ATOM     33  O   GLU C 746      20.262 -18.267 -33.907  1.00 63.66           O
ATOM     34  N   ASP C 747      21.847 -18.295 -35.513  1.00 69.15           N
ATOM     35  CA  ASP C 747      22.173 -16.876 -35.356  1.00 69.63           C
ATOM     36  CB  ASP C 747      23.457 -16.567 -36.090  1.00 76.03           C
ATOM     37  CG  ASP C 747      24.197 -17.828 -36.523  1.00 91.80           C
ATOM     38  OD1 ASP C 747      24.443 -18.720 -35.682  1.00 99.45           O
ATOM     39  OD2 ASP C 747      24.534  17.930  37.716  1.00 98.70           O
ATOM     40  C   ASP C 747      21.019 -16.029 -35.894  1.00 70.43           C
ATOM     41  O   ASP C 747      20.446 -15.173 -35.191  1.00 62.28           O
ATOM     42  N   ILE C 748      20.667 -16.316 -37.141  1.00 68.09           N
ATOM     43  CA  ILE C 748      19.453 -15.812 -37.776  1.00 68.30           C
ATOM     44  CB  ILE C 748      19.079 -16.715 -38.984  1.00 70.48           C
ATOM     45  CG1 ILE C 748      20.233 -16.767 -40.008  1.00 74.94           C
ATOM     46  CD1 ILE C 748      20.024 -17.740 -41.161  1.00 87.18           C
ATOM     47  CG2 ILE C 748      17.748 -16.303 -39.598  1.00 63.22           C
ATOM     48  C   ILE C 748      18.286 -15.726 -36.778  1.00 69.76           C
ATOM     49  O   ILE C 748      17.694 -14.675 -36.592  1.00 69.70           O
ATOM     50  N   ILE C 749      17.965  16.829  36.114  1.00 77.01           N
ATOM     51  CA  ILE C 749      16.871 -16.820 -35.140  1.00 71.15           C
ATOM     52  CB  ILE C 749      16.530 -18.250 -34.683  1.00 75.56           C
ATOM     53  CG1 ILE C 749      15.622 -18.885 -35.730  1.00 73.54           C
ATOM     54  CD1 ILE C 749      15.410 -20.362 -35.526  1.00 78.13           C
ATOM     55  CG2 ILE C 749      15.868 -18.265 -33.307  1.00 74.37           C
ATOM     56  C   ILE C 749      17.136 -15.900 -33.960  1.00 64.02           C
ATOM     57  O   ILE C 749      16.232 -15.196 -33.534  1.00 53.41           O
ATOM     58  N   ARG C 750      18.382 -15.913 -33.463  1.00 72.34           N
```

[0309]

```
ATOM    59  CA  ARG C 750      18.858 -15.014 -32.400  1.00 72.35           C
ATOM    60  CB  ARG C 750      20.357 -15.163 -32.217  1.00 77.09           C
ATOM    61  CG  ARG C 750      20.752 -16.104 -31.106  1.00 85.77           C
ATOM    62  CD  ARG C 750      22.121 -16.701 -31.339  1.00 79.21           C
ATOM    63  NE  ARG C 750      22.046  18.149  31.170  1.00 86.81           N
ATOM    64  CZ  ARG C 750      23.093 -18.962 -31.035  1.00 91.04           C
ATOM    65  NH1 ARG C 750      24.326 -18.472 -31.041  1.00109.64           N
ATOM    66  NH2 ARG C 750      22.914 -20.272 -30.903  1.00 83.60           N
ATOM    67  C   ARG C 750      18.565 -13.576 -32.764  1.00 74.44           C
ATOM    68  O   ARG C 750      17.906 -12.846 -32.002  1.00 75.97           O
ATOM    69  N   LYS C 751      19.035 -13.185 -33.951  1.00 66.12           N
ATOM    70  CA  LYS C 751      18.756 -11.847 -34.470  1.00 61.01           C
ATOM    71  CB  LYS C 751      19.497 -11.571 -35.801  1.00 51.19           C
ATOM    72  C   LYS C 751      17.229 -11.653 -34.540  1.00 62.27           C
ATOM    73  O   LYS C 751      16.679 -10.834 -33.794  1.00 61.37           O
ATOM    74  N   ALA C 752      16.553  12.470  35.355  1.00 62.36           N
ATOM    75  CA  ALA C 752      15.099 -12.366 -35.582  1.00 58.29           C
ATOM    76  CB  ALA C 752      14.586 -13.528 -36.388  1.00 58.51           C
ATOM    77  C   ALA C 752      14.305 -12.287 -34.329  1.00 57.74           C
ATOM    78  O   ALA C 752      13.249 -11.680 -34.335  1.00 57.26           O
ATOM    79  N   LEU C 753      14.809 -12.884 -33.252  1.00 58.72           N
ATOM    80  CA  LEU C 753      14.177 -12.708 -31.959  1.00 64.81           C
ATOM    81  CB  LEU C 753      14.858 -13.543 -30.903  1.00 63.92           C
ATOM    82  CG  LEU C 753      14.133 -14.882 -30.757  1.00 64.45           C
ATOM    83  CD1 LEU C 753      14.938 -15.892 -29.938  1.00 60.54           C
ATOM    84  CD2 LEU C 753      12.734 -14.687 -30.190  1.00 58.51           C
ATOM    85  C   LEU C 753      14.009  11.249  31.503  1.00 77.30           C
ATOM    86  O   LEU C 753      13.056 -10.946 -30.796  1.00 71.00           O
ATOM    87  N   MET C 754      14.910 -10.348 -31.908  1.00 89.88           N
ATOM    88  CA  MET C 754      14.580  -8.909 -31.913  1.00 96.47           C
ATOM    89  CB  MET C 754      14.871  -8.222 -30.574  1.00105.54           C
ATOM    90  CG  MET C 754      16.333  -8.170 -30.186  1.00118.35           C
ATOM    91  SD  MET C 754      16.916  -9.746 -29.548  1.00127.08           S
ATOM    92  CE  MET C 754      16.384  -9.571 -27.846  1.00126.50           C
ATOM    93  C   MET C 754      15.202  -8.127 -33.062  1.00104.49           C
ATOM    94  O   MET C 754      14.493  -7.710 -33.979  1.00106.03           O
ATOM    95  N   GLY C 755      16.524  -7.949 -32.997  1.00121.99           N
ATOM    96  CA  GLY C 755      17.307   7.116  33.927  1.00118.97           C
ATOM    97  C   GLY C 755      16.762  -7.010 -35.340  1.00116.77           C
ATOM    98  O   GLY C 755      16.031  -6.069 -35.661  1.00116.42           O
ATOM    99  N   SER C 756      17.105  -7.986 -36.174  1.00106.56           N
ATOM   100  CA  SER C 756      16.639  -8.040 -37.559  1.00110.81           C
ATOM   101  CB  SER C 756      17.092  -9.356 -38.202  1.00114.09           C
ATOM   102  OG  SER C 756      16.528  -9.514 -39.494  1.00117.80           O
ATOM   103  C   SER C 756      15.115  -7.827 -37.770  1.00117.97           C
ATOM   104  O   SER C 756      14.586  -8.164 -38.839  1.00123.88           O
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[0355]

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ATOM    105  N   PHE C 757      14.425  -7.282 -36.761  1.00116.00           N
ATOM    106  CA  PHE C 757      12.999  -6.883 -36.857  1.00120.77           C
ATOM    107  CB  PHE C 757      12.868  -5.458 -37.434  1.00130.68           C
ATOM    108  CG  PHE C 757      11.510  -4.817 -37.223  1.00134.39           C
ATOM    109  CD1 PHE C 757      10.491   4.956  38.177  1.00138.03           C
ATOM    110  CE1 PHE C 757       9.248  -4.362 -37.990  1.00133.12           C
ATOM    111  CZ  PHE C 757       9.011  -3.610 -36.846  1.00137.06           C
ATOM    112  CE2 PHE C 757      10.014  -3.454 -35.894  1.00132.83           C
ATOM    113  CD2 PHE C 757      11.256  -4.048 -36.086  1.00131.69           C
ATOM    114  C   PHE C 757      12.130  -7.862 -37.651  1.00107.91           C
ATOM    115  O   PHE C 757      10.930  -7.987 -37.395  1.00106.12           O
ATOM    116  N   GLU A 244     -18.325 -25.540 -26.704  1.00 95.16           N
ATOM    117  CA  GLU A 244     -18.073 -26.244 -25.400  1.00101.28           C
ATOM    118  CB  GLU A 244     -18.336 -27.763 -25.573  1.00 99.29           C
ATOM    119  CG  GLU A 244     -17.696 -28.716 -24.565  1.00100.52           C
ATOM    120  CD  GLU A 244      18.378  28.717  23.208  1.00100.97           C
ATOM    121  OE1 GLU A 244     -19.216 -27.823 -22.947  1.00106.04           O
ATOM    122  OE2 GLU A 244     -18.070 -29.617 -22.395  1.00 95.65           O
ATOM    123  C   GLU A 244     -16.698 -25.915 -24.733  1.00 96.26           C
ATOM    124  O   GLU A 244     -16.376 -26.425 -23.654  1.00 91.42           O
ATOM    125  N   LEU A 245     -15.902 -25.053 -25.367  1.00 86.02           N
ATOM    126  CA  LEU A 245     -14.650 -24.578 -24.766  1.00 79.26           C
ATOM    127  CB  LEU A 245     -13.912 -23.608 -25.697  1.00 72.49           C
ATOM    128  CG  LEU A 245     -13.676 -24.003 -27.156  1.00 65.58           C
ATOM    129  CD1 LEU A 245     -13.116 -22.821 -27.923  1.00 63.46           C
ATOM    130  CD2 LEU A 245     -12.725 -25.174 -27.243  1.00 66.62           C
ATOM    131  C   LEU A 245      14.915  23.858  23.453  1.00 85.34           C
ATOM    132  O   LEU A 245     -16.017 -23.352 -23.211  1.00 97.34           O
ATOM    133  N   THR A 246     -13.895 -23.806 -22.610  1.00 80.64           N
ATOM    134  CA  THR A 246     -13.954 -23.015 -21.405  1.00 71.62           C
ATOM    135  CB  THR A 246     -13.166 -23.660 -20.268  1.00 68.45           C
ATOM    136  OG1 THR A 246     -11.815 -23.194 -20.318  1.00 71.61           O
ATOM    137  CG2 THR A 246     -13.194 -25.166 -20.379  1.00 66.14           C
ATOM    138  C   THR A 246     -13.313 -21.657 -21.687  1.00 77.31           C
ATOM    139  O   THR A 246     -12.360 -21.573 -22.461  1.00 71.90           O
ATOM    155  N   GLN A 249      -9.922 -21.529 -22.706  1.00 70.74           N
ATOM    156  CA  GLN A 249      -9.787 -22.016 -24.066  1.00 72.02           C
ATOM    157  CB  GLN A 249      10.566  23.323  24.241  1.00 70.29           C
ATOM    158  CG  GLN A 249     -10.366 -24.294 -23.083  1.00 67.41           C
ATOM    159  CD  GLN A 249     -10.995 -25.663 -23.314  1.00 73.99           C
ATOM    160  OE1 GLN A 249     -11.815 -25.866 -24.217  1.00 80.54           O
ATOM    161  NE2 GLN A 249     -10.606 -26.612 -22.496  1.00 70.10           N
ATOM    162  C   GLN A 249     -10.201 -20.962 -25.100  1.00 68.00           C
ATOM    163  O   GLN A 249      -9.379 -20.577 -25.918  1.00 66.11           O
ATOM    164  N   GLN A 250     -11.455 -20.490 -25.047  1.00 70.12           N
ATOM    165  CA  GLN A 250     -11.955 -19.507 -26.027  1.00 68.86           C
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[0401]

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 166 | CB | GLN | A | 250 | -13.415 | -19.106 | -25.789 | 1.00 | 63.79 | C |
| ATOM | 167 | CG | GLN | A | 250 | -13.694 | -18.507 | -24.426 | 1.00 | 79.63 | C |
| ATOM | 168 | CD | GLN | A | 250 | -14.867 | -17.520 | -24.406 | 1.00 | 85.93 | C |
| ATOM | 169 | OE1 | GLN | A | 250 | -16.017 | -17.868 | -24.709 | 1.00 | 77.91 | O |
| ATOM | 170 | NE2 | GLN | A | 250 | 14.572 | 16.274 | 24.026 | 1.00 | 89.83 | N |
| ATOM | 171 | C | GLN | A | 250 | -11.050 | -18.285 | -26.135 | 1.00 | 68.81 | C |
| ATOM | 172 | O | GLN | A | 250 | -10.808 | -17.754 | -27.242 | 1.00 | 69.99 | O |
| ATOM | 173 | N | THR | A | 251 | -10.522 | -17.871 | -24.986 | 1.00 | 63.77 | N |
| ATOM | 174 | CA | THR | A | 251 | -9.563 | -16.783 | -24.930 | 1.00 | 58.96 | C |
| ATOM | 175 | CB | THR | A | 251 | -9.225 | -16.440 | -23.485 | 1.00 | 63.49 | C |
| ATOM | 176 | OG1 | THR | A | 251 | -10.429 | -16.098 | -22.788 | 1.00 | 66.97 | O |
| ATOM | 177 | CG2 | THR | A | 251 | -8.242 | -15.284 | -23.439 | 1.00 | 61.32 | C |
| ATOM | 178 | C | THR | A | 251 | -8.283 | -17.139 | -25.655 | 1.00 | 59.05 | C |
| ATOM | 179 | O | THR | A | 251 | -7.866 | -16.409 | -26.540 | 1.00 | 57.34 | O |
| ATOM | 180 | N | LEU | A | 252 | -7.666 | -18.264 | -25.269 | 1.00 | 61.91 | N |
| ATOM | 181 | CA | LEU | A | 252 | 6.488 | 18.792 | 25.958 | 1.00 | 56.00 | C |
| ATOM | 182 | CB | LEU | A | 252 | -6.068 | -20.138 | -25.374 | 1.00 | 52.70 | C |
| ATOM | 183 | CG | LEU | A | 252 | -4.775 | -20.857 | -25.817 | 1.00 | 54.52 | C |
| ATOM | 184 | CD1 | LEU | A | 252 | -3.528 | -19.974 | -25.862 | 1.00 | 52.01 | C |
| ATOM | 185 | CD2 | LEU | A | 252 | -4.499 | -22.045 | -24.907 | 1.00 | 52.94 | C |
| ATOM | 186 | C | LEU | A | 252 | -6.736 | -18.932 | -27.465 | 1.00 | 60.72 | C |
| ATOM | 187 | O | LEU | A | 252 | -5.851 | -18.608 | -28.264 | 1.00 | 61.91 | O |
| ATOM | 188 | N | LEU | A | 253 | -7.933 | -19.381 | -27.850 | 1.00 | 56.02 | N |
| ATOM | 189 | CA | LEU | A | 253 | -8.187 | -19.656 | -29.240 | 1.00 | 59.39 | C |
| ATOM | 190 | CB | LEU | A | 253 | -9.485 | -20.449 | -29.472 | 1.00 | 64.88 | C |
| ATOM | 191 | CG | LEU | A | 253 | -9.899 | -20.878 | -30.910 | 1.00 | 57.78 | C |
| ATOM | 192 | CD1 | LEU | A | 253 | 8.724 | 21.139 | 31.849 | 1.00 | 48.72 | C |
| ATOM | 193 | CD2 | LEU | A | 253 | -10.863 | -22.067 | -30.889 | 1.00 | 50.34 | C |
| ATOM | 194 | C | LEU | A | 253 | -8.139 | -18.371 | -30.026 | 1.00 | 62.44 | C |
| ATOM | 195 | O | LEU | A | 253 | -7.288 | -18.232 | -30.904 | 1.00 | 73.67 | O |
| ATOM | 196 | N | HIS | A | 254 | -9.012 | -17.428 | -29.686 | 1.00 | 66.91 | N |
| ATOM | 197 | CA | HIS | A | 254 | -8.997 | -16.065 | -30.256 | 1.00 | 60.28 | C |
| ATOM | 198 | CB | HIS | A | 254 | -9.904 | -15.163 | -29.423 | 1.00 | 67.43 | C |
| ATOM | 199 | CG | HIS | A | 254 | -10.138 | -13.804 | -30.030 | 1.00 | 85.22 | C |
| ATOM | 200 | ND1 | HIS | A | 254 | -11.356 | -13.390 | -30.423 | 1.00 | 95.51 | N |
| ATOM | 201 | CE1 | HIS | A | 254 | -11.259 | -12.136 | -30.924 | 1.00 | 108.55 | C |
| ATOM | 202 | NE2 | HIS | A | 254 | -9.966 | -11.752 | -30.856 | 1.00 | 100.11 | N |
| ATOM | 203 | CD2 | HIS | A | 254 | 9.250 | 12.751 | 30.308 | 1.00 | 92.23 | C |
| ATOM | 204 | C | HIS | A | 254 | -7.610 | -15.455 | -30.386 | 1.00 | 55.25 | C |
| ATOM | 205 | O | HIS | A | 254 | -7.232 | -14.945 | -31.443 | 1.00 | 50.40 | O |
| ATOM | 206 | N | PHE | A | 255 | -6.823 | -15.506 | -29.322 | 1.00 | 54.31 | N |
| ATOM | 207 | CA | PHE | A | 255 | -5.484 | -14.970 | -29.386 | 1.00 | 63.11 | C |
| ATOM | 208 | CB | PHE | A | 255 | -4.757 | -15.177 | -28.053 | 1.00 | 70.70 | C |
| ATOM | 209 | CG | PHE | A | 255 | -3.557 | -14.283 | -27.881 | 1.00 | 75.50 | C |
| ATOM | 210 | CD1 | PHE | A | 255 | -3.681 | -13.033 | -27.286 | 1.00 | 77.17 | C |
| ATOM | 211 | CE1 | PHE | A | 255 | -2.584 | -12.192 | -27.149 | 1.00 | 82.65 | C |

[0447]

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 212 | CZ | PHE | A | 255 | -1.345 | -12.600 | -27.608 | 1.00 | 87.31 | C |
| ATOM | 213 | CE2 | PHE | A | 255 | -1.208 | -13.848 | -28.197 | 1.00 | 87.35 | C |
| ATOM | 214 | CD2 | PHE | A | 255 | -2.309 | -14.682 | -28.333 | 1.00 | 81.81 | C |
| ATOM | 215 | C | PHE | A | 255 | -4.698 | -15.592 | -30.545 | 1.00 | 67.99 | C |
| ATOM | 216 | O | PHE | A | 255 | 4.097 | 14.896 | 31.360 | 1.00 | 69.92 | O |
| ATOM | 217 | N | ILE | A | 256 | -4.736 | -16.918 | -30.624 | 1.00 | 76.76 | N |
| ATOM | 218 | CA | ILE | A | 256 | -3.997 | -17.650 | -31.642 | 1.00 | 66.02 | C |
| ATOM | 219 | CB | ILE | A | 256 | -4.103 | -19.180 | -31.465 | 1.00 | 62.35 | C |
| ATOM | 220 | CG1 | ILE | A | 256 | -3.790 | -19.608 | -30.018 | 1.00 | 57.61 | C |
| ATOM | 221 | CD1 | ILE | A | 256 | -2.455 | -19.134 | -29.485 | 1.00 | 54.28 | C |
| ATOM | 222 | CG2 | ILE | A | 256 | -3.146 | -19.869 | -32.432 | 1.00 | 68.80 | C |
| ATOM | 223 | C | ILE | A | 256 | -4.451 | -17.237 | -33.033 | 1.00 | 63.36 | C |
| ATOM | 224 | O | ILE | A | 256 | -3.632 | -16.795 | -33.842 | 1.00 | 65.01 | O |
| ATOM | 225 | N | MET | A | 257 | -5.753 | -17.368 | -33.295 | 1.00 | 58.44 | N |
| ATOM | 226 | CA | MET | A | 257 | -6.351 | -16.964 | -34.571 | 1.00 | 59.19 | C |
| ATOM | 227 | CB | MET | A | 257 | 7.866 | 16.961 | 34.458 | 1.00 | 60.01 | C |
| ATOM | 228 | CG | MET | A | 257 | -8.512 | -18.308 | -34.750 | 1.00 | 71.78 | C |
| ATOM | 229 | SD | MET | A | 257 | -7.679 | -19.356 | -35.974 | 1.00 | 79.41 | S |
| ATOM | 230 | CE | MET | A | 257 | -7.641 | -18.326 | -37.462 | 1.00 | 66.46 | C |
| ATOM | 231 | C | MET | A | 257 | -5.884 | -15.597 | -35.067 | 1.00 | 68.24 | C |
| ATOM | 232 | O | MET | A | 257 | -5.263 | -15.483 | -36.139 | 1.00 | 67.00 | O |
| ATOM | 233 | N | ASP | A | 258 | -6.219 | -14.577 | -34.269 | 1.00 | 70.44 | N |
| ATOM | 234 | CA | ASP | A | 258 | -5.693 | -13.221 | -34.348 | 1.00 | 63.65 | C |
| ATOM | 235 | CB | ASP | A | 258 | -5.765 | -12.619 | -32.946 | 1.00 | 72.46 | C |
| ATOM | 236 | CG | ASP | A | 258 | -6.322 | -11.179 | -32.923 | 1.00 | 83.30 | C |
| ATOM | 237 | OD1 | ASP | A | 258 | -7.393 | -10.904 | -33.558 | 1.00 | 74.31 | O |
| ATOM | 238 | OD2 | ASP | A | 258 | 5.684 | 10.345 | 32.219 | 1.00 | 74.91 | O |
| ATOM | 239 | C | ASP | A | 258 | -4.247 | -13.175 | -34.833 | 1.00 | 64.43 | C |
| ATOM | 240 | O | ASP | A | 258 | -3.915 | -12.466 | -35.825 | 1.00 | 62.93 | O |
| ATOM | 241 | N | SER | A | 259 | -3.392 | -13.936 | -34.141 | 1.00 | 58.22 | N |
| ATOM | 242 | CA | SER | A | 259 | -1.959 | -13.889 | -34.403 | 1.00 | 61.61 | C |
| ATOM | 243 | CB | SER | A | 259 | -1.171 | -14.453 | -33.242 | 1.00 | 60.41 | C |
| ATOM | 244 | OG | SER | A | 259 | -1.833 | -14.177 | -32.038 | 1.00 | 65.05 | O |
| ATOM | 245 | C | SER | A | 259 | -1.593 | -14.640 | -35.649 | 1.00 | 67.47 | C |
| ATOM | 246 | O | SER | A | 259 | -0.703 | -14.218 | -36.382 | 1.00 | 87.04 | O |
| ATOM | 247 | N | TYR | A | 260 | -2.282 | -15.751 | -35.891 | 1.00 | 66.41 | N |
| ATOM | 248 | CA | TYR | A | 260 | -2.053 | -16.556 | -37.075 | 1.00 | 65.84 | C |
| ATOM | 249 | CB | TYR | A | 260 | 2.831 | 17.875 | 36.986 | 1.00 | 66.79 | C |
| ATOM | 250 | CG | TYR | A | 260 | -2.453 | -18.880 | -38.044 | 1.00 | 61.65 | C |
| ATOM | 251 | CD1 | TYR | A | 260 | -1.137 | -19.322 | -38.162 | 1.00 | 66.20 | C |
| ATOM | 252 | CE1 | TYR | A | 260 | -0.764 | -20.228 | -39.144 | 1.00 | 69.32 | C |
| ATOM | 253 | CZ | TYR | A | 260 | -1.721 | -20.702 | -40.013 | 1.00 | 72.88 | C |
| ATOM | 254 | OH | TYR | A | 260 | -1.315 | -21.606 | -40.964 | 1.00 | 88.07 | O |
| ATOM | 255 | CE2 | TYR | A | 260 | -3.045 | -20.282 | -39.924 | 1.00 | 62.54 | C |
| ATOM | 256 | CD2 | TYR | A | 260 | -3.404 | -19.384 | -38.934 | 1.00 | 58.02 | C |
| ATOM | 257 | C | TYR | A | 260 | -2.455 | -15.778 | -38.301 | 1.00 | 72.22 | C |

[0493]

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| ATOM | 258 | O | TYR A 260 | -1.938 | -16.011 | -39.380 | 1.00 | 84.34 | O |
| ATOM | 259 | N | ASN A 261 | -3.355 | -14.818 | -38.121 | 1.00 | 84.01 | N |
| ATOM | 260 | CA | ASN A 261 | -3.862 | -14.003 | -39.222 | 1.00 | 84.78 | C |
| ATOM | 261 | CB | ASN A 261 | -5.254 | -13.491 | -38.883 | 1.00 | 78.70 | C |
| ATOM | 262 | CG | ASN A 261 | 6.327 | 14.540 | 39.109 | 1.00 | 89.69 | C |
| ATOM | 263 | OD1 | ASN A 261 | -7.489 | -14.206 | -39.353 | 1.00 | 95.40 | O |
| ATOM | 264 | ND2 | ASN A 261 | -5.944 | -15.816 | -39.061 | 1.00 | 89.29 | N |
| ATOM | 265 | C | ASN A 261 | -2.989 | -12.856 | -39.723 | 1.00 | 90.69 | C |
| ATOM | 266 | O | ASN A 261 | -2.962 | -12.600 | -40.925 | 1.00 | 97.65 | O |
| ATOM | 267 | N | LYS A 262 | -2.292 | -12.164 | -38.819 | 1.00 | 99.07 | N |
| ATOM | 268 | CA | LYS A 262 | -1.544 | -10.938 | -39.174 | 1.00 | 115.04 | C |
| ATOM | 269 | CB | LYS A 262 | -0.854 | -10.327 | -37.938 | 1.00 | 127.18 | C |
| ATOM | 270 | CG | LYS A 262 | -1.764 | -9.527 | -37.004 | 1.00 | 123.16 | C |
| ATOM | 271 | CD | LYS A 262 | -0.986 | -8.972 | -35.809 | 1.00 | 109.97 | C |
| ATOM | 272 | CE | LYS A 262 | -1.905 | -8.608 | -34.646 | 1.00 | 104.09 | C |
| ATOM | 273 | NZ | LYS A 262 | 2.355 | 7.184 | 34.641 | 1.00 | 101.50 | N |
| ATOM | 274 | C | LYS A 262 | -0.516 | -11.133 | -40.292 | 1.00 | 122.59 | C |
| ATOM | 275 | O | LYS A 262 | 0.115 | -10.174 | -40.739 | 1.00 | 127.12 | O |
| ATOM | 276 | N | GLN A 263 | -0.356 | -12.381 | -40.730 | 1.00 | 132.27 | N |
| ATOM | 277 | CA | GLN A 263 | 0.559 | -12.749 | -41.814 | 1.00 | 123.34 | C |
| ATOM | 278 | CB | GLN A 263 | 1.392 | -13.970 | -41.396 | 1.00 | 125.96 | C |
| ATOM | 279 | CG | GLN A 263 | 0.611 | -15.072 | -40.677 | 1.00 | 130.55 | C |
| ATOM | 280 | CD | GLN A 263 | 1.177 | -15.439 | -39.305 | 1.00 | 129.11 | C |
| ATOM | 281 | OE1 | GLN A 263 | 1.676 | -16.555 | -39.094 | 1.00 | 117.78 | O |
| ATOM | 282 | NE2 | GLN A 263 | 1.094 | -14.500 | -38.363 | 1.00 | 124.45 | N |
| ATOM | 283 | C | GLN A 263 | -0.192 | -12.979 | -43.140 | 1.00 | 124.40 | C |
| ATOM | 284 | O | GLN A 263 | 0.897 | 13.984 | 43.310 | 1.00 | 115.00 | O |
| ATOM | 285 | N | ARG A 264 | -0.038 | -12.023 | -44.063 | 1.00 | 132.30 | N |
| ATOM | 286 | CA | ARG A 264 | -0.781 | -11.978 | -45.343 | 1.00 | 129.94 | C |
| ATOM | 287 | CB | ARG A 264 | -1.708 | -10.737 | -45.403 | 1.00 | 127.72 | C |
| ATOM | 288 | CG | ARG A 264 | -2.281 | -10.214 | -44.079 | 1.00 | 119.54 | C |
| ATOM | 289 | CD | ARG A 264 | -1.470 | -9.012 | -43.608 | 1.00 | 118.18 | C |
| ATOM | 290 | NE | ARG A 264 | -1.869 | -8.480 | -42.307 | 1.00 | 116.51 | N |
| ATOM | 291 | CZ | ARG A 264 | -1.100 | -7.689 | -41.556 | 1.00 | 117.13 | C |
| ATOM | 292 | NH1 | ARG A 264 | 0.123 | -7.354 | -41.963 | 1.00 | 104.97 | N |
| ATOM | 293 | NH2 | ARG A 264 | -1.542 | -7.246 | -40.383 | 1.00 | 113.28 | N |
| ATOM | 294 | C | ARG A 264 | 0.188 | -12.123 | -46.571 | 1.00 | 127.91 | C |
| ATOM | 295 | O | ARG A 264 | 1.012 | -13.046 | -46.557 | 1.00 | 115.47 | O |
| ATOM | 296 | N | ALA A 265 | 0.118 | -11.311 | -47.640 | 1.00 | 127.10 | N |
| ATOM | 297 | CA | ALA A 265 | -0.948 | -10.368 | -47.997 | 1.00 | 129.76 | C |
| ATOM | 298 | CB | ALA A 265 | -0.353 | -9.008 | -48.347 | 1.00 | 117.15 | C |
| ATOM | 299 | C | ALA A 265 | -1.676 | -10.955 | -49.206 | 1.00 | 134.71 | C |
| ATOM | 300 | O | ALA A 265 | -1.384 | -10.566 | -50.344 | 1.00 | 119.71 | O |
| ATOM | 301 | N | PRO A 266 | -2.650 | -11.870 | -48.959 | 1.00 | 150.65 | N |
| ATOM | 302 | CA | PRO A 266 | -3.128 | -12.910 | -49.900 | 1.00 | 152.52 | C |
| ATOM | 303 | CB | PRO A 266 | 4.425 | 13.414 | 49.249 | 1.00 | 160.97 | C |

[0539]

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 304 | CG | PRO | A | 266 | -4.864 | -12.301 | -48.359 | 1.00163.35 | C |
| ATOM | 305 | CD | PRO | A | 266 | -3.587 | -11.712 | -47.831 | 1.00155.40 | C |
| ATOM | 306 | C | PRO | A | 266 | -3.411 | -12.396 | -51.303 | 1.00149.59 | C |
| ATOM | 307 | O | PRO | A | 266 | -3.525 | -13.184 | -52.248 | 1.00146.68 | O |
| ATOM | 308 | N | GLN | A | 267 | 3.538 | 11.078 | 51.409 | 1.00138.45 | N |
| ATOM | 309 | CA | GLN | A | 267 | -3.607 | -10.396 | -52.678 | 1.00131.68 | C |
| ATOM | 310 | CB | GLN | A | 267 | -3.642 | -8.878 | -52.438 | 1.00140.27 | C |
| ATOM | 311 | CG | GLN | A | 267 | -4.150 | -8.038 | -53.601 | 1.00138.05 | C |
| ATOM | 312 | CD | GLN | A | 267 | -3.036 | -7.618 | -54.546 | 1.00145.63 | C |
| ATOM | 313 | OE1 | GLN | A | 267 | -2.003 | -7.089 | -54.120 | 1.00140.46 | O |
| ATOM | 314 | NE2 | GLN | A | 267 | -3.244 | -7.848 | -55.839 | 1.00152.12 | N |
| ATOM | 315 | C | GLN | A | 267 | -2.415 | -10.830 | -53.539 | 1.00121.93 | C |
| ATOM | 316 | O | GLN | A | 267 | -2.587 | -11.638 | -54.452 | 1.00116.81 | O |
| ATOM | 317 | N | GLU | A | 268 | -1.208 | -10.351 | -53.231 | 1.00119.78 | N |
| ATOM | 318 | CA | GLU | A | 268 | -0.061 | -10.593 | -54.129 | 1.00125.48 | C |
| ATOM | 319 | CB | GLU | A | 268 | 0.928 | 9.392 | 54.144 | 1.00112.97 | C |
| ATOM | 320 | CG | GLU | A | 268 | 2.219 | -9.514 | -53.339 | 1.00106.41 | C |
| ATOM | 321 | CD | GLU | A | 268 | 2.087 | -10.412 | -52.126 | 1.00104.30 | C |
| ATOM | 322 | OE1 | GLU | A | 268 | 0.975 | -10.450 | -51.531 | 1.00 98.89 | O |
| ATOM | 323 | OE2 | GLU | A | 268 | 3.095 | -11.088 | -51.790 | 1.00 93.62 | O |
| ATOM | 324 | C | GLU | A | 268 | 0.590 | -11.983 | -53.911 | 1.00124.23 | C |
| ATOM | 325 | O | GLU | A | 268 | 1.667 | -12.297 | -54.433 | 1.00125.70 | O |
| ATOM | 326 | N | ALA | A | 269 | -0.094 | -12.809 | -53.129 | 1.00115.97 | N |
| ATOM | 327 | CA | ALA | A | 269 | 0.129 | -14.235 | -53.165 | 1.00108.38 | C |
| ATOM | 328 | CB | ALA | A | 269 | -0.625 | -14.907 | -52.030 | 1.00110.59 | C |
| ATOM | 329 | C | ALA | A | 269 | -0.345 | -14.750 | -54.534 | 1.00107.90 | C |
| ATOM | 330 | O | ALA | A | 269 | 0.140 | 15.921 | 54.883 | 1.00 99.12 | O |
| ATOM | 331 | N | ALA | A | 270 | -0.983 | -13.856 | -55.298 | 1.00109.25 | N |
| ATOM | 332 | CA | ALA | A | 270 | -1.369 | -14.127 | -56.681 | 1.00107.03 | C |
| ATOM | 333 | CB | ALA | A | 270 | -2.531 | -13.247 | -57.105 | 1.00100.51 | C |
| ATOM | 334 | C | ALA | A | 270 | -0.170 | -13.920 | -57.596 | 1.00109.39 | C |
| ATOM | 335 | O | ALA | A | 270 | -0.025 | -14.615 | -58.606 | 1.00107.46 | O |
| ATOM | 336 | N | ASN | A | 271 | 0.689 | -12.966 | -57.234 | 1.00114.24 | N |
| ATOM | 337 | CA | ASN | A | 271 | 1.976 | -12.763 | -57.920 | 1.00112.80 | C |
| ATOM | 338 | CB | ASN | A | 271 | 2.775 | -11.606 | -57.271 | 1.00112.16 | C |
| ATOM | 339 | CG | ASN | A | 271 | 4.195 | -11.463 | -57.830 | 1.00119.82 | C |
| ATOM | 340 | OD1 | ASN | A | 271 | 4.402 | -11.324 | -59.046 | 1.00114.47 | O |
| ATOM | 341 | ND2 | ASN | A | 271 | 5.183 | 11.483 | 56.933 | 1.00115.46 | N |
| ATOM | 342 | C | ASN | A | 271 | 2.796 | -14.061 | -57.969 | 1.00 98.58 | C |
| ATOM | 343 | O | ASN | A | 271 | 3.546 | -14.291 | -58.926 | 1.00 97.96 | O |
| ATOM | 344 | N | ALA | A | 272 | 2.635 | -14.898 | -56.938 | 1.00 88.05 | N |
| ATOM | 345 | CA | ALA | A | 272 | 3.300 | -16.199 | -56.862 | 1.00 85.04 | C |
| ATOM | 346 | CB | ALA | A | 272 | 3.707 | -16.516 | -55.436 | 1.00 77.63 | C |
| ATOM | 347 | C | ALA | A | 272 | 2.432 | -17.313 | -57.435 | 1.00 87.63 | C |
| ATOM | 348 | O | ALA | A | 272 | 2.950 | -18.332 | -57.903 | 1.00 95.95 | O |
| ATOM | 349 | N | ALA | A | 273 | 1.116 | -17.112 | -57.396 | 1.00 93.09 | N |

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ATOM    350  CA  ALA A 273       0.167 -18.060 -57.970  1.00100.97           C
ATOM    351  CB  ALA A 273      -1.247 -17.771 -57.482  1.00108.89           C
ATOM    352  C   ALA A 273       0.241 -18.050 -59.500  1.00106.49           C
ATOM    353  O   ALA A 273       0.993 -18.834 -60.089  1.00115.25           O
ATOM    354  N   ALA A 274       0.527  17.164  60.142  1.00118.27           N
ATOM    355  CA  ALA A 274      -0.486 -17.048 -61.604  1.00111.38           C
ATOM    356  CB  ALA A 274      -1.829 -16.595 -62.165  1.00103.45           C
ATOM    357  C   ALA A 274       0.651 -16.148 -62.093  1.00105.32           C
ATOM    358  O   ALA A 274       1.300 -15.446 -61.308  1.00 96.60           O
ATOM    359  N   LYS A 275       0.866 -16.183 -63.404  1.00105.29           N
ATOM    360  CA  LYS A 275       2.003 -15.558 -64.061  1.00105.91           C
ATOM    361  CB  LYS A 275       1.806 -14.048 -64.228  1.00117.63           C
ATOM    362  CG  LYS A 275       2.729 -13.393 -65.252  1.00118.40           C
ATOM    363  CD  LYS A 275       2.768 -11.889 -65.029  1.00115.55           C
ATOM    364  CE  LYS A 275       3.557 -11.173 -66.107  1.00112.60           C
ATOM    365  NZ  LYS A 275       3.762   9.754  65.709  1.00108.50           N
ATOM    366  C   LYS A 275       3.297 -15.889 -63.332  1.00103.87           C
ATOM    367  O   LYS A 275       3.823 -15.092 -62.554  1.00100.28           O
ATOM    368  N   GLU A 276       3.760 -17.110 -63.561  1.00108.80           N
ATOM    369  CA  GLU A 276       5.133 -17.509 -63.273  1.00111.99           C
ATOM    370  CB  GLU A 276       5.278 -18.162 -61.885  1.00112.59           C
ATOM    371  CG  GLU A 276       5.269 -17.185 -60.704  1.00 98.17           C
ATOM    372  CD  GLU A 276       6.420 -16.180 -60.719  1.00 94.70           C
ATOM    373  OE1 GLU A 276       7.516 -16.507 -61.253  1.00 77.13           O
ATOM    374  OE2 GLU A 276       6.221 -15.061 -60.183  1.00 86.67           O
ATOM    375  C   GLU A 276       5.550 -18.463 -64.375  1.00104.30           C
ATOM    376  O   GLU A 276       4.955  18.460  65.454  1.00104.04           O
ATOM    377  N   PHE A 278       7.055 -15.266 -64.815  1.00140.26           N
ATOM    378  CA  PHE A 278       8.510 -15.178 -64.733  1.00141.37           C
ATOM    379  CB  PHE A 278       8.954 -13.933 -63.941  1.00144.78           C
ATOM    380  CG  PHE A 278       8.144 -12.683 -64.193  1.00154.75           C
ATOM    381  CD1 PHE A 278       7.601 -12.396 -65.450  1.00155.25           C
ATOM    382  CE1 PHE A 278       6.871 -11.233 -65.646  1.00154.54           C
ATOM    383  CZ  PHE A 278       6.693 -10.330 -64.591  1.00147.84           C
ATOM    384  CE2 PHE A 278       7.242 -10.592 -63.346  1.00151.53           C
ATOM    385  CD2 PHE A 278       7.968 -11.757 -63.153  1.00158.31           C
ATOM    386  C   PHE A 278       9.094 -16.420 -64.044  1.00134.30           C
ATOM    387  O   PHE A 278       9.234  16.431  62.818  1.00139.39           O
ATOM    388  N   SER A 279       9.466 -17.443 -64.820  1.00121.35           N
ATOM    389  CA  SER A 279       9.854 -18.748 -64.245  1.00112.11           C
ATOM    390  CB  SER A 279       8.917 -19.840 -64.763  1.00113.62           C
ATOM    391  OG  SER A 279       7.579 -19.527 -64.427  1.00113.92           O
ATOM    392  C   SER A 279      11.329 -19.183 -64.388  1.00102.09           C
ATOM    393  O   SER A 279      12.165 -18.422 -64.887  1.00101.57           O
ATOM    394  N   ALA A 280      11.611 -20.417 -63.950  1.00 92.83           N
ATOM    395  CA  ALA A 280      12.963 -20.987 -63.824  1.00 84.34           C
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[0631]

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 396 | CB | ALA | A | 280 | 13.676 | -21.026 | -65.161 | 1.00 96.16 | C |
| ATOM | 397 | C | ALA | A | 280 | 13.793 | -20.253 | -62.779 | 1.00 85.65 | C |
| ATOM | 398 | O | ALA | A | 280 | 13.285 | -19.927 | -61.717 | 1.00 90.92 | O |
| ATOM | 399 | N | GLU | A | 281 | 15.066 | -19.998 | -63.067 | 1.00 90.94 | N |
| ATOM | 400 | CA | GLU | A | 281 | 15.972 | 19.302 | 62.128 | 1.00 89.85 | C |
| ATOM | 401 | CB | GLU | A | 281 | 17.341 | -18.999 | -62.766 | 1.00 85.75 | C |
| ATOM | 402 | CG | GLU | A | 281 | 17.772 | -19.897 | -63.923 | 1.00 91.98 | C |
| ATOM | 403 | CD | GLU | A | 281 | 17.132 | -19.539 | -65.269 | 1.00 97.70 | C |
| ATOM | 404 | OE1 | GLU | A | 281 | 16.410 | -18.515 | -65.365 | 1.00 96.11 | O |
| ATOM | 405 | OE2 | GLU | A | 281 | 17.340 | -20.301 | -66.247 | 1.00 99.07 | O |
| ATOM | 406 | C | GLU | A | 281 | 15.370 | -17.993 | -61.575 | 1.00 88.23 | C |
| ATOM | 407 | O | GLU | A | 281 | 15.892 | -17.411 | -60.620 | 1.00 86.47 | O |
| ATOM | 408 | N | GLU | A | 282 | 14.288 | -17.520 | -62.189 | 1.00 87.96 | N |
| ATOM | 409 | CA | GLU | A | 282 | 13.575 | -16.365 | -61.663 | 1.00 87.97 | C |
| ATOM | 410 | CB | GLU | A | 282 | 12.500 | -15.890 | -62.635 | 1.00 91.23 | C |
| ATOM | 411 | CG | GLU | A | 282 | 13.048 | 15.308 | 63.928 | 1.00105.43 | C |
| ATOM | 412 | CD | GLU | A | 282 | 12.089 | -14.314 | -64.566 | 1.00118.44 | C |
| ATOM | 413 | OE1 | GLU | A | 282 | 11.763 | -13.296 | -63.915 | 1.00118.34 | O |
| ATOM | 414 | OE2 | GLU | A | 282 | 11.659 | -14.539 | -65.721 | 1.00124.25 | O |
| ATOM | 415 | C | GLU | A | 282 | 12.953 | -16.826 | -60.376 | 1.00 78.42 | C |
| ATOM | 416 | O | GLU | A | 282 | 13.403 | -16.472 | -59.297 | 1.00 72.59 | O |
| ATOM | 417 | N | ASN | A | 283 | 11.918 | -17.640 | -60.543 | 1.00 84.63 | N |
| ATOM | 418 | CA | ASN | A | 283 | 11.330 | -18.527 | -59.536 | 1.00 79.24 | C |
| ATOM | 419 | CB | ASN | A | 283 | 10.810 | -19.770 | -60.265 | 1.00 77.40 | C |
| ATOM | 420 | CG | ASN | A | 283 | 10.048 | -20.715 | -59.369 | 1.00 78.83 | C |
| ATOM | 421 | OD1 | ASN | A | 283 | 8.993 | -20.369 | -58.838 | 1.00 82.39 | O |
| ATOM | 422 | ND2 | ASN | A | 283 | 10.559 | 21.936 | 59.232 | 1.00 71.64 | N |
| ATOM | 423 | C | ASN | A | 283 | 12.210 | -18.928 | -58.339 | 1.00 79.44 | C |
| ATOM | 424 | O | ASN | A | 283 | 11.727 | -18.876 | -57.210 | 1.00 89.20 | O |
| ATOM | 425 | N | PHE | A | 284 | 13.470 | -19.326 | -58.567 | 1.00 71.11 | N |
| ATOM | 426 | CA | PHE | A | 284 | 14.427 | -19.546 | -57.465 | 1.00 72.23 | C |
| ATOM | 427 | CB | PHE | A | 284 | 15.833 | -19.774 | -58.035 | 1.00 77.60 | C |
| ATOM | 428 | CG | PHE | A | 284 | 16.854 | -20.257 | -57.032 | 1.00 76.28 | C |
| ATOM | 429 | CD1 | PHE | A | 284 | 17.001 | -19.662 | -55.801 | 1.00 72.00 | C |
| ATOM | 430 | CE1 | PHE | A | 284 | 17.954 | -20.116 | -54.895 | 1.00 74.65 | C |
| ATOM | 431 | CZ | PHE | A | 284 | 18.791 | -21.163 | -55.217 | 1.00 72.20 | C |
| ATOM | 432 | CE2 | PHE | A | 284 | 18.671 | -21.762 | -56.453 | 1.00 84.26 | C |
| ATOM | 433 | CD2 | PHE | A | 284 | 17.712 | 21.304 | 57.358 | 1.00 87.48 | C |
| ATOM | 434 | C | PHE | A | 284 | 14.444 | -18.315 | -56.549 | 1.00 81.18 | C |
| ATOM | 435 | O | PHE | A | 284 | 14.144 | -18.402 | -55.356 | 1.00 78.49 | O |
| ATOM | 436 | N | LEU | A | 285 | 14.769 | -17.170 | -57.154 | 1.00 93.53 | N |
| ATOM | 437 | CA | LEU | A | 285 | 15.046 | -15.915 | -56.469 | 1.00 85.95 | C |
| ATOM | 438 | CB | LEU | A | 285 | 15.429 | -14.822 | -57.487 | 1.00 88.31 | C |
| ATOM | 439 | CG | LEU | A | 285 | 16.613 | -13.921 | -57.087 | 1.00 96.45 | C |
| ATOM | 440 | CD1 | LEU | A | 285 | 17.708 | -14.737 | -56.417 | 1.00 98.87 | C |
| ATOM | 441 | CD2 | LEU | A | 285 | 17.211 | -13.145 | -58.257 | 1.00102.19 | C |

[0677]

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 442 | C | LEU | A | 285 | 13.864 | -15.475 | -55.642 | 1.00 85.35 | C |
| ATOM | 443 | O | LEU | A | 285 | 14.025 | -14.886 | -54.571 | 1.00 95.25 | O |
| ATOM | 444 | N | ILE | A | 286 | 12.670 | -15.765 | -56.132 | 1.00 80.06 | N |
| ATOM | 445 | CA | ILE | A | 286 | 11.473 | -15.407 | -55.386 | 1.00 90.54 | C |
| ATOM | 446 | CB | ILE | A | 286 | 10.216 | 15.334 | 56.286 | 1.00 91.89 | C |
| ATOM | 447 | CG1 | ILE | A | 286 | 10.165 | -13.950 | -56.964 | 1.00 81.12 | C |
| ATOM | 448 | CD1 | ILE | A | 286 | 8.850 | -13.626 | -57.640 | 1.00 85.33 | C |
| ATOM | 449 | CG2 | ILE | A | 286 | 8.951 | -15.657 | -55.491 | 1.00 84.91 | C |
| ATOM | 450 | C | ILE | A | 286 | 11.283 | -16.271 | -54.131 | 1.00 93.99 | C |
| ATOM | 451 | O | ILE | A | 286 | 11.092 | -15.730 | -53.038 | 1.00100.04 | O |
| ATOM | 452 | N | LEU | A | 287 | 11.366 | -17.595 | -54.285 | 1.00 85.53 | N |
| ATOM | 453 | CA | LEU | A | 287 | 11.288 | -18.513 | -53.151 | 1.00 71.91 | C |
| ATOM | 454 | CB | LEU | A | 287 | 11.526 | -19.931 | -53.603 | 1.00 67.48 | C |
| ATOM | 455 | CG | LEU | A | 287 | 10.463 | -20.454 | -54.538 | 1.00 65.28 | C |
| ATOM | 456 | CD1 | LEU | A | 287 | 11.056 | -21.651 | -55.272 | 1.00 69.35 | C |
| ATOM | 457 | CD2 | LEU | A | 287 | 9.213 | 20.798 | 53.744 | 1.00 57.94 | C |
| ATOM | 458 | C | LEU | A | 287 | 12.307 | -18.162 | -52.099 | 1.00 72.99 | C |
| ATOM | 459 | O | LEU | A | 287 | 11.935 | -17.834 | -50.982 | 1.00 76.16 | O |
| ATOM | 460 | N | THR | A | 288 | 13.591 | -18.214 | -52.454 | 1.00 71.57 | N |
| ATOM | 461 | CA | THR | A | 288 | 14.642 | -17.810 | -51.517 | 1.00 72.32 | C |
| ATOM | 462 | CB | THR | A | 288 | 15.979 | -17.502 | -52.207 | 1.00 69.94 | C |
| ATOM | 463 | OG1 | THR | A | 288 | 15.773 | -17.477 | -53.619 | 1.00 77.96 | O |
| ATOM | 464 | CG2 | THR | A | 288 | 16.996 | -18.580 | -51.898 | 1.00 64.56 | C |
| ATOM | 465 | C | THR | A | 288 | 14.193 | -16.629 | -50.676 | 1.00 69.95 | C |
| ATOM | 466 | O | THR | A | 288 | 14.423 | -16.614 | -49.469 | 1.00 71.59 | O |
| ATOM | 467 | N | ALA | A | 289 | 13.518 | -15.665 | -51.300 | 1.00 70.83 | N |
| ATOM | 468 | CA | ALA | A | 289 | 12.961 | 14.536 | 50.554 | 1.00 73.78 | C |
| ATOM | 469 | CB | ALA | A | 289 | 12.466 | -13.445 | -51.488 | 1.00 76.74 | C |
| ATOM | 470 | C | ALA | A | 289 | 11.841 | -15.018 | -49.650 | 1.00 68.56 | C |
| ATOM | 471 | O | ALA | A | 289 | 11.990 | -15.019 | -48.443 | 1.00 66.45 | O |
| ATOM | 472 | N | MET | A | 290 | 10.728 | -15.414 | -50.260 | 1.00 72.99 | N |
| ATOM | 473 | CA | MET | A | 290 | 9.598 | -16.084 | -49.607 | 1.00 74.60 | C |
| ATOM | 474 | CB | MET | A | 290 | 8.920 | -16.983 | -50.628 | 1.00 81.05 | C |
| ATOM | 475 | CG | MET | A | 290 | 8.256 | -16.225 | -51.759 | 1.00 84.99 | C |
| ATOM | 476 | SD | MET | A | 290 | 6.476 | -16.162 | -51.496 | 1.00 83.30 | S |
| ATOM | 477 | CE | MET | A | 290 | 6.045 | -17.836 | -52.002 | 1.00 94.29 | C |
| ATOM | 478 | C | MET | A | 290 | 9.975 | -16.937 | -48.398 | 1.00 72.53 | C |
| ATOM | 479 | O | MET | A | 290 | 9.335 | 16.846 | 47.367 | 1.00 82.38 | O |
| ATOM | 480 | N | ALA | A | 291 | 11.000 | -17.770 | -48.543 | 1.00 64.19 | N |
| ATOM | 481 | CA | ALA | A | 291 | 11.496 | -18.617 | -47.475 | 1.00 58.96 | C |
| ATOM | 482 | CB | ALA | A | 291 | 12.705 | -19.420 | -47.959 | 1.00 57.05 | C |
| ATOM | 483 | C | ALA | A | 291 | 11.861 | -17.764 | -46.272 | 1.00 61.23 | C |
| ATOM | 484 | O | ALA | A | 291 | 11.101 | -17.672 | -45.301 | 1.00 62.79 | O |
| ATOM | 485 | N | THR | A | 292 | 13.059 | -17.192 | -46.327 | 1.00 65.17 | N |
| ATOM | 486 | CA | THR | A | 292 | 13.448 | -15.999 | -45.568 | 1.00 64.26 | C |
| ATOM | 487 | CB | THR | A | 292 | 14.110 | -15.007 | -46.532 | 1.00 69.50 | C |

[0723]

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ATOM    488  OG1 THR A 292      15.323 -15.587 -47.059  1.00 71.55           O
ATOM    489  CG2 THR A 292      14.347 -13.671 -45.844  1.00 62.95           C
ATOM    490  C   THR A 292      12.298 -15.218 -44.986  1.00 58.22           C
ATOM    491  O   THR A 292      12.337 -14.791 -43.850  1.00 64.54           O
ATOM    492  N   ASN A 293      11.265 -15.020 -45.784  1.00 59.03           N
ATOM    493  CA  ASN A 293      10.222 -14.127 -45.389  1.00 61.00           C
ATOM    494  CB  ASN A 293       9.642 -13.395 -46.603  1.00 71.01           C
ATOM    495  CG  ASN A 293       8.787 -12.202 -46.208  1.00 71.83           C
ATOM    496  OD1 ASN A 293       9.194 -11.355 -45.384  1.00 61.50           O
ATOM    497  ND2 ASN A 293       7.578  12.139  46.780  1.00 77.71           N
ATOM    498  C   ASN A 293       9.173 -14.883 -44.683  1.00 58.68           C
ATOM    499  O   ASN A 293       8.038 -14.429 -44.595  1.00 70.28           O
ATOM    500  N   HIS A 294       9.556 -16.059 -44.197  1.00 64.32           N
ATOM    501  CA  HIS A 294       8.653  17.004  43.542  1.00 55.39           C
ATOM    502  CB  HIS A 294       8.692 -18.308 -44.289  1.00 53.93           C
ATOM    503  CG  HIS A 294       8.443 -19.526 -43.437  1.00 56.62           C
ATOM    504  ND1 HIS A 294       7.207 -19.896 -43.015  1.00 48.22           N
ATOM    505  CE1 HIS A 294       7.317 -21.012 -42.306  1.00 44.18           C
ATOM    506  NE2 HIS A 294       8.602 -21.380 -42.292  1.00 45.06           N
ATOM    507  CD2 HIS A 294       9.316 -20.498 -42.989  1.00 51.36           C
ATOM    508  C   HIS A 294       9.087 -17.160 -42.137  1.00 55.50           C
ATOM    509  O   HIS A 294       8.249 -17.221 -41.223  1.00 51.52           O
ATOM    510  N   VAL A 295      10.416 -17.199 -41.973  1.00 56.73           N
ATOM    511  CA  VAL A 295      11.112 -17.067 -40.683  1.00 53.77           C
ATOM    512  CB  VAL A 295      12.630 -17.160 -40.875  1.00 48.81           C
ATOM    513  CG1 VAL A 295      13.364 -16.725 -39.627  1.00 53.50           C
ATOM    514  CG2 VAL A 295      13.019 -18.574 -41.232  1.00 45.35           C
ATOM    515  C   VAL A 295      10.752 -15.791 -39.895  1.00 58.82           C
ATOM    516  O   VAL A 295      10.439  15.864  38.701  1.00 61.37           O
ATOM    517  N   GLN A 296      10.763 -14.625 -40.529  1.00 61.41           N
ATOM    518  CA  GLN A 296      10.319 -13.436 -39.769  1.00 74.30           C
ATOM    519  CB  GLN A 296      10.510 -12.121 -40.562  1.00 86.54           C
ATOM    520  CG  GLN A 296      11.920  11.517  40.469  1.00102.26           C
ATOM    521  CD  GLN A 296      13.045 -12.465 -40.929  1.00112.04           C
ATOM    522  OE1 GLN A 296      12.848 -13.287 -41.829  1.00116.70           O
ATOM    523  NE2 GLN A 296      14.230 -12.352 -40.303  1.00 95.06           N
ATOM    524  C   GLN A 296       8.877 -13.596 -39.240  1.00 69.72           C
ATOM    525  O   GLN A 296       8.551 -13.145 -38.140  1.00 60.95           O
ATOM    526  N   VAL A 297       8.028 -14.262 -40.029  1.00 73.16           N
ATOM    527  CA  VAL A 297       6.624 -14.475 -39.649  1.00 66.44           C
ATOM    528  CB  VAL A 297       5.763 -14.949 -40.817  1.00 60.71           C
ATOM    529  CG1 VAL A 297       4.329 -15.126 -40.357  1.00 58.39           C
ATOM    530  CG2 VAL A 297       5.819 -13.961 -41.956  1.00 65.33           C
ATOM    531  C   VAL A 297       6.513 -15.526 -38.572  1.00 61.83           C
ATOM    532  O   VAL A 297       5.738 -15.384 -37.619  1.00 57.20           O
ATOM    533  N   LEU A 298       7.290 -16.589 -38.740  1.00 61.66           N
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[0769]

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 534 | CA | LEU | A | 298 | 7.267 | -17.664 | -37.781 | 1.00 | 57.85 | C |
| ATOM | 535 | CB | LEU | A | 298 | 8.180 | -18.814 | -38.198 | 1.00 | 49.61 | C |
| ATOM | 536 | CG | LEU | A | 298 | 8.151 | -19.949 | -37.167 | 1.00 | 48.36 | C |
| ATOM | 537 | CD1 | LEU | A | 298 | 6.720 | -20.452 | -36.968 | 1.00 | 47.54 | C |
| ATOM | 538 | CD2 | LEU | A | 298 | 9.118 | -21.084 | -37.531 | 1.00 | 47.32 | C |
| ATOM | 539 | C | LEU | A | 298 | 7.632 | -17.104 | -36.414 | 1.00 | 55.51 | C |
| ATOM | 540 | O | LEU | A | 298 | 6.858 | -17.269 | -35.462 | 1.00 | 54.73 | O |
| ATOM | 541 | N | VAL | A | 299 | 8.772 | -16.407 | -36.353 | 1.00 | 53.02 | N |
| ATOM | 542 | CA | VAL | A | 299 | 9.273 | -15.813 | -35.110 | 1.00 | 57.28 | C |
| ATOM | 543 | CB | VAL | A | 299 | 10.656 | -15.151 | -35.252 | 1.00 | 57.91 | C |
| ATOM | 544 | CG1 | VAL | A | 299 | 11.101 | -14.594 | -33.912 | 1.00 | 52.51 | C |
| ATOM | 545 | CG2 | VAL | A | 299 | 11.694 | -16.145 | -35.776 | 1.00 | 59.83 | C |
| ATOM | 546 | C | VAL | A | 299 | 8.321 | -14.804 | -34.485 | 1.00 | 58.79 | C |
| ATOM | 547 | O | VAL | A | 299 | 8.205 | -14.783 | -33.279 | 1.00 | 65.64 | O |
| ATOM | 548 | N | GLU | A | 300 | 7.643 | -13.989 | -35.293 | 1.00 | 60.03 | N |
| ATOM | 549 | CA | GLU | A | 300 | 6.649 | -13.042 | -34.798 | 1.00 | 60.63 | C |
| ATOM | 550 | CB | GLU | A | 300 | 6.157 | -12.104 | -35.927 | 1.00 | 80.96 | C |
| ATOM | 551 | CG | GLU | A | 300 | 4.777 | -11.416 | -35.735 | 1.00 | 88.19 | C |
| ATOM | 552 | CD | GLU | A | 300 | 3.581 | -12.193 | -36.339 | 1.00 | 95.22 | C |
| ATOM | 553 | OE1 | GLU | A | 300 | 3.762 | 12.923 | 37.345 | 1.00 | 94.41 | O |
| ATOM | 554 | OE2 | GLU | A | 300 | 2.442 | -12.078 | -35.815 | 1.00 | 96.81 | O |
| ATOM | 555 | C | GLU | A | 300 | 5.483 | -13.770 | -34.177 | 1.00 | 59.89 | C |
| ATOM | 556 | O | GLU | A | 300 | 4.957 | -13.343 | -33.140 | 1.00 | 66.98 | O |
| ATOM | 557 | N | PHE | A | 301 | 5.054 | -14.848 | -34.833 | 1.00 | 61.04 | N |
| ATOM | 558 | CA | PHE | A | 301 | 3.930 | -15.673 | -34.360 | 1.00 | 56.15 | C |
| ATOM | 559 | CB | PHE | A | 301 | 3.575 | -16.727 | -35.407 | 1.00 | 47.18 | C |
| ATOM | 560 | CG | PHE | A | 301 | 2.497 | -17.671 | -34.977 | 1.00 | 44.94 | C |
| ATOM | 561 | CD1 | PHE | A | 301 | 1.215 | -17.218 | -34.730 | 1.00 | 47.68 | C |
| ATOM | 562 | CE1 | PHE | A | 301 | 0.226 | -18.089 | -34.325 | 1.00 | 45.74 | C |
| ATOM | 563 | CZ | PHE | A | 301 | 0.525 | -19.426 | -34.173 | 1.00 | 48.04 | C |
| ATOM | 564 | CE2 | PHE | A | 301 | 1.789 | 19.892 | 34.433 | 1.00 | 42.87 | C |
| ATOM | 565 | CD2 | PHE | A | 301 | 2.765 | -19.015 | -34.824 | 1.00 | 45.13 | C |
| ATOM | 566 | C | PHE | A | 301 | 4.293 | -16.338 | -33.034 | 1.00 | 61.65 | C |
| ATOM | 567 | O | PHE | A | 301 | 3.469 | -16.442 | -32.114 | 1.00 | 62.89 | O |
| ATOM | 568 | N | THR | A | 302 | 5.548 | -16.755 | -32.942 | 1.00 | 61.58 | N |
| ATOM | 569 | CA | THR | A | 302 | 6.015 | -17.495 | -31.819 | 1.00 | 68.91 | C |
| ATOM | 570 | CB | THR | A | 302 | 7.312 | -18.226 | -32.191 | 1.00 | 73.55 | C |
| ATOM | 571 | OG1 | THR | A | 302 | 7.101 | -18.931 | -33.421 | 1.00 | 77.09 | O |
| ATOM | 572 | CG2 | THR | A | 302 | 7.701 | -19.228 | -31.124 | 1.00 | 69.21 | C |
| ATOM | 573 | C | THR | A | 302 | 6.125 | -16.629 | -30.558 | 1.00 | 74.14 | C |
| ATOM | 574 | O | THR | A | 302 | 5.550 | -16.971 | -29.532 | 1.00 | 79.79 | O |
| ATOM | 575 | N | LYS | A | 303 | 6.827 | 15.503 | 30.642 | 1.00 | 74.35 | N |
| ATOM | 576 | CA | LYS | A | 303 | 6.922 | -14.540 | -29.525 | 1.00 | 74.29 | C |
| ATOM | 577 | CB | LYS | A | 303 | 7.520 | -13.217 | -29.998 | 1.00 | 75.35 | C |
| ATOM | 578 | CG | LYS | A | 303 | 9.027 | -13.125 | -29.874 | 1.00 | 79.85 | C |
| ATOM | 579 | CD | LYS | A | 303 | 9.519 | -11.856 | -30.533 | 1.00 | 91.13 | C |

[0815]

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 580 | CE | LYS | A | 303 | 10.364 | -11.039 | -29.575 | 1.00 | 104.04 | C |
| ATOM | 581 | NZ | LYS | A | 303 | 10.659 | -9.712 | -30.190 | 1.00 | 124.50 | N |
| ATOM | 582 | C | LYS | A | 303 | 5.593 | -14.235 | -28.844 | 1.00 | 72.45 | C |
| ATOM | 583 | O | LYS | A | 303 | 5.542 | -14.097 | -27.619 | 1.00 | 75.10 | O |
| ATOM | 584 | N | LYS | A | 304 | 4.533 | 14.114 | 29.642 | 1.00 | 63.63 | N |
| ATOM | 585 | CA | LYS | A | 304 | 3.200 | -13.852 | -29.113 | 1.00 | 61.93 | C |
| ATOM | 586 | CB | LYS | A | 304 | 2.375 | -13.023 | -30.115 | 1.00 | 49.28 | C |
| ATOM | 587 | C | LYS | A | 304 | 2.440 | -15.130 | -28.651 | 1.00 | 66.56 | C |
| ATOM | 588 | O | LYS | A | 304 | 1.241 | -15.067 | -28.373 | 1.00 | 71.71 | O |
| ATOM | 589 | N | LEU | A | 305 | 3.119 | -16.277 | -28.569 | 1.00 | 61.25 | N |
| ATOM | 590 | CA | LEU | A | 305 | 2.480 | -17.479 | -28.033 | 1.00 | 60.69 | C |
| ATOM | 591 | CB | LEU | A | 305 | 3.126 | -18.784 | -28.550 | 1.00 | 65.44 | C |
| ATOM | 592 | CG | LEU | A | 305 | 2.806 | -19.404 | -29.943 | 1.00 | 62.71 | C |
| ATOM | 593 | CD1 | LEU | A | 305 | 2.513 | -20.888 | -29.814 | 1.00 | 59.26 | C |
| ATOM | 594 | CD2 | LEU | A | 305 | 1.620 | -18.739 | -30.627 | 1.00 | 61.96 | C |
| ATOM | 595 | C | LEU | A | 305 | 2.512 | 17.433 | 26.517 | 1.00 | 60.98 | C |
| ATOM | 596 | O | LEU | A | 305 | 3.576 | -17.233 | -25.922 | 1.00 | 64.73 | O |
| ATOM | 597 | N | PRO | A | 306 | 1.339 | -17.605 | -25.880 | 1.00 | 60.84 | N |
| ATOM | 598 | CA | PRO | A | 306 | 1.170 | -17.555 | -24.428 | 1.00 | 54.57 | C |
| ATOM | 599 | CB | PRO | A | 306 | -0.160 | -18.253 | -24.215 | 1.00 | 53.41 | C |
| ATOM | 600 | CG | PRO | A | 306 | -0.951 | -17.928 | -25.451 | 1.00 | 58.61 | C |
| ATOM | 601 | CD | PRO | A | 306 | 0.041 | -17.727 | -26.575 | 1.00 | 62.98 | C |
| ATOM | 602 | C | PRO | A | 306 | 2.215 | -18.349 | -23.738 | 1.00 | 61.37 | C |
| ATOM | 603 | O | PRO | A | 306 | 2.059 | -19.566 | -23.641 | 1.00 | 73.69 | O |
| ATOM | 604 | N | GLY | A | 307 | 3.283 | -17.679 | -23.294 | 1.00 | 64.42 | N |
| ATOM | 605 | CA | GLY | A | 307 | 4.299 | -18.275 | -22.410 | 1.00 | 61.23 | C |
| ATOM | 606 | C | GLY | A | 307 | 5.670 | -18.332 | -23.030 | 1.00 | 65.02 | C |
| ATOM | 607 | O | GLY | A | 307 | 6.655 | 18.705 | 22.361 | 1.00 | 58.20 | O |
| ATOM | 608 | N | PHE | A | 308 | 5.749 | -17.955 | -24.309 | 1.00 | 65.58 | N |
| ATOM | 609 | CA | PHE | A | 308 | 6.999 | -18.148 | -25.039 | 1.00 | 68.30 | C |
| ATOM | 610 | CB | PHE | A | 308 | 6.923 | -17.822 | -26.523 | 1.00 | 67.39 | C |
| ATOM | 611 | CG | PHE | A | 308 | 8.024 | -18.481 | -27.318 | 1.00 | 65.20 | C |
| ATOM | 612 | CD1 | PHE | A | 308 | 7.941 | -19.835 | -27.658 | 1.00 | 60.02 | C |
| ATOM | 613 | CE1 | PHE | A | 308 | 8.948 | -20.452 | -28.361 | 1.00 | 57.45 | C |
| ATOM | 614 | CZ | PHE | A | 308 | 10.073 | -19.735 | -28.732 | 1.00 | 65.44 | C |
| ATOM | 615 | CE2 | PHE | A | 308 | 10.180 | -18.399 | -28.381 | 1.00 | 69.70 | C |
| ATOM | 616 | CD2 | PHE | A | 308 | 9.158 | -17.781 | -27.668 | 1.00 | 64.72 | C |
| ATOM | 617 | C | PHE | A | 308 | 8.188 | -17.423 | -24.483 | 1.00 | 70.98 | C |
| ATOM | 618 | O | PHE | A | 308 | 9.241 | -18.028 | -24.327 | 1.00 | 78.86 | O |
| ATOM | 619 | N | GLN | A | 309 | 8.029 | 16.128 | 24.229 | 1.00 | 75.46 | N |
| ATOM | 620 | CA | GLN | A | 309 | 9.131 | -15.292 | -23.760 | 1.00 | 73.33 | C |
| ATOM | 621 | CB | GLN | A | 309 | 8.718 | -13.822 | -23.738 | 1.00 | 72.57 | C |
| ATOM | 622 | CG | GLN | A | 309 | 7.690 | -13.486 | -24.812 | 1.00 | 83.43 | C |
| ATOM | 623 | CD | GLN | A | 309 | 8.129 | -12.398 | -25.777 | 1.00 | 82.55 | C |
| ATOM | 624 | OE1 | GLN | A | 309 | 9.308 | -12.279 | -26.102 | 1.00 | 93.67 | O |
| ATOM | 625 | NE2 | GLN | A | 309 | 7.171 | -11.611 | -26.263 | 1.00 | 79.68 | N |

[0861]

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 626 | C | GLN | A | 309 | 9.575 | -15.790 | -22.386 | 1.00 | 76.61 | C |
| ATOM | 627 | O | GLN | A | 309 | 10.769 | -15.777 | -22.055 | 1.00 | 74.14 | O |
| ATOM | 628 | N | THR | A | 310 | 8.603 | -16.295 | -21.624 | 1.00 | 77.23 | N |
| ATOM | 629 | CA | THR | A | 310 | 8.838 | 16.864 | 20.293 | 1.00 | 70.75 | C |
| ATOM | 630 | CB | THR | A | 310 | 7.504 | -17.109 | -19.534 | 1.00 | 67.36 | C |
| ATOM | 631 | OG1 | THR | A | 310 | 7.128 | -18.487 | -19.608 | 1.00 | 74.51 | O |
| ATOM | 632 | CG2 | THR | A | 310 | 6.380 | -16.249 | -20.114 | 1.00 | 67.47 | C |
| ATOM | 633 | C | THR | A | 310 | 9.752 | -18.114 | -20.301 | 1.00 | 65.70 | C |
| ATOM | 634 | O | THR | A | 310 | 10.323 | -18.474 | -19.283 | 1.00 | 67.90 | O |
| ATOM | 635 | N | LEU | A | 311 | 9.918 | -18.759 | -21.445 | 1.00 | 66.28 | N |
| ATOM | 636 | CA | LEU | A | 311 | 10.856 | 19.875 | 21.528 | 1.00 | 73.71 | C |
| ATOM | 637 | CB | LEU | A | 311 | 10.674 | -20.648 | -22.830 | 1.00 | 77.09 | C |
| ATOM | 638 | CG | LEU | A | 311 | 9.391 | -21.473 | -22.965 | 1.00 | 85.59 | C |
| ATOM | 639 | CD1 | LEU | A | 311 | 9.540 | -22.322 | -24.221 | 1.00 | 96.45 | C |
| ATOM | 640 | CD2 | LEU | A | 311 | 9.053 | -22.356 | -21.764 | 1.00 | 65.05 | C |
| ATOM | 641 | C | LEU | A | 311 | 12.291 | -19.414 | -21.423 | 1.00 | 75.89 | C |
| ATOM | 642 | O | LEU | A | 311 | 12.551 | -18.215 | -21.379 | 1.00 | 87.18 | O |
| ATOM | 643 | N | ASP | A | 312 | 13.223 | -20.365 | -21.401 | 1.00 | 80.65 | N |
| ATOM | 644 | CA | ASP | A | 312 | 14.653 | -20.054 | -21.361 | 1.00 | 84.19 | C |
| ATOM | 645 | CB | ASP | A | 312 | 15.488 | 21.343 | 21.386 | 1.00 | 91.90 | C |
| ATOM | 646 | CG | ASP | A | 312 | 16.722 | -21.282 | -20.475 | 1.00 | 99.46 | C |
| ATOM | 647 | OD1 | ASP | A | 312 | 16.624 | -20.734 | -19.352 | 1.00 | 111.81 | O |
| ATOM | 648 | OD2 | ASP | A | 312 | 17.787 | -21.809 | -20.873 | 1.00 | 95.02 | O |
| ATOM | 649 | C | ASP | A | 312 | 14.977 | -19.178 | -22.558 | 1.00 | 83.46 | C |
| ATOM | 650 | O | ASP | A | 312 | 14.104 | -18.489 | -23.065 | 1.00 | 82.51 | O |
| ATOM | 651 | N | HIS | A | 313 | 16.224 | -19.194 | -23.011 | 1.00 | 87.88 | N |
| ATOM | 652 | CA | HIS | A | 313 | 16.629 | -18.383 | -24.154 | 1.00 | 86.21 | C |
| ATOM | 653 | CB | HIS | A | 313 | 17.734 | -17.400 | -23.759 | 1.00 | 86.64 | C |
| ATOM | 654 | CG | HIS | A | 313 | 18.578 | -16.924 | -24.924 | 1.00 | 102.61 | C |
| ATOM | 655 | ND1 | HIS | A | 313 | 18.093 | -16.121 | -25.897 | 1.00 | 107.37 | N |
| ATOM | 656 | CE1 | HIS | A | 313 | 19.068 | -15.862 | -26.794 | 1.00 | 108.17 | C |
| ATOM | 657 | NE2 | HIS | A | 313 | 20.183 | -16.508 | -26.398 | 1.00 | 109.77 | N |
| ATOM | 658 | CD2 | HIS | A | 313 | 19.917 | -17.171 | -25.248 | 1.00 | 105.73 | C |
| ATOM | 659 | C | HIS | A | 313 | 17.074 | -19.294 | -25.247 | 1.00 | 81.94 | C |
| ATOM | 660 | O | HIS | A | 313 | 16.713 | -19.131 | -26.410 | 1.00 | 74.47 | O |
| ATOM | 661 | N | GLU | A | 314 | 17.872 | 20.277 | 24.871 | 1.00 | 84.93 | N |
| ATOM | 662 | CA | GLU | A | 314 | 18.319 | -21.277 | -25.818 | 1.00 | 92.99 | C |
| ATOM | 663 | CB | GLU | A | 314 | 19.602 | -21.910 | -25.309 | 1.00 | 97.74 | C |
| ATOM | 664 | CG | GLU | A | 314 | 20.756 | -20.928 | -25.395 | 1.00 | 104.21 | C |
| ATOM | 665 | CD | GLU | A | 314 | 21.936 | -21.345 | -24.559 | 1.00 | 117.42 | C |
| ATOM | 666 | OE1 | GLU | A | 314 | 22.139 | -20.729 | -23.487 | 1.00 | 135.67 | O |
| ATOM | 667 | OE2 | GLU | A | 314 | 22.651 | -22.286 | -24.971 | 1.00 | 115.15 | O |
| ATOM | 668 | C | GLU | A | 314 | 17.218 | -22.302 | -26.116 | 1.00 | 91.59 | C |
| ATOM | 669 | O | GLU | A | 314 | 17.133 | -22.837 | -27.220 | 1.00 | 86.97 | O |
| ATOM | 670 | N | ASP | A | 315 | 16.367 | 22.550 | 25.123 | 1.00 | 91.37 | N |
| ATOM | 671 | CA | ASP | A | 315 | 15.148 | -23.296 | -25.334 | 1.00 | 79.39 | C |

[0907]

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 672 | CB | ASP | A | 315 | 14.327 | -23.372 | -24.042 | 1.00 77.31 | C |
| ATOM | 673 | CG | ASP | A | 315 | 14.754 | -24.557 | -23.119 | 1.00 86.47 | C |
| ATOM | 674 | OD1 | ASP | A | 315 | 15.774 | -25.241 | -23.406 | 1.00 85.05 | O |
| ATOM | 675 | OD2 | ASP | A | 315 | 14.060 | -24.808 | -22.096 | 1.00 82.62 | O |
| ATOM | 676 | C | ASP | A | 315 | 14.376 | 22.626 | 26.468 | 1.00 80.29 | C |
| ATOM | 677 | O | ASP | A | 315 | 14.005 | -23.277 | -27.451 | 1.00 87.76 | O |
| ATOM | 678 | N | GLN | A | 316 | 14.188 | -21.317 | -26.361 | 1.00 68.47 | N |
| ATOM | 679 | CA | GLN | A | 316 | 13.529 | -20.570 | -27.415 | 1.00 58.86 | C |
| ATOM | 680 | CB | GLN | A | 316 | 13.459 | -19.099 | -27.073 | 1.00 57.75 | C |
| ATOM | 681 | CG | GLN | A | 316 | 12.668 | -18.837 | -25.819 | 1.00 62.68 | C |
| ATOM | 682 | CD | GLN | A | 316 | 12.523 | -17.374 | -25.543 | 1.00 61.67 | C |
| ATOM | 683 | OE1 | GLN | A | 316 | 12.790 | -16.558 | -26.425 | 1.00 61.14 | O |
| ATOM | 684 | NE2 | GLN | A | 316 | 12.090 | -17.020 | -24.317 | 1.00 58.67 | N |
| ATOM | 685 | C | GLN | A | 316 | 14.217 | -20.747 | -28.746 | 1.00 60.12 | C |
| ATOM | 686 | O | GLN | A | 316 | 13.546 | -20.926 | -29.761 | 1.00 71.58 | O |
| ATOM | 687 | N | ILE | A | 317 | 15.543 | -20.716 | -28.766 | 1.00 52.73 | N |
| ATOM | 688 | CA | ILE | A | 317 | 16.218 | -20.880 | -30.044 | 1.00 53.71 | C |
| ATOM | 689 | CB | ILE | A | 317 | 17.712 | -20.537 | -29.986 | 1.00 52.18 | C |
| ATOM | 690 | CG1 | ILE | A | 317 | 17.951 | -19.250 | -29.203 | 1.00 60.47 | C |
| ATOM | 691 | CD1 | ILE | A | 317 | 17.144 | -18.084 | -29.714 | 1.00 73.43 | C |
| ATOM | 692 | CG2 | ILE | A | 317 | 18.264 | 20.361 | 31.374 | 1.00 46.56 | C |
| ATOM | 693 | C | ILE | A | 317 | 15.993 | -22.279 | -30.630 | 1.00 52.73 | C |
| ATOM | 694 | O | ILE | A | 317 | 15.635 | -22.408 | -31.798 | 1.00 49.64 | O |
| ATOM | 695 | N | ALA | A | 318 | 16.166 | -23.302 | -29.796 | 1.00 55.99 | N |
| ATOM | 696 | CA | ALA | A | 318 | 16.036 | -24.701 | -30.205 | 1.00 58.60 | C |
| ATOM | 697 | CB | ALA | A | 318 | 16.460 | -25.629 | -29.089 | 1.00 60.99 | C |
| ATOM | 698 | C | ALA | A | 318 | 14.634 | -25.074 | -30.712 | 1.00 60.06 | C |
| ATOM | 699 | O | ALA | A | 318 | 14.515 | -25.807 | -31.716 | 1.00 52.87 | O |
| ATOM | 700 | N | LEU | A | 319 | 13.599 | -24.560 | -30.040 | 1.00 52.58 | N |
| ATOM | 701 | CA | LEU | A | 319 | 12.224 | 24.658 | 30.548 | 1.00 53.33 | C |
| ATOM | 702 | CB | LEU | A | 319 | 11.245 | -23.762 | -29.773 | 1.00 46.69 | C |
| ATOM | 703 | CG | LEU | A | 319 | 11.044 | -24.241 | -28.350 | 1.00 47.08 | C |
| ATOM | 704 | CD1 | LEU | A | 319 | 10.111 | -23.275 | -27.674 | 1.00 55.32 | C |
| ATOM | 705 | CD2 | LEU | A | 319 | 10.469 | -25.653 | -28.288 | 1.00 44.56 | C |
| ATOM | 706 | C | LEU | A | 319 | 12.201 | -24.288 | -32.010 | 1.00 55.40 | C |
| ATOM | 707 | O | LEU | A | 319 | 12.082 | -25.175 | -32.857 | 1.00 53.56 | O |
| ATOM | 708 | N | LEU | A | 320 | 12.351 | -22.982 | -32.275 | 1.00 59.00 | N |
| ATOM | 709 | CA | LEU | A | 320 | 12.311 | -22.372 | -33.613 | 1.00 55.52 | C |
| ATOM | 710 | CB | LEU | A | 320 | 12.664 | -20.893 | -33.481 | 1.00 59.19 | C |
| ATOM | 711 | CG | LEU | A | 320 | 11.676 | -19.713 | -33.524 | 1.00 62.42 | C |
| ATOM | 712 | CD1 | LEU | A | 320 | 10.262 | -20.088 | -33.129 | 1.00 61.77 | C |
| ATOM | 713 | CD2 | LEU | A | 320 | 12.180 | -18.546 | -32.673 | 1.00 62.36 | C |
| ATOM | 714 | C | LEU | A | 320 | 13.226 | -23.049 | -34.664 | 1.00 56.61 | C |
| ATOM | 715 | O | LEU | A | 320 | 12.822 | -23.265 | -35.794 | 1.00 52.97 | O |
| ATOM | 716 | N | LYS | A | 321 | 14.455 | -23.392 | -34.300 | 1.00 59.91 | N |
| ATOM | 717 | CA | LYS | A | 321 | 15.317 | 24.133 | 35.214 | 1.00 64.97 | C |

[0953]

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 718 | CB | LYS | A | 321 | 16.718 | -24.370 | -34.612 | 1.00 | 80.34 | C |
| ATOM | 719 | CG | LYS | A | 321 | 17.607 | -25.332 | -35.405 | 1.00 | 75.85 | C |
| ATOM | 720 | CD | LYS | A | 321 | 18.992 | -25.466 | -34.790 | 1.00 | 90.17 | C |
| ATOM | 721 | CE | LYS | A | 321 | 19.656 | -26.769 | -35.243 | 1.00 | 109.74 | C |
| ATOM | 722 | NZ | LYS | A | 321 | 20.940 | -27.111 | -34.545 | 1.00 | 110.75 | N |
| ATOM | 723 | C | LYS | A | 321 | 14.662 | -25.455 | -35.556 | 1.00 | 62.81 | C |
| ATOM | 724 | O | LYS | A | 321 | 14.874 | 25.968 | 36.645 | 1.00 | 68.21 | O |
| ATOM | 725 | N | GLY | A | 322 | 13.869 | -25.991 | -34.621 | 1.00 | 60.22 | N |
| ATOM | 726 | CA | GLY | A | 322 | 13.135 | -27.255 | -34.812 | 1.00 | 52.21 | C |
| ATOM | 727 | C | GLY | A | 322 | 11.868 | -27.108 | -35.622 | 1.00 | 50.83 | C |
| ATOM | 728 | O | GLY | A | 322 | 11.531 | -27.988 | -36.429 | 1.00 | 55.11 | O |
| ATOM | 729 | N | SER | A | 323 | 11.187 | -25.977 | -35.451 | 1.00 | 48.32 | N |
| ATOM | 730 | CA | SER | A | 323 | 9.925 | -25.725 | -36.150 | 1.00 | 47.38 | C |
| ATOM | 731 | CB | SER | A | 323 | 9.050 | -24.764 | -35.375 | 1.00 | 47.62 | C |
| ATOM | 732 | OG | SER | A | 323 | 9.558 | -24.504 | -34.092 | 1.00 | 61.38 | O |
| ATOM | 733 | C | SER | A | 323 | 10.053 | -25.189 | -37.581 | 1.00 | 49.65 | C |
| ATOM | 734 | O | SER | A | 323 | 9.205 | -25.521 | -38.420 | 1.00 | 51.45 | O |
| ATOM | 735 | N | ALA | A | 324 | 11.073 | 24.370 | 37.872 | 1.00 | 46.07 | N |
| ATOM | 736 | CA | ALA | A | 324 | 11.127 | 23.634 | 39.166 | 1.00 | 46.31 | C |
| ATOM | 737 | CB | ALA | A | 324 | 12.506 | -23.010 | -39.405 | 1.00 | 42.02 | C |
| ATOM | 738 | C | ALA | A | 324 | 10.677 | -24.441 | -40.405 | 1.00 | 44.46 | C |
| ATOM | 739 | O | ALA | A | 324 | 9.881 | -23.995 | -41.227 | 1.00 | 42.56 | O |
| ATOM | 740 | N | VAL | A | 325 | 11.205 | -25.636 | -40.556 | 1.00 | 47.80 | N |
| ATOM | 741 | CA | VAL | A | 325 | 10.810 | -26.419 | -41.698 | 1.00 | 48.87 | C |
| ATOM | 742 | CB | VAL | A | 325 | 11.911 | -27.400 | -42.095 | 1.00 | 47.56 | C |
| ATOM | 743 | CG1 | VAL | A | 325 | 11.345 | -28.592 | -42.833 | 1.00 | 61.86 | C |
| ATOM | 744 | CG2 | VAL | A | 325 | 12.913 | -26.684 | -42.984 | 1.00 | 50.22 | C |
| ATOM | 745 | C | VAL | A | 325 | 9.412 | -27.009 | -41.493 | 1.00 | 50.85 | C |
| ATOM | 746 | O | VAL | A | 325 | 8.488 | -26.682 | -42.205 | 1.00 | 53.67 | O |
| ATOM | 747 | N | GLU | A | 326 | 9.229 | 27.853 | 40.496 | 1.00 | 56.64 | N |
| ATOM | 748 | CA | GLU | A | 326 | 7.878 | -28.339 | -40.237 | 1.00 | 53.58 | C |
| ATOM | 749 | CB | GLU | A | 326 | 7.733 | -28.904 | -38.809 | 1.00 | 50.94 | C |
| ATOM | 750 | CG | GLU | A | 326 | 8.804 | -29.939 | -38.467 | 1.00 | 55.81 | C |
| ATOM | 751 | CD | GLU | A | 326 | 8.540 | -30.778 | -37.207 | 1.00 | 61.68 | C |
| ATOM | 752 | OE1 | GLU | A | 326 | 7.453 | -30.657 | -36.600 | 1.00 | 71.26 | O |
| ATOM | 753 | OE2 | GLU | A | 326 | 9.425 | -31.583 | -36.821 | 1.00 | 54.78 | O |
| ATOM | 754 | C | GLU | A | 326 | 6.850 | -27.243 | -40.558 | 1.00 | 47.09 | C |
| ATOM | 755 | O | GLU | A | 326 | 6.023 | -27.425 | -41.446 | 1.00 | 41.35 | O |
| ATOM | 756 | N | ALA | A | 327 | 6.938 | -26.098 | -39.885 | 1.00 | 48.19 | N |
| ATOM | 757 | CA | ALA | A | 327 | 5.874 | -25.061 | -39.968 | 1.00 | 52.80 | C |
| ATOM | 758 | CB | ALA | A | 327 | 6.054 | -24.019 | -38.866 | 1.00 | 51.08 | C |
| ATOM | 759 | C | ALA | A | 327 | 5.690 | 24.382 | 41.358 | 1.00 | 48.67 | C |
| ATOM | 760 | O | ALA | A | 327 | 4.658 | -23.800 | -41.667 | 1.00 | 49.66 | O |
| ATOM | 761 | N | MET | A | 328 | 6.706 | -24.447 | -42.183 | 1.00 | 47.36 | N |
| ATOM | 762 | CA | MET | A | 328 | 6.573 | -24.026 | -43.554 | 1.00 | 50.68 | C |
| ATOM | 763 | CB | MET | A | 328 | 7.967 | -23.787 | -44.146 | 1.00 | 54.59 | C |

[0999]

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 764 | CG | MET | A | 328 | 8.074 | -23.785 | -45.660 | 1.00 59.86 | C |
| ATOM | 765 | SD | MET | A | 328 | 9.781 | -23.343 | -46.062 | 1.00 77.23 | S |
| ATOM | 766 | CE | MET | A | 328 | 10.432 | -24.944 | -46.515 | 1.00 64.46 | C |
| ATOM | 767 | C | MET | A | 328 | 5.780 | -25.064 | -44.344 | 1.00 51.40 | C |
| ATOM | 768 | O | MET | A | 328 | 4.924 | -24.689 | -45.125 | 1.00 55.19 | O |
| ATOM | 769 | N | PHE | A | 329 | 6.049 | 26.358 | 44.136 | 1.00 54.63 | N |
| ATOM | 770 | CA | PHE | A | 329 | 5.265 | -27.446 | -44.770 | 1.00 56.60 | C |
| ATOM | 771 | CB | PHE | A | 329 | 5.824 | -28.807 | -44.399 | 1.00 52.94 | C |
| ATOM | 772 | CG | PHE | A | 329 | 6.943 | -29.217 | -45.274 | 1.00 59.50 | C |
| ATOM | 773 | CD1 | PHE | A | 329 | 6.842 | -30.346 | -46.060 | 1.00 59.15 | C |
| ATOM | 774 | CE1 | PHE | A | 329 | 7.871 | -30.694 | -46.903 | 1.00 71.77 | C |
| ATOM | 775 | CZ | PHE | A | 329 | 9.017 | -29.893 | -46.991 | 1.00 75.62 | C |
| ATOM | 776 | CE2 | PHE | A | 329 | 9.125 | -28.755 | -46.225 | 1.00 67.35 | C |
| ATOM | 777 | CD2 | PHE | A | 329 | 8.085 | -28.417 | -45.372 | 1.00 65.39 | C |
| ATOM | 778 | C | PHE | A | 329 | 3.789 | -27.370 | -44.442 | 1.00 59.10 | C |
| ATOM | 779 | O | PHE | A | 329 | 2.932 | -27.664 | -45.264 | 1.00 63.93 | O |
| ATOM | 780 | N | LEU | A | 330 | 3.510 | -26.926 | -43.235 | 1.00 56.91 | N |
| ATOM | 781 | CA | LEU | A | 330 | 2.171 | -26.765 | -42.788 | 1.00 56.48 | C |
| ATOM | 782 | CB | LEU | A | 330 | 2.227 | 26.638 | 41.276 | 1.00 56.95 | C |
| ATOM | 783 | CG | LEU | A | 330 | 1.002 | -27.135 | -40.546 | 1.00 56.77 | C |
| ATOM | 784 | CD1 | LEU | A | 330 | 0.548 | -28.475 | -41.126 | 1.00 51.23 | C |
| ATOM | 785 | CD2 | LEU | A | 330 | 1.394 | -27.209 | -39.078 | 1.00 56.46 | C |
| ATOM | 786 | C | LEU | A | 330 | 1.479 | -25.549 | -43.434 | 1.00 54.93 | C |
| ATOM | 787 | O | LEU | A | 330 | 0.285 | -25.575 | -43.708 | 1.00 54.41 | O |
| ATOM | 788 | N | ARG | A | 331 | 2.230 | -24.477 | -43.650 | 1.00 59.45 | N |
| ATOM | 789 | CA | ARG | A | 331 | 1.710 | -23.299 | -44.316 | 1.00 59.74 | C |
| ATOM | 790 | CB | ARG | A | 331 | 2.755 | -22.198 | -44.350 | 1.00 63.71 | C |
| ATOM | 791 | CG | ARG | A | 331 | 2.153 | -20.821 | -44.556 | 1.00 71.31 | C |
| ATOM | 792 | CD | ARG | A | 331 | 2.078 | -20.077 | -43.229 | 1.00 71.87 | C |
| ATOM | 793 | NE | ARG | A | 331 | 0.747 | -19.532 | -43.008 | 1.00 68.91 | N |
| ATOM | 794 | CZ | ARG | A | 331 | 0.394 | -18.779 | -41.964 | 1.00 73.36 | C |
| ATOM | 795 | NH1 | ARG | A | 331 | 1.278 | 18.465 | 41.022 | 1.00 67.47 | N |
| ATOM | 796 | NH2 | ARG | A | 331 | -0.862 | -18.330 | -41.865 | 1.00 76.61 | N |
| ATOM | 797 | C | ARG | A | 331 | 1.368 | -23.671 | -45.746 | 1.00 62.02 | C |
| ATOM | 798 | O | ARG | A | 331 | 0.323 | -23.262 | -46.288 | 1.00 64.71 | O |
| ATOM | 799 | N | SER | A | 332 | 2.254 | -24.444 | -46.361 | 1.00 53.41 | N |
| ATOM | 800 | CA | SER | A | 332 | 2.112 | 24.713 | 47.764 | 1.00 59.33 | C |
| ATOM | 801 | CB | SER | A | 332 | 3.216 | -25.630 | -48.250 | 1.00 65.17 | C |
| ATOM | 802 | OG | SER | A | 332 | 4.452 | -25.278 | -47.679 | 1.00 69.68 | O |
| ATOM | 803 | C | SER | A | 332 | 0.814 | -25.429 | -47.901 | 1.00 57.30 | C |
| ATOM | 804 | O | SER | A | 332 | -0.005 | -25.111 | -48.747 | 1.00 54.74 | O |
| ATOM | 805 | N | ALA | A | 333 | 0.638 | -26.399 | -47.020 | 1.00 63.13 | N |
| ATOM | 806 | CA | ALA | A | 333 | -0.484 | -27.297 | -47.075 | 1.00 61.51 | C |
| ATOM | 807 | CB | ALA | A | 333 | -0.357 | -28.335 | -45.969 | 1.00 62.00 | C |
| ATOM | 808 | C | ALA | A | 333 | 1.806 | 26.514 | 47.002 | 1.00 60.01 | C |
| ATOM | 809 | O | ALA | A | 333 | -2.690 | -26.756 | -47.802 | 1.00 60.51 | O |

[1045]

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 810 | N | GLU | A | 334 | -1.921 | -25.562 | -46.075 | 1.00 | 62.61 | N |
| ATOM | 811 | CA | GLU | A | 334 | -3.060 | -24.633 | -46.045 | 1.00 | 66.75 | C |
| ATOM | 812 | CB | GLU | A | 334 | -2.861 | -23.574 | -44.949 | 1.00 | 66.73 | C |
| ATOM | 813 | CG | GLU | A | 334 | -3.982 | -22.541 | -44.830 | 1.00 | 73.35 | C |
| ATOM | 814 | CD | GLU | A | 334 | -3.878 | -21.695 | -43.567 | 1.00 | 84.01 | C |
| ATOM | 815 | OE1 | GLU | A | 334 | -2.802 | -21.681 | -42.930 | 1.00 | 94.13 | O |
| ATOM | 816 | OE2 | GLU | A | 334 | -4.866 | -21.036 | -43.194 | 1.00 | 82.24 | O |
| ATOM | 817 | C | GLU | A | 334 | -3.274 | -23.968 | -47.430 | 1.00 | 69.28 | C |
| ATOM | 818 | O | GLU | A | 334 | -4.357 | -24.081 | -48.021 | 1.00 | 59.62 | O |
| ATOM | 819 | N | ILE | A | 335 | -2.248 | -23.293 | -47.952 | 1.00 | 62.70 | N |
| ATOM | 820 | CA | ILE | A | 335 | -2.352 | -22.729 | -49.292 | 1.00 | 67.98 | C |
| ATOM | 821 | CB | ILE | A | 335 | -1.025 | -22.056 | -49.744 | 1.00 | 74.77 | C |
| ATOM | 822 | CG1 | ILE | A | 335 | -0.700 | -20.870 | -48.829 | 1.00 | 67.09 | C |
| ATOM | 823 | CD1 | ILE | A | 335 | -1.919 | -20.039 | -48.504 | 1.00 | 58.03 | C |
| ATOM | 824 | CG2 | ILE | A | 335 | -1.070 | -21.638 | -51.220 | 1.00 | 68.45 | C |
| ATOM | 825 | C | ILE | A | 335 | -2.875 | -23.773 | -50.296 | 1.00 | 68.48 | C |
| ATOM | 826 | O | ILE | A | 335 | 4.069 | 23.746 | 50.616 | 1.00 | 70.77 | O |
| ATOM | 827 | N | PHE | A | 336 | -1.996 | -24.685 | -50.742 | 1.00 | 66.07 | N |
| ATOM | 828 | CA | PHE | A | 336 | 2.296 | 25.856 | 51.636 | 1.00 | 70.37 | C |
| ATOM | 829 | CB | PHE | A | 336 | -1.266 | -26.971 | -51.364 | 1.00 | 73.56 | C |
| ATOM | 830 | CG | PHE | A | 336 | 1.267 | 28.133 | 52.347 | 1.00 | 83.32 | C |
| ATOM | 831 | CD1 | PHE | A | 336 | -0.289 | -28.228 | -53.331 | 1.00 | 85.23 | C |
| ATOM | 832 | CE1 | PHE | A | 336 | -0.260 | -29.325 | -54.202 | 1.00 | 86.89 | C |
| ATOM | 833 | CZ | PHE | A | 336 | -1.188 | -30.358 | -54.075 | 1.00 | 85.97 | C |
| ATOM | 834 | CE2 | PHE | A | 336 | -2.152 | -30.306 | -53.079 | 1.00 | 78.88 | C |
| ATOM | 835 | CD2 | PHE | A | 336 | -2.177 | -29.210 | -52.212 | 1.00 | 93.50 | C |
| ATOM | 836 | C | PHE | A | 336 | -3.742 | -26.403 | -51.661 | 1.00 | 73.69 | C |
| ATOM | 837 | O | PHE | A | 336 | -4.162 | -26.922 | -52.692 | 1.00 | 82.48 | O |
| ATOM | 838 | N | ASN | A | 337 | -4.498 | -26.286 | -50.567 | 1.00 | 72.78 | N |
| ATOM | 839 | CA | ASN | A | 337 | -5.924 | -26.658 | -50.580 | 1.00 | 82.91 | C |
| ATOM | 840 | CB | ASN | A | 337 | -6.135 | -28.099 | -50.089 | 1.00 | 85.87 | C |
| ATOM | 841 | CG | ASN | A | 337 | -5.188 | -28.485 | -48.978 | 1.00 | 80.60 | C |
| ATOM | 842 | OD1 | ASN | A | 337 | -4.661 | -29.593 | -48.960 | 1.00 | 85.60 | O |
| ATOM | 843 | ND2 | ASN | A | 337 | -4.984 | -27.587 | -48.033 | 1.00 | 96.17 | N |
| ATOM | 844 | C | ASN | A | 337 | -6.970 | -25.731 | -49.920 | 1.00 | 89.01 | C |
| ATOM | 845 | O | ASN | A | 337 | -8.174 | -25.922 | -50.127 | 1.00 | 90.54 | O |
| ATOM | 846 | N | LYS | A | 338 | -6.534 | -24.759 | -49.119 | 1.00 | 93.60 | N |
| ATOM | 847 | CA | LYS | A | 338 | 7.475 | 23.778 | 48.562 | 1.00 | 91.06 | C |
| ATOM | 848 | CB | LYS | A | 338 | -7.135 | -23.375 | -47.120 | 1.00 | 80.07 | C |
| ATOM | 849 | C | LYS | A | 338 | 7.520 | 22.574 | 49.489 | 1.00 | 92.41 | C |
| ATOM | 850 | O | LYS | A | 338 | -8.576 | -22.277 | -50.045 | 1.00 | 92.60 | O |
| ATOM | 851 | N | LYS | A | 339 | -6.381 | -21.897 | -49.664 | 1.00 | 91.02 | N |
| ATOM | 852 | CA | LYS | A | 339 | -6.241 | -20.891 | -50.713 | 1.00 | 100.48 | C |
| ATOM | 853 | CB | LYS | A | 339 | -4.898 | -20.168 | -50.571 | 1.00 | 109.14 | C |
| ATOM | 854 | CG | LYS | A | 339 | -4.796 | -18.797 | -51.247 | 1.00 | 120.94 | C |
| ATOM | 855 | CD | LYS | A | 339 | -3.999 | -18.876 | -52.552 | 1.00 | 133.47 | C |

[1091]

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 856 | CE | LYS | A | 339 | -3.153 | -17.622 | -52.813 | 1.00 | 139.65 | C |
| ATOM | 857 | NZ | LYS | A | 339 | -2.052 | -17.804 | -53.819 | 1.00 | 126.30 | N |
| ATOM | 858 | C | LYS | A | 339 | -6.370 | -21.650 | -52.047 | 1.00 | 96.18 | C |
| ATOM | 859 | O | LYS | A | 339 | -6.694 | -22.843 | -52.026 | 1.00 | 96.13 | O |
| ATOM | 860 | N | LEU | A | 340 | -6.155 | -20.980 | -53.183 | 1.00 | 83.77 | N |
| ATOM | 861 | CA | LEU | A | 340 | 6.213 | 21.630 | 54.504 | 1.00 | 99.84 | C |
| ATOM | 862 | CB | LEU | A | 340 | -5.086 | -22.673 | -54.630 | 1.00 | 95.45 | C |
| ATOM | 863 | CG | LEU | A | 340 | -5.251 | -24.063 | -55.263 | 1.00 | 86.80 | C |
| ATOM | 864 | CD1 | LEU | A | 340 | -3.878 | -24.682 | -55.445 | 1.00 | 74.75 | C |
| ATOM | 865 | CD2 | LEU | A | 340 | -6.138 | -24.984 | -54.431 | 1.00 | 91.28 | C |
| ATOM | 866 | C | LEU | A | 340 | 7.604 | 22.219 | 54.880 | 1.00 | 122.11 | C |
| ATOM | 867 | O | LEU | A | 340 | -8.332 | -22.714 | -54.000 | 1.00 | 124.19 | O |
| ATOM | 868 | N | PRO | A | 341 | -7.972 | -22.165 | -56.189 | 1.00 | 129.21 | N |
| ATOM | 869 | CA | PRO | A | 341 | -9.256 | -22.681 | -56.699 | 1.00 | 123.39 | C |
| ATOM | 870 | CB | PRO | A | 341 | -9.156 | -22.440 | -58.209 | 1.00 | 116.59 | C |
| ATOM | 871 | CG | PRO | A | 341 | -8.243 | -21.277 | -58.334 | 1.00 | 120.32 | C |
| ATOM | 872 | CD | PRO | A | 341 | -7.223 | -21.459 | -57.249 | 1.00 | 122.04 | C |
| ATOM | 873 | C | PRO | A | 341 | -9.490 | -24.164 | -56.402 | 1.00 | 126.17 | C |
| ATOM | 874 | O | PRO | A | 341 | -9.887 | -24.505 | -55.285 | 1.00 | 119.75 | O |
| ATOM | 875 | N | SER | A | 342 | -9.249 | -25.027 | -57.392 | 1.00 | 139.18 | N |
| ATOM | 876 | CA | SER | A | 342 | -9.495 | -26.468 | -57.249 | 1.00 | 144.09 | C |
| ATOM | 877 | CB | SER | A | 342 | -10.695 | -26.899 | -58.106 | 1.00 | 136.31 | C |
| ATOM | 878 | OG | SER | A | 342 | -11.188 | -28.169 | -57.695 | 1.00 | 136.81 | O |
| ATOM | 879 | C | SER | A | 342 | 8.264 | 27.361 | 57.523 | 1.00 | 144.85 | C |
| ATOM | 880 | O | SER | A | 342 | -8.282 | -28.198 | -58.433 | 1.00 | 145.23 | O |
| ATOM | 881 | N | GLY | A | 343 | -7.201 | -27.148 | -56.738 | 1.00 | 145.23 | N |
| ATOM | 882 | CA | GLY | A | 343 | -6.060 | -28.077 | -56.605 | 1.00 | 138.81 | C |
| ATOM | 883 | C | GLY | A | 343 | -5.120 | -28.315 | -57.778 | 1.00 | 142.49 | C |
| ATOM | 884 | O | GLY | A | 343 | -4.456 | -27.391 | -58.258 | 1.00 | 142.71 | O |
| ATOM | 885 | N | HIS | A | 344 | -5.075 | -29.575 | -58.216 | 1.00 | 143.40 | N |
| ATOM | 886 | CA | HIS | A | 344 | -4.155 | -30.083 | -59.250 | 1.00 | 141.02 | C |
| ATOM | 887 | CB | HIS | A | 344 | -4.699 | -31.379 | -59.866 | 1.00 | 133.69 | C |
| ATOM | 888 | CG | HIS | A | 344 | -6.106 | -31.262 | -60.411 | 1.00 | 131.68 | C |
| ATOM | 889 | ND1 | HIS | A | 344 | -6.364 | -31.153 | -61.729 | 1.00 | 130.33 | N |
| ATOM | 890 | CE1 | HIS | A | 344 | -7.696 | -31.074 | -61.922 | 1.00 | 130.19 | C |
| ATOM | 891 | NE2 | HIS | A | 344 | -8.295 | -31.134 | -60.721 | 1.00 | 137.10 | N |
| ATOM | 892 | CD2 | HIS | A | 344 | 7.343 | 31.253 | 59.765 | 1.00 | 130.93 | C |
| ATOM | 893 | C | HIS | A | 344 | -3.704 | -29.108 | -60.326 | 1.00 | 145.45 | C |
| ATOM | 894 | O | HIS | A | 344 | -4.452 | -28.807 | -61.255 | 1.00 | 157.91 | O |
| ATOM | 895 | N | SER | A | 345 | -2.472 | -28.604 | -60.221 | 1.00 | 134.15 | N |
| ATOM | 896 | CA | SER | A | 345 | -1.552 | -28.895 | -59.112 | 1.00 | 137.25 | C |
| ATOM | 897 | CB | SER | A | 345 | -1.286 | -30.411 | -58.957 | 1.00 | 141.52 | C |
| ATOM | 898 | OG | SER | A | 345 | -0.741 | -30.969 | -60.144 | 1.00 | 144.70 | O |
| ATOM | 899 | C | SER | A | 345 | -0.230 | -28.144 | -59.305 | 1.00 | 124.13 | C |
| ATOM | 900 | O | SER | A | 345 | 0.857 | -28.719 | -59.142 | 1.00 | 101.11 | O |
| ATOM | 901 | N | ASP | A | 346 | -0.328 | -26.864 | -59.663 | 1.00 | 106.09 | N |

[1137]

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| ATOM | 902 | CA | ASP | A | 346 | 0.849 | -26.015 | -59.820 | 1.00 | 102.92 | C |
| ATOM | 903 | CB | ASP | A | 346 | 1.392 | -25.598 | -58.447 | 1.00 | 97.96 | C |
| ATOM | 904 | CG | ASP | A | 346 | 0.323 | -24.950 | -57.567 | 1.00 | 90.88 | C |
| ATOM | 905 | OD1 | ASP | A | 346 | -0.730 | -24.581 | -58.112 | 1.00 | 92.13 | O |
| ATOM | 906 | OD2 | ASP | A | 346 | 0.520 | 24.814 | 56.337 | 1.00 | 85.92 | O |
| ATOM | 907 | C | ASP | A | 346 | 1.910 | -26.697 | -60.698 | 1.00 | 106.08 | C |
| ATOM | 908 | O | ASP | A | 346 | 2.592 | -26.040 | -61.505 | 1.00 | 110.93 | O |
| ATOM | 909 | N | LEU | A | 347 | 2.032 | -28.015 | -60.520 | 1.00 | 99.50 | N |
| ATOM | 910 | CA | LEU | A | 347 | 2.561 | -28.940 | -61.537 | 1.00 | 107.46 | C |
| ATOM | 911 | CB | LEU | A | 347 | 1.412 | -29.437 | -62.440 | 1.00 | 101.24 | C |
| ATOM | 912 | CG | LEU | A | 347 | 0.243 | -28.482 | -62.750 | 1.00 | 104.48 | C |
| ATOM | 913 | CD1 | LEU | A | 347 | 0.549 | -27.515 | -63.893 | 1.00 | 96.33 | C |
| ATOM | 914 | CD2 | LEU | A | 347 | -1.032 | -29.267 | -63.021 | 1.00 | 107.17 | C |
| ATOM | 915 | C | LEU | A | 347 | 3.713 | -28.396 | -62.379 | 1.00 | 107.53 | C |
| ATOM | 916 | O | LEU | A | 347 | 3.880 | -28.773 | -63.542 | 1.00 | 91.70 | O |
| ATOM | 917 | N | LEU | A | 348 | 4.502 | -27.513 | -61.772 | 1.00 | 108.64 | N |
| ATOM | 918 | CA | LEU | A | 348 | 5.669 | -26.925 | -62.411 | 1.00 | 112.26 | C |
| ATOM | 919 | CB | LEU | A | 348 | 6.278 | -25.869 | -61.486 | 1.00 | 110.90 | C |
| ATOM | 920 | CG | LEU | A | 348 | 7.049 | 26.305 | 60.216 | 1.00 | 113.90 | C |
| ATOM | 921 | CD1 | LEU | A | 348 | 6.334 | -27.364 | -59.361 | 1.00 | 103.95 | C |
| ATOM | 922 | CD2 | LEU | A | 348 | 8.485 | -26.728 | -60.534 | 1.00 | 97.57 | C |
| ATOM | 923 | C | LEU | A | 348 | 6.742 | -27.964 | -62.762 | 1.00 | 117.26 | C |
| ATOM | 924 | O | LEU | A | 348 | 7.511 | -27.749 | -63.685 | 1.00 | 109.91 | O |
| ATOM | 925 | N | GLU | A | 349 | 6.763 | 29.080 | 62.025 | 1.00 | 123.79 | N |
| ATOM | 926 | CA | GLU | A | 349 | 7.914 | -30.007 | -61.921 | 1.00 | 119.63 | C |
| ATOM | 927 | CB | GLU | A | 349 | 7.476 | -31.431 | -61.631 | 1.00 | 110.22 | C |
| ATOM | 928 | CG | GLU | A | 349 | 6.190 | -31.552 | -60.859 | 1.00 | 104.40 | C |
| ATOM | 929 | CD | GLU | A | 349 | 5.606 | -32.923 | -61.030 | 1.00 | 103.59 | C |
| ATOM | 930 | OE1 | GLU | A | 349 | 4.365 | -33.029 | -61.109 | 1.00 | 100.55 | O |
| ATOM | 931 | OE2 | GLU | A | 349 | 6.402 | -33.889 | -61.108 | 1.00 | 107.55 | O |
| ATOM | 932 | C | GLU | A | 349 | 8.852 | -30.063 | -63.097 | 1.00 | 121.05 | C |
| ATOM | 933 | O | GLU | A | 349 | 10.054 | -30.243 | -62.911 | 1.00 | 125.00 | O |
| ATOM | 934 | N | GLU | A | 350 | 8.295 | -29.956 | -64.302 | 1.00 | 125.72 | N |
| ATOM | 935 | CA | GLU | A | 350 | 9.092 | -29.788 | -65.523 | 1.00 | 130.12 | C |
| ATOM | 936 | CB | GLU | A | 350 | 8.204 | -29.858 | -66.776 | 1.00 | 120.02 | C |
| ATOM | 937 | CG | GLU | A | 350 | 6.892 | -29.092 | -66.676 | 1.00 | 116.65 | C |
| ATOM | 938 | CD | GLU | A | 350 | 5.684 | -29.941 | -67.039 | 1.00 | 124.47 | C |
| ATOM | 939 | OE1 | GLU | A | 350 | 5.538 | 31.068 | 66.491 | 1.00 | 122.57 | O |
| ATOM | 940 | OE2 | GLU | A | 350 | 4.867 | -29.475 | -67.864 | 1.00 | 118.46 | O |
| ATOM | 941 | C | GLU | A | 350 | 9.869 | -28.470 | -65.433 | 1.00 | 136.14 | C |
| ATOM | 942 | O | GLU | A | 350 | 10.347 | -27.935 | -66.443 | 1.00 | 135.13 | O |
| ATOM | 943 | N | ARG | A | 351 | 9.983 | -27.978 | -64.193 | 1.00 | 139.80 | N |
| ATOM | 944 | CA | ARG | A | 351 | 10.716 | 26.767 | 63.848 | 1.00 | 133.48 | C |
| ATOM | 945 | CB | ARG | A | 351 | 9.780 | -25.547 | -63.861 | 1.00 | 123.93 | C |
| ATOM | 946 | C | ARG | A | 351 | 11.448 | -26.857 | -62.499 | 1.00 | 130.90 | C |
| ATOM | 947 | O | ARG | A | 351 | 12.004 | -25.854 | -62.047 | 1.00 | 133.48 | O |

[1183]

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 948 | N | ILE | A | 352 | 11.468 | -28.029 | -61.857 | 1.00130.23 | N |
| ATOM | 949 | CA | ILE | A | 352 | 12.181 | -28.143 | -60.563 | 1.00140.25 | C |
| ATOM | 950 | CB | ILE | A | 352 | 11.679 | -29.296 | -59.637 | 1.00135.27 | C |
| ATOM | 951 | CG1 | ILE | A | 352 | 12.534 | -30.579 | -59.735 | 1.00133.63 | C |
| ATOM | 952 | CD1 | ILE | A | 352 | 12.260 | -31.484 | -60.922 | 1.00145.05 | C |
| ATOM | 953 | CG2 | ILE | A | 352 | 10.183 | -29.504 | -59.799 | 1.00141.81 | C |
| ATOM | 954 | C | ILE | A | 352 | 13.706 | 28.165 | 60.705 | 1.00143.17 | C |
| ATOM | 955 | O | ILE | A | 352 | 14.279 | -29.076 | -61.316 | 1.00153.89 | O |
| ATOM | 956 | N | ARG | A | 353 | 14.344 | -27.126 | -60.159 | 1.00146.73 | N |
| ATOM | 957 | CA | ARG | A | 353 | 15.803 | -27.023 | -60.126 | 1.00150.03 | C |
| ATOM | 958 | CB | ARG | A | 353 | 16.253 | -25.598 | -60.514 | 1.00138.30 | C |
| ATOM | 959 | CG | ARG | A | 353 | 17.697 | -25.438 | -61.001 | 1.00125.87 | C |
| ATOM | 960 | CD | ARG | A | 353 | 18.158 | -26.530 | -61.967 | 1.00131.21 | C |
| ATOM | 961 | NE | ARG | A | 353 | 19.071 | -27.495 | -61.337 | 1.00127.85 | N |
| ATOM | 962 | CZ | ARG | A | 353 | 19.719 | -28.473 | -61.976 | 1.00122.02 | C |
| ATOM | 963 | NH1 | ARG | A | 353 | 19.572 | -28.654 | -63.286 | 1.00126.04 | N |
| ATOM | 964 | NH2 | ARG | A | 353 | 20.526 | -29.276 | -61.301 | 1.00110.49 | N |
| ATOM | 965 | C | ARG | A | 353 | 16.271 | -27.421 | -58.721 | 1.00152.03 | C |
| ATOM | 966 | O | ARG | A | 353 | 15.433 | 27.803 | 57.871 | 1.00154.63 | O |
| ATOM | 967 | N | ASN | A | 354 | 17.594 | -27.367 | -58.490 | 1.00152.81 | N |
| ATOM | 968 | CA | ASN | A | 354 | 18.153 | -27.602 | -57.161 | 1.00139.59 | C |
| ATOM | 969 | CB | ASN | A | 354 | 19.581 | -28.167 | -57.236 | 1.00142.59 | C |
| ATOM | 970 | CG | ASN | A | 354 | 19.612 | -29.655 | -57.555 | 1.00143.59 | C |
| ATOM | 971 | OD1 | ASN | A | 354 | 18.909 | -30.127 | -58.452 | 1.00135.70 | O |
| ATOM | 972 | ND2 | ASN | A | 354 | 20.439 | -30.404 | -56.823 | 1.00139.02 | N |
| ATOM | 973 | C | ASN | A | 354 | 18.096 | -26.330 | -56.320 | 1.00136.02 | C |
| ATOM | 974 | O | ASN | A | 354 | 17.340 | -25.398 | -56.657 | 1.00111.48 | O |
| ATOM | 975 | N | SER | A | 355 | 18.900 | -26.313 | -55.244 | 1.00132.96 | N |
| ATOM | 976 | CA | SER | A | 355 | 18.945 | -25.235 | -54.229 | 1.00123.60 | C |
| ATOM | 977 | CB | SER | A | 355 | 17.589 | 25.082 | 53.528 | 1.00114.25 | C |
| ATOM | 978 | OG | SER | A | 355 | 17.746 | -24.450 | -52.270 | 1.00106.25 | O |
| ATOM | 979 | C | SER | A | 355 | 20.066 | -25.312 | -53.154 | 1.00115.95 | C |
| ATOM | 980 | O | SER | A | 355 | 20.366 | -24.297 | -52.519 | 1.00110.19 | O |
| ATOM | 981 | N | GLY | A | 356 | 20.665 | -26.478 | -52.905 | 1.00113.67 | N |
| ATOM | 982 | CA | GLY | A | 356 | 20.295 | -27.747 | -53.503 | 1.00119.68 | C |
| ATOM | 983 | C | GLY | A | 356 | 18.968 | -28.241 | -52.968 | 1.00117.39 | C |
| ATOM | 984 | O | GLY | A | 356 | 18.816 | -28.467 | -51.765 | 1.00110.81 | O |
| ATOM | 985 | N | ILE | A | 357 | 18.008 | -28.358 | -53.882 | 1.00107.57 | N |
| ATOM | 986 | CA | ILE | A | 357 | 16.685 | -28.898 | -53.628 | 1.00117.36 | C |
| ATOM | 987 | CB | ILE | A | 357 | 15.700 | -27.818 | -53.077 | 1.00111.80 | C |
| ATOM | 988 | CG1 | ILE | A | 357 | 15.872 | -27.645 | -51.552 | 1.00107.36 | C |
| ATOM | 989 | CD1 | ILE | A | 357 | 15.197 | 26.440 | 50.914 | 1.00 82.84 | C |
| ATOM | 990 | CG2 | ILE | A | 357 | 14.251 | -28.169 | -53.400 | 1.00112.35 | C |
| ATOM | 991 | C | ILE | A | 357 | 16.247 | -29.483 | -54.977 | 1.00129.31 | C |
| ATOM | 992 | O | ILE | A | 357 | 16.179 | -28.750 | -55.955 | 1.00 35.23 | O |
| ATOM | 993 | N | SER | A | 358 | 15.987 | -30.795 | -55.036 | 1.00130.11 | N |

[1229]

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 994 | CA | SER | A | 358 | 15.687 | 31.483 | 56.310 | 1.00 120.57 | C |
| ATOM | 995 | CB | SER | A | 358 | 16.666 | -32.637 | -56.555 | 1.00 138.50 | C |
| ATOM | 996 | OG | SER | A | 358 | 17.827 | -32.194 | -57.243 | 1.00 154.78 | O |
| ATOM | 997 | C | SER | A | 358 | 14.232 | -31.932 | -56.520 | 1.00 110.13 | C |
| ATOM | 998 | O | SER | A | 358 | 13.355 | -31.096 | -56.726 | 1.00 109.57 | O |
| ATOM | 999 | N | ALA | A | 359 | 13.994 | -33.248 | -56.485 | 1.00 109.37 | N |
| ATOM | 1000 | CA | ALA | A | 359 | 12.678 | -33.840 | -56.795 | 1.00 103.82 | C |
| ATOM | 1001 | CB | ALA | A | 359 | 12.747 | -34.686 | -58.058 | 1.00 99.74 | C |
| ATOM | 1002 | C | ALA | A | 359 | 12.122 | -34.667 | -55.648 | 1.00 104.08 | C |
| ATOM | 1003 | O | ALA | A | 359 | 10.941 | -35.011 | -55.648 | 1.00 104.63 | O |
| ATOM | 1004 | N | GLU | A | 360 | 12.981 | -34.992 | -54.682 | 1.00 109.76 | N |
| ATOM | 1005 | CA | GLU | A | 360 | 12.566 | 35.650 | 53.434 | 1.00 108.21 | C |
| ATOM | 1006 | CB | GLU | A | 360 | 13.681 | -36.543 | -52.871 | 1.00 127.93 | C |
| ATOM | 1007 | CG | GLU | A | 360 | 15.040 | -35.869 | -52.732 | 1.00 135.98 | C |
| ATOM | 1008 | CD | GLU | A | 360 | 15.837 | -35.907 | -54.024 | 1.00 152.50 | C |
| ATOM | 1009 | OE1 | GLU | A | 360 | 16.214 | -34.812 | -54.518 | 1.00 155.98 | O |
| ATOM | 1010 | OE2 | GLU | A | 360 | 16.074 | -37.031 | -54.555 | 1.00 168.11 | O |
| ATOM | 1011 | C | GLU | A | 360 | 12.142 | -34.631 | -52.383 | 1.00 97.30 | C |
| ATOM | 1012 | O | GLU | A | 360 | 12.044 | -34.947 | -51.204 | 1.00 91.08 | O |
| ATOM | 1013 | N | TYR | A | 361 | 11.929 | -33.400 | -52.830 | 1.00 98.35 | N |
| ATOM | 1014 | CA | TYR | A | 361 | 11.324 | -32.345 | -52.037 | 1.00 92.99 | C |
| ATOM | 1015 | CB | TYR | A | 361 | 12.101 | -31.048 | -52.229 | 1.00 91.01 | C |
| ATOM | 1016 | CG | TYR | A | 361 | 13.369 | 30.939 | 51.415 | 1.00 89.37 | C |
| ATOM | 1017 | CD1 | TYR | A | 361 | 14.607 | -31.246 | -51.969 | 1.00 88.29 | C |
| ATOM | 1018 | CE1 | TYR | A | 361 | 15.783 | -31.140 | -51.230 | 1.00 88.98 | C |
| ATOM | 1019 | CZ | TYR | A | 361 | 15.726 | -30.710 | -49.916 | 1.00 94.54 | C |
| ATOM | 1020 | OH | TYR | A | 361 | 16.880 | -30.610 | -49.171 | 1.00 93.87 | O |
| ATOM | 1021 | CE2 | TYR | A | 361 | 14.505 | -30.388 | -49.345 | 1.00 98.67 | C |
| ATOM | 1022 | CD2 | TYR | A | 361 | 13.336 | -30.502 | -50.093 | 1.00 97.22 | C |
| ATOM | 1023 | C | TYR | A | 361 | 9.872 | -32.156 | -52.505 | 1.00 103.53 | C |
| ATOM | 1024 | O | TYR | A | 361 | 8.973 | -31.804 | -51.706 | 1.00 95.81 | O |
| ATOM | 1025 | N | ILE | A | 362 | 9.671 | -32.392 | -53.810 | 1.00 98.24 | N |
| ATOM | 1026 | CA | ILE | A | 362 | 8.372 | -32.305 | -54.487 | 1.00 82.37 | C |
| ATOM | 1027 | CB | ILE | A | 362 | 8.536 | 32.386 | 56.023 | 1.00 85.79 | C |
| ATOM | 1028 | CG1 | ILE | A | 362 | 8.789 | -30.997 | -56.632 | 1.00 80.82 | C |
| ATOM | 1029 | CD1 | ILE | A | 362 | 10.148 | -30.394 | -56.309 | 1.00 74.96 | C |
| ATOM | 1030 | CG2 | ILE | A | 362 | 7.347 | -33.074 | -56.697 | 1.00 83.00 | C |
| ATOM | 1031 | C | ILE | A | 362 | 7.421 | -33.389 | -54.011 | 1.00 82.56 | C |
| ATOM | 1032 | O | ILE | A | 362 | 6.339 | -33.083 | -53.491 | 1.00 80.16 | O |
| ATOM | 1033 | N | THR | A | 363 | 7.841 | -34.644 | -54.170 | 1.00 76.76 | N |
| ATOM | 1034 | CA | THR | A | 363 | 7.012 | -35.790 | -53.825 | 1.00 76.06 | C |
| ATOM | 1035 | CB | THR | A | 363 | 7.732 | -37.100 | -54.160 | 1.00 77.55 | C |
| ATOM | 1036 | OG1 | THR | A | 363 | 8.015 | -37.124 | -55.569 | 1.00 79.24 | O |
| ATOM | 1037 | CG2 | THR | A | 363 | 6.872 | -38.313 | -53.769 | 1.00 80.03 | C |
| ATOM | 1038 | C | THR | A | 363 | 6.466 | 35.772 | 52.379 | 1.00 81.70 | C |
| ATOM | 1039 | O | THR | A | 363 | 5.247 | -35.854 | -52.199 | 1.00 91.74 | O |

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 1040 | N | PRO | A | 364 | 7.347 | -35.644 | -51.353 | 1.00 | 80.43 | N |
| ATOM | 1041 | CA | PRO | A | 364 | 6.973 | -35.488 | -49.912 | 1.00 | 74.92 | C |
| ATOM | 1042 | CB | PRO | A | 364 | 8.276 | -34.994 | -49.255 | 1.00 | 78.13 | C |
| ATOM | 1043 | CG | PRO | A | 364 | 9.317 | -34.957 | -50.336 | 1.00 | 85.76 | C |
| ATOM | 1044 | CD | PRO | A | 364 | 8.808 | -35.756 | -51.505 | 1.00 | 85.25 | C |
| ATOM | 1045 | C | PRO | A | 364 | 5.850 | -34.487 | -49.617 | 1.00 | 73.29 | C |
| ATOM | 1046 | O | PRO | A | 364 | 4.772 | 34.870 | 49.177 | 1.00 | 69.00 | O |
| ATOM | 1047 | N | MET | A | 365 | 6.139 | -33.212 | -49.861 | 1.00 | 84.65 | N |
| ATOM | 1048 | CA | MET | A | 365 | 5.175 | -32.104 | -49.909 | 1.00 | 88.39 | C |
| ATOM | 1049 | CB | MET | A | 365 | 5.897 | -30.899 | -50.532 | 1.00 | 92.97 | C |
| ATOM | 1050 | CG | MET | A | 365 | 5.034 | 29.751 | 51.037 | 1.00 | 93.89 | C |
| ATOM | 1051 | SD | MET | A | 365 | 4.127 | -28.946 | -49.721 | 1.00 | 103.94 | S |
| ATOM | 1052 | CE | MET | A | 365 | 5.482 | -28.425 | -48.662 | 1.00 | 97.87 | C |
| ATOM | 1053 | C | MET | A | 365 | 3.833 | -32.397 | -50.633 | 1.00 | 89.73 | C |
| ATOM | 1054 | O | MET | A | 365 | 2.819 | -31.709 | -50.395 | 1.00 | 85.51 | O |
| ATOM | 1055 | N | PHE | A | 366 | 3.821 | -33.417 | -51.495 | 1.00 | 88.21 | N |
| ATOM | 1056 | CA | PHE | A | 366 | 2.597 | -33.808 | -52.212 | 1.00 | 86.77 | C |
| ATOM | 1057 | CB | PHE | A | 366 | 2.906 | -34.372 | -53.599 | 1.00 | 90.71 | C |
| ATOM | 1058 | CG | PHE | A | 366 | 2.931 | -33.325 | -54.667 | 1.00 | 96.60 | C |
| ATOM | 1059 | CD1 | PHE | A | 366 | 1.853 | -32.464 | -54.831 | 1.00 | 90.84 | C |
| ATOM | 1060 | CE1 | PHE | A | 366 | 1.883 | -31.489 | -55.808 | 1.00 | 93.74 | C |
| ATOM | 1061 | CZ | PHE | A | 366 | 2.987 | -31.366 | -56.640 | 1.00 | 92.51 | C |
| ATOM | 1062 | CE2 | PHE | A | 366 | 4.063 | -32.217 | -56.492 | 1.00 | 88.85 | C |
| ATOM | 1063 | CD2 | PHE | A | 366 | 4.036 | -33.187 | -55.504 | 1.00 | 97.23 | C |
| ATOM | 1064 | C | PHE | A | 366 | 1.704 | -34.768 | -51.458 | 1.00 | 75.40 | C |
| ATOM | 1065 | O | PHE | A | 366 | 0.526 | 34.485 | 51.230 | 1.00 | 64.93 | O |
| ATOM | 1066 | N | SER | A | 367 | 2.262 | -35.917 | -51.107 | 1.00 | 73.43 | N |
| ATOM | 1067 | CA | SER | A | 367 | 1.558 | -36.874 | -50.273 | 1.00 | 73.75 | C |
| ATOM | 1068 | CB | SER | A | 367 | 2.481 | -38.002 | -49.827 | 1.00 | 72.74 | C |
| ATOM | 1069 | OG | SER | A | 367 | 3.840 | 37.578 | 49.801 | 1.00 | 77.50 | O |
| ATOM | 1070 | C | SER | A | 367 | 1.032 | -36.141 | -49.063 | 1.00 | 73.43 | C |
| ATOM | 1071 | O | SER | A | 367 | -0.123 | -36.332 | -48.649 | 1.00 | 74.91 | O |
| ATOM | 1072 | N | PHE | A | 368 | 1.866 | -35.262 | -48.522 | 1.00 | 66.23 | N |
| ATOM | 1073 | CA | PHE | A | 368 | 1.486 | -34.583 | -47.319 | 1.00 | 65.18 | C |
| ATOM | 1074 | CB | PHE | A | 368 | 2.628 | -33.757 | -46.767 | 1.00 | 62.36 | C |
| ATOM | 1075 | CG | PHE | A | 368 | 2.285 | -33.087 | -45.482 | 1.00 | 58.53 | C |
| ATOM | 1076 | CD1 | PHE | A | 368 | 1.981 | -33.844 | -44.354 | 1.00 | 56.95 | C |
| ATOM | 1077 | CE1 | PHE | A | 368 | 1.635 | -33.225 | -43.159 | 1.00 | 55.86 | C |
| ATOM | 1078 | CZ | PHE | A | 368 | 1.592 | -31.845 | -43.096 | 1.00 | 55.02 | C |
| ATOM | 1079 | CE2 | PHE | A | 368 | 1.886 | -31.091 | -44.222 | 1.00 | 52.14 | C |
| ATOM | 1080 | CD2 | PHE | A | 368 | 2.217 | -31.708 | -45.405 | 1.00 | 52.50 | C |
| ATOM | 1081 | C | PHE | A | 368 | 0.250 | -33.716 | -47.535 | 1.00 | 71.37 | C |
| ATOM | 1082 | O | PHE | A | 368 | -0.774 | -33.916 | -46.863 | 1.00 | 68.60 | O |
| ATOM | 1083 | N | ALA | A | 369 | 0.347 | -32.774 | -48.479 | 1.00 | 70.98 | N |
| ATOM | 1084 | CA | ALA | A | 369 | 0.763 | 31.874 | 48.805 | 1.00 | 70.24 | C |
| ATOM | 1085 | CB | ALA | A | 369 | -0.412 | -31.050 | -50.028 | 1.00 | 72.65 | C |

[1321]

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 1086 | C | ALA A 369 | -2.115 | -32.605 | -48.989 | 1.00 | 66.31 | C |
| ATOM | 1087 | O | ALA A 369 | -3.079 | -32.359 | -48.254 | 1.00 | 63.23 | O |
| ATOM | 1088 | N | LYS A 370 | -2.154 | -33.518 | -49.951 | 1.00 | 61.44 | N |
| ATOM | 1089 | CA | LYS A 370 | 3.300 | 34.375 | 50.201 | 1.00 | 62.54 | C |
| ATOM | 1090 | CB | LYS A 370 | -2.912 | -35.366 | -51.311 | 1.00 | 67.66 | C |
| ATOM | 1091 | CG | LYS A 370 | -4.032 | -36.216 | -51.913 | 1.00 | 72.21 | C |
| ATOM | 1092 | CD | LYS A 370 | -4.388 | -37.412 | -51.028 | 1.00 | 71.57 | C |
| ATOM | 1093 | CE | LYS A 370 | -5.296 | -38.412 | -51.715 | 1.00 | 68.99 | C |
| ATOM | 1094 | NZ | LYS A 370 | -6.683 | -37.902 | -51.895 | 1.00 | 71.58 | N |
| ATOM | 1095 | C | LYS A 370 | -3.822 | -35.090 | -48.924 | 1.00 | 66.68 | C |
| ATOM | 1096 | O | LYS A 370 | 5.030 | 35.308 | 48.779 | 1.00 | 59.74 | O |
| ATOM | 1097 | N | SER A 371 | -2.930 | -35.454 | -47.999 | 1.00 | 69.86 | N |
| ATOM | 1098 | CA | SER A 371 | -3.378 | -36.051 | -46.731 | 1.00 | 68.12 | C |
| ATOM | 1099 | CB | SER A 371 | -2.270 | -36.840 | -46.054 | 1.00 | 71.30 | C |
| ATOM | 1100 | OG | SER A 371 | -1.704 | -37.769 | -46.950 | 1.00 | 87.23 | O |
| ATOM | 1101 | C | SER A 371 | -3.946 | -35.048 | -45.737 | 1.00 | 72.47 | C |
| ATOM | 1102 | O | SER A 371 | -4.796 | -35.403 | -44.929 | 1.00 | 76.17 | O |
| ATOM | 1103 | N | ILE A 372 | -3.453 | -33.812 | -45.763 | 1.00 | 73.44 | N |
| ATOM | 1104 | CA | ILE A 372 | -3.971 | -32.775 | -44.880 | 1.00 | 67.91 | C |
| ATOM | 1105 | CB | ILE A 372 | 2.946 | 31.618 | 44.674 | 1.00 | 68.64 | C |
| ATOM | 1106 | CG1 | ILE A 372 | -2.754 | -31.305 | -43.191 | 1.00 | 64.31 | C |
| ATOM | 1107 | CD1 | ILE A 372 | -1.917 | -32.328 | -42.464 | 1.00 | 63.49 | C |
| ATOM | 1108 | CG2 | ILE A 372 | -3.352 | -30.344 | -45.414 | 1.00 | 70.98 | C |
| ATOM | 1109 | C | ILE A 372 | -5.306 | -32.270 | -45.449 | 1.00 | 72.11 | C |
| ATOM | 1110 | O | ILE A 372 | -6.242 | -31.964 | -44.696 | 1.00 | 71.84 | O |
| ATOM | 1111 | N | GLY A 373 | -5.386 | -32.181 | -46.779 | 1.00 | 69.44 | N |
| ATOM | 1112 | CA | GLY A 373 | -6.621 | -31.788 | -47.447 | 1.00 | 67.40 | C |
| ATOM | 1113 | C | GLY A 373 | -7.701 | -32.790 | -47.102 | 1.00 | 66.76 | C |
| ATOM | 1114 | O | GLY A 373 | -8.797 | -32.443 | -46.657 | 1.00 | 66.85 | O |
| ATOM | 1115 | N | GLU A 374 | -7.350 | -34.055 | -47.256 | 1.00 | 69.53 | N |
| ATOM | 1116 | CA | GLU A 374 | -8.238 | -35.146 | -46.928 | 1.00 | 73.06 | C |
| ATOM | 1117 | CB | GLU A 374 | -7.481 | -36.475 | -47.014 | 1.00 | 82.42 | C |
| ATOM | 1118 | CG | GLU A 374 | -8.356 | -37.689 | -47.287 | 1.00 | 100.77 | C |
| ATOM | 1119 | CD | GLU A 374 | -7.854 | -38.946 | -46.586 | 1.00 | 115.64 | C |
| ATOM | 1120 | OE1 | GLU A 374 | -8.628 | -39.540 | -45.791 | 1.00 | 111.23 | O |
| ATOM | 1121 | OE2 | GLU A 374 | 6.685 | 39.338 | 46.821 | 1.00 | 125.97 | O |
| ATOM | 1122 | C | GLU A 374 | -8.814 | -34.965 | -45.540 | 1.00 | 72.67 | C |
| ATOM | 1123 | O | GLU A 374 | -9.812 | -35.567 | -45.215 | 1.00 | 81.77 | O |
| ATOM | 1124 | N | LEU A 375 | -8.175 | -34.146 | -44.710 | 1.00 | 80.11 | N |
| ATOM | 1125 | CA | LEU A 375 | -8.648 | -33.936 | -43.351 | 1.00 | 72.20 | C |
| ATOM | 1126 | CB | LEU A 375 | -7.504 | -33.611 | -42.390 | 1.00 | 70.01 | C |
| ATOM | 1127 | CG | LEU A 375 | -6.680 | -34.773 | -41.813 | 1.00 | 70.41 | C |
| ATOM | 1128 | CD1 | LEU A 375 | -5.608 | -34.283 | -40.859 | 1.00 | 63.13 | C |
| ATOM | 1129 | CD2 | LEU A 375 | -7.554 | -35.777 | -41.087 | 1.00 | 69.19 | C |
| ATOM | 1130 | C | LEU A 375 | 9.676 | 32.841 | 43.305 | 1.00 | 75.31 | C |
| ATOM | 1131 | O | LEU A 375 | -10.358 | -32.694 | -42.303 | 1.00 | 83.28 | O |

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 1132 | N | LYS | A | 376 | -9.802 | -32.065 | -44.373 | 1.00 70.79 | N |
| ATOM | 1133 | CA | LYS | A | 376 | -10.815 | -31.038 | -44.374 | 1.00 79.70 | C |
| ATOM | 1134 | CB | LYS | A | 376 | -12.202 | -31.668 | -44.602 | 1.00 87.06 | C |
| ATOM | 1135 | CG | LYS | A | 376 | -12.591 | -31.822 | -46.069 | 1.00 96.72 | C |
| ATOM | 1136 | CD | LYS | A | 376 | -13.487 | -33.035 | -46.292 | 1.00100.56 | C |
| ATOM | 1137 | CE | LYS | A | 376 | 13.435 | 33.534 | 47.739 | 1.00106.56 | C |
| ATOM | 1138 | NZ | LYS | A | 376 | -14.322 | -32.797 | -48.693 | 1.00108.43 | N |
| ATOM | 1139 | C | LYS | A | 376 | -10.757 | -30.280 | -43.034 | 1.00 79.43 | C |
| ATOM | 1140 | O | LYS | A | 376 | -11.715 | -30.277 | -42.262 | 1.00 80.05 | O |
| ATOM | 1141 | N | MET | A | 377 | -9.617 | -29.655 | -42.751 | 1.00 80.32 | N |
| ATOM | 1142 | CA | MET | A | 377 | -9.434 | -28.965 | -41.477 | 1.00 79.71 | C |
| ATOM | 1143 | CB | MET | A | 377 | -8.079 | -29.320 | -40.826 | 1.00 81.73 | C |
| ATOM | 1144 | CG | MET | A | 377 | -6.864 | -29.376 | -41.741 | 1.00 88.56 | C |
| ATOM | 1145 | SD | MET | A | 377 | -5.353 | -29.926 | -40.888 | 1.00 85.37 | S |
| ATOM | 1146 | CE | MET | A | 377 | 5.157 | 28.629 | 39.663 | 1.00 79.81 | C |
| ATOM | 1147 | C | MET | A | 377 | -9.656 | -27.455 | -41.551 | 1.00 73.59 | C |
| ATOM | 1148 | O | MET | A | 377 | -9.228 | -26.821 | -42.500 | 1.00 79.36 | O |
| ATOM | 1149 | N | THR | A | 378 | -10.331 | -26.890 | -40.547 | 1.00 62.12 | N |
| ATOM | 1150 | CA | THR | A | 378 | -10.590 | -25.453 | -40.489 | 1.00 62.33 | C |
| ATOM | 1151 | CB | THR | A | 378 | -11.699 | -25.155 | -39.487 | 1.00 63.90 | C |
| ATOM | 1152 | OG1 | THR | A | 378 | -11.220 | -25.390 | -38.164 | 1.00 65.30 | O |
| ATOM | 1153 | CG2 | THR | A | 378 | -12.883 | -26.059 | -39.747 | 1.00 68.86 | C |
| ATOM | 1154 | C | THR | A | 378 | -9.351 | -24.625 | -40.126 | 1.00 65.47 | C |
| ATOM | 1155 | O | THR | A | 378 | -8.333 | -25.180 | -39.718 | 1.00 70.07 | O |
| ATOM | 1156 | N | GLN | A | 379 | -9.423 | -23.304 | -40.271 | 1.00 61.70 | N |
| ATOM | 1157 | CA | GLN | A | 379 | -8.246 | -22.463 | -40.015 | 1.00 67.70 | C |
| ATOM | 1158 | CB | GLN | A | 379 | -8.511 | -21.005 | -40.401 | 1.00 72.61 | C |
| ATOM | 1159 | CG | GLN | A | 379 | -7.722 | -20.508 | -41.619 | 1.00 82.67 | C |
| ATOM | 1160 | CD | GLN | A | 379 | -7.846 | -21.375 | -42.882 | 1.00 95.64 | C |
| ATOM | 1161 | OE1 | GLN | A | 379 | -7.177 | -21.108 | -43.885 | 1.00102.19 | O |
| ATOM | 1162 | NE2 | GLN | A | 379 | 8.696 | 22.408 | 42.842 | 1.00 99.62 | N |
| ATOM | 1163 | C | GLN | A | 379 | -7.724 | -22.567 | -38.587 | 1.00 68.42 | C |
| ATOM | 1164 | O | GLN | A | 379 | -6.520 | -22.623 | -38.342 | 1.00 67.20 | O |
| ATOM | 1165 | N | GLU | A | 380 | -8.647 | -22.632 | -37.647 | 1.00 70.33 | N |
| ATOM | 1166 | CA | GLU | A | 380 | -8.316 | -22.773 | -36.251 | 1.00 69.04 | C |
| ATOM | 1167 | CB | GLU | A | 380 | -9.608 | -22.919 | -35.477 | 1.00 74.52 | C |
| ATOM | 1168 | CG | GLU | A | 380 | -10.809 | -22.509 | -36.316 | 1.00 88.66 | C |
| ATOM | 1169 | CD | GLU | A | 380 | -12.093 | -22.552 | -35.536 | 1.00 98.17 | C |
| ATOM | 1170 | OE1 | GLU | A | 380 | -12.034 | -22.286 | -34.305 | 1.00 96.75 | O |
| ATOM | 1171 | OE2 | GLU | A | 380 | 13.142 | 22.852 | 36.158 | 1.00 98.26 | O |
| ATOM | 1172 | C | GLU | A | 380 | -7.421 | -23.990 | -36.056 | 1.00 67.06 | C |
| ATOM | 1173 | O | GLU | A | 380 | -6.470 | -23.969 | -35.270 | 1.00 67.14 | O |
| ATOM | 1174 | N | GLU | A | 381 | -7.722 | -25.043 | -36.806 | 1.00 66.66 | N |
| ATOM | 1175 | CA | GLU | A | 381 | -6.959 | -26.278 | -36.765 | 1.00 57.00 | C |
| ATOM | 1176 | CB | GLU | A | 381 | -7.761 | -27.408 | -37.429 | 1.00 55.47 | C |
| ATOM | 1177 | CG | GLU | A | 381 | -9.098 | -27.651 | -36.722 | 1.00 61.50 | C |

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 1178 | CD | GLU | A | 381 | -9.982 | -28.762 | -37.310 | 1.00 | 64.99 | C |
| ATOM | 1179 | OE1 | GLU | A | 381 | -9.924 | -29.026 | -38.519 | 1.00 | 69.41 | O |
| ATOM | 1180 | OE2 | GLU | A | 381 | -10.787 | -29.365 | -36.555 | 1.00 | 70.72 | O |
| ATOM | 1181 | C | GLU | A | 381 | -5.588 | -26.047 | -37.404 | 1.00 | 55.03 | C |
| ATOM | 1182 | O | GLU | A | 381 | -4.632 | -26.683 | -37.059 | 1.00 | 56.08 | O |
| ATOM | 1183 | N | TYR | A | 382 | -5.471 | -25.104 | -38.317 | 1.00 | 55.69 | N |
| ATOM | 1184 | CA | TYR | A | 382 | -4.163 | -24.842 | -38.882 | 1.00 | 57.76 | C |
| ATOM | 1185 | CB | TYR | A | 382 | 4.298 | 24.141 | 40.212 | 1.00 | 54.77 | C |
| ATOM | 1186 | CG | TYR | A | 382 | -4.451 | -25.107 | -41.341 | 1.00 | 61.55 | C |
| ATOM | 1187 | CD1 | TYR | A | 382 | -3.366 | -25.845 | -41.804 | 1.00 | 58.62 | C |
| ATOM | 1188 | CE1 | TYR | A | 382 | -3.510 | -26.723 | -42.856 | 1.00 | 61.61 | C |
| ATOM | 1189 | CZ | TYR | A | 382 | -4.749 | -26.877 | -43.455 | 1.00 | 63.50 | C |
| ATOM | 1190 | OH | TYR | A | 382 | -4.929 | -27.752 | -44.519 | 1.00 | 71.14 | O |
| ATOM | 1191 | CE2 | TYR | A | 382 | -5.830 | -26.163 | -43.000 | 1.00 | 60.38 | C |
| ATOM | 1192 | CD2 | TYR | A | 382 | -5.682 | -25.288 | -41.950 | 1.00 | 60.51 | C |
| ATOM | 1193 | C | TYR | A | 382 | -3.306 | -24.011 | -37.954 | 1.00 | 61.17 | C |
| ATOM | 1194 | O | TYR | A | 382 | -2.119 | -24.271 | -37.801 | 1.00 | 57.91 | O |
| ATOM | 1195 | N | ALA | A | 383 | -3.915 | -22.993 | -37.358 | 1.00 | 60.41 | N |
| ATOM | 1196 | CA | ALA | A | 383 | -3.258 | -22.222 | -36.335 | 1.00 | 61.02 | C |
| ATOM | 1197 | CB | ALA | A | 383 | -4.193 | -21.149 | -35.810 | 1.00 | 64.92 | C |
| ATOM | 1198 | C | ALA | A | 383 | 2.762 | 23.126 | 35.195 | 1.00 | 61.33 | C |
| ATOM | 1199 | O | ALA | A | 383 | -1.566 | -23.243 | -34.991 | 1.00 | 63.06 | O |
| ATOM | 1200 | N | LEU | A | 384 | -3.658 | -23.788 | -34.473 | 1.00 | 56.90 | N |
| ATOM | 1201 | CA | LEU | A | 384 | -3.233 | -24.535 | -33.291 | 1.00 | 61.52 | C |
| ATOM | 1202 | CB | LEU | A | 384 | -4.409 | -25.217 | -32.610 | 1.00 | 63.43 | C |
| ATOM | 1203 | CG | LEU | A | 384 | 5.701 | 24.453 | 32.390 | 1.00 | 61.80 | C |
| ATOM | 1204 | CD1 | LEU | A | 384 | -6.613 | -25.410 | -31.633 | 1.00 | 65.49 | C |
| ATOM | 1205 | CD2 | LEU | A | 384 | -5.443 | -23.168 | -31.623 | 1.00 | 58.06 | C |
| ATOM | 1206 | C | LEU | A | 384 | -2.190 | -25.592 | -33.602 | 1.00 | 63.01 | C |
| ATOM | 1207 | O | LEU | A | 384 | -1.136 | -25.691 | -32.946 | 1.00 | 67.06 | O |
| ATOM | 1208 | N | LEU | A | 385 | -2.499 | -26.389 | -34.611 | 1.00 | 58.63 | N |
| ATOM | 1209 | CA | LEU | A | 385 | -1.622 | -27.449 | -35.057 | 1.00 | 52.95 | C |
| ATOM | 1210 | CB | LEU | A | 385 | -2.154 | -28.002 | -36.353 | 1.00 | 56.62 | C |
| ATOM | 1211 | CG | LEU | A | 385 | 2.155 | 29.468 | 36.699 | 1.00 | 52.07 | C |
| ATOM | 1212 | CD1 | LEU | A | 385 | -1.113 | -29.643 | -37.792 | 1.00 | 47.35 | C |
| ATOM | 1213 | CD2 | LEU | A | 385 | -1.960 | -30.350 | -35.464 | 1.00 | 52.18 | C |
| ATOM | 1214 | C | LEU | A | 385 | -0.262 | -26.895 | -35.325 | 1.00 | 51.90 | C |
| ATOM | 1215 | O | LEU | A | 385 | 0.665 | -27.648 | -35.421 | 1.00 | 62.42 | O |
| ATOM | 1216 | N | THR | A | 386 | 0.144 | 25.578 | 35.463 | 1.00 | 51.79 | N |
| ATOM | 1217 | CA | THR | A | 386 | 1.127 | -24.949 | -35.788 | 1.00 | 50.01 | C |
| ATOM | 1218 | CB | THR | A | 386 | 0.941 | -23.649 | -36.556 | 1.00 | 48.66 | C |
| ATOM | 1219 | OG1 | THR | A | 386 | 0.256 | -23.916 | -37.786 | 1.00 | 62.76 | O |
| ATOM | 1220 | CG2 | THR | A | 386 | 2.262 | -23.007 | -36.850 | 1.00 | 46.46 | C |
| ATOM | 1221 | C | THR | A | 386 | 1.833 | -24.610 | -34.517 | 1.00 | 56.25 | C |
| ATOM | 1222 | O | THR | A | 386 | 3.063 | -24.810 | -34.414 | 1.00 | 62.43 | O |
| ATOM | 1223 | N | ALA | A | 387 | 1.072 | -24.078 | -33.559 | 1.00 | 51.85 | N |

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ATOM   1224  CA  ALA A 387       1.618  23.782  32.247  1.00 51.84           C
ATOM   1225  CB  ALA A 387       0.614 -23.049 -31.408  1.00 54.80           C
ATOM   1226  C   ALA A 387       2.037 -25.056 -31.546  1.00 54.72           C
ATOM   1227  O   ALA A 387       3.071 -25.078 -30.874  1.00 53.97           O
ATOM   1228  N   ILE A 388       1.239 -26.114 -31.718  1.00 52.55           N
ATOM   1229  CA  ILE A 388       1.586 -27.423 -31.192  1.00 49.29           C
ATOM   1230  CB  ILE A 388       0.523 -28.471 -31.550  1.00 48.21           C
ATOM   1231  CG1 ILE A 388      -0.601 -28.382 -30.551  1.00 49.02           C
ATOM   1232  CD1 ILE A 388      -1.940 -28.678 -31.179  1.00 53.80           C
ATOM   1233  CG2 ILE A 388       1.072 -29.885 -31.478  1.00 46.19           C
ATOM   1234  C   ILE A 388       2.942 -27.834 -31.725  1.00 47.95           C
ATOM   1235  O   ILE A 388       3.756 -28.403 -30.984  1.00 50.26           O
ATOM   1236  N   VAL A 389       3.196 -27.531 -32.992  1.00 44.58           N
ATOM   1237  CA  VAL A 389       4.453 -27.944 -33.617  1.00 48.78           C
ATOM   1238  CB  VAL A 389       4.391  27.901  35.147  1.00 49.00           C
ATOM   1239  CG1 VAL A 389       5.794 -27.903 -35.732  1.00 48.38           C
ATOM   1240  CG2 VAL A 389       3.648 -29.122 -35.636  1.00 51.92           C
ATOM   1241  C   VAL A 389       5.678 -27.175 -33.161  1.00 50.05           C
ATOM   1242  O   VAL A 389       6.775 -27.733 -33.124  1.00 50.82           O
ATOM   1243  N   ILE A 390       5.515  25.892  32.852  1.00 52.16           N
ATOM   1244  CA  ILE A 390       6.654 -25.117 -32.394  1.00 48.94           C
ATOM   1245  CB  ILE A 390       6.393 -23.604 -32.437  1.00 51.15           C
ATOM   1246  CG1 ILE A 390       6.071 -23.163 -33.869  1.00 54.64           C
ATOM   1247  CD1 ILE A 390       5.219 -21.902 -33.931  1.00 58.23           C
ATOM   1248  CG2 ILE A 390       7.571 -22.837 -31.860  1.00 47.19           C
ATOM   1249  C   ILE A 390       6.899 -25.576 -30.983  1.00 42.50           C
ATOM   1250  O   ILE A 390       7.994 -25.964 -30.639  1.00 46.94           O
ATOM   1251  N   LEU A 391       5.852 -25.577 -30.193  1.00 38.46           N
ATOM   1252  CA  LEU A 391       5.965 -25.865 -28.783  1.00 42.84           C
ATOM   1253  CB  LEU A 391       4.714 -25.393 -28.078  1.00 40.16           C
ATOM   1254  CG  LEU A 391       4.791 -23.881 -27.828  1.00 43.05           C
ATOM   1255  CD1 LEU A 391       3.506 -23.313 -27.227  1.00 42.47           C
ATOM   1256  CD2 LEU A 391       5.977 -23.642 -26.927  1.00 44.73           C
ATOM   1257  C   LEU A 391       6.156  27.322  28.459  1.00 47.29           C
ATOM   1258  O   LEU A 391       5.381 -27.875 -27.698  1.00 52.99           O
ATOM   1259  N   SER A 392       7.192 -27.935 -29.010  1.00 45.21           N
ATOM   1260  CA  SER A 392       7.332 -29.367 -28.964  1.00 47.68           C
ATOM   1261  CB  SER A 392       7.564 -29.914 -30.365  1.00 48.60           C
ATOM   1262  OG  SER A 392       6.391  29.720  31.150  1.00 55.97           O
ATOM   1263  C   SER A 392       8.461 -29.747 -28.042  1.00 53.30           C
ATOM   1264  O   SER A 392       9.623 -29.498 -28.354  1.00 59.83           O
ATOM   1265  N   PRO A 393       8.133 -30.357 -26.900  1.00 51.03           N
ATOM   1266  CA  PRO A 393       9.130 -30.619 -25.885  1.00 54.95           C
ATOM   1267  CB  PRO A 393       8.303 -30.838 -24.607  1.00 55.32           C
ATOM   1268  CG  PRO A 393       6.909 -30.489 -24.958  1.00 58.13           C
ATOM   1269  CD  PRO A 393       6.785 -30.669 -26.426  1.00 55.17           C
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[1505]

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| ATOM | 1270 | C | PRO | A | 393 | 10.078 | -31.786 | -26.147 | 1.00 58.89 | C |
| ATOM | 1271 | O | PRO | A | 393 | 10.857 | -32.150 | -25.269 | 1.00 62.84 | O |
| ATOM | 1272 | N | ASP | A | 394 | 10.048 | 32.355 | 27.339 | 1.00 64.81 | N |
| ATOM | 1273 | CA | ASP | A | 394 | 11.028 | -33.373 | -27.667 | 1.00 60.13 | C |
| ATOM | 1274 | CB | ASP | A | 394 | 10.326 | -34.689 | -27.986 | 1.00 65.44 | C |
| ATOM | 1275 | CG | ASP | A | 394 | 9.454 | -34.600 | -29.216 | 1.00 70.53 | C |
| ATOM | 1276 | OD1 | ASP | A | 394 | 8.539 | -33.754 | -29.214 | 1.00 78.68 | O |
| ATOM | 1277 | OD2 | ASP | A | 394 | 9.675 | -35.374 | -30.179 | 1.00 69.45 | O |
| ATOM | 1278 | C | ASP | A | 394 | 11.943 | -32.952 | -28.808 | 1.00 56.55 | C |
| ATOM | 1279 | O | ASP | A | 394 | 12.413 | -33.794 | -29.546 | 1.00 67.78 | O |
| ATOM | 1280 | N | ARG | A | 395 | 12.174 | -31.654 | -28.976 | 1.00 52.10 | N |
| ATOM | 1281 | CA | ARG | A | 395 | 13.197 | -31.169 | -29.911 | 1.00 52.11 | C |
| ATOM | 1282 | CB | ARG | A | 395 | 13.138 | -29.639 | -30.106 | 1.00 48.46 | C |
| ATOM | 1283 | CG | ARG | A | 395 | 11.931 | -29.086 | -30.830 | 1.00 47.46 | C |
| ATOM | 1284 | CD | ARG | A | 395 | 11.892 | -29.511 | -32.291 | 1.00 48.83 | C |
| ATOM | 1285 | NE | ARG | A | 395 | 10.622 | -29.142 | -32.909 | 1.00 59.19 | N |
| ATOM | 1286 | CZ | ARG | A | 395 | 9.976 | 29.882 | 33.810 | 1.00 60.59 | C |
| ATOM | 1287 | NH1 | ARG | A | 395 | 10.469 | -31.040 | -34.207 | 1.00 64.00 | N |
| ATOM | 1288 | NH2 | ARG | A | 395 | 8.834 | -29.456 | -34.325 | 1.00 62.02 | N |
| ATOM | 1289 | C | ARG | A | 395 | 14.531 | -31.482 | -29.289 | 1.00 56.44 | C |
| ATOM | 1290 | O | ARG | A | 395 | 14.673 | -31.395 | -28.059 | 1.00 59.21 | O |
| ATOM | 1291 | N | GLN | A | 396 | 15.517 | 31.839 | 30.103 | 1.00 61.16 | N |
| ATOM | 1292 | CA | GLN | A | 396 | 16.815 | -32.113 | -29.526 | 1.00 76.54 | C |
| ATOM | 1293 | CB | GLN | A | 396 | 17.731 | -32.891 | -30.478 | 1.00 80.97 | C |
| ATOM | 1294 | CG | GLN | A | 396 | 18.797 | -32.066 | -31.185 | 1.00 93.33 | C |
| ATOM | 1295 | CD | GLN | A | 396 | 19.987 | -32.896 | -31.635 | 1.00103.47 | C |
| ATOM | 1296 | OE1 | GLN | A | 396 | 20.066 | -34.103 | -31.362 | 1.00102.37 | O |
| ATOM | 1297 | NE2 | GLN | A | 396 | 20.926 | -32.249 | -32.330 | 1.00103.13 | N |
| ATOM | 1298 | C | GLN | A | 396 | 17.381 | -30.767 | -29.104 | 1.00 82.16 | C |
| ATOM | 1299 | O | GLN | A | 396 | 17.186 | -29.773 | -29.803 | 1.00 84.74 | O |
| ATOM | 1300 | N | TYR | A | 397 | 18.011 | -30.735 | -27.929 | 1.00 89.04 | N |
| ATOM | 1301 | CA | TYR | A | 397 | 18.654 | -29.526 | -27.379 | 1.00 90.57 | C |
| ATOM | 1302 | CB | TYR | A | 397 | 19.177 | -28.582 | -28.485 | 1.00 98.66 | C |
| ATOM | 1303 | CG | TYR | A | 397 | 20.417 | -29.096 | -29.186 | 1.00105.03 | C |
| ATOM | 1304 | CD1 | TYR | A | 397 | 21.361 | -29.864 | -28.493 | 1.00110.81 | C |
| ATOM | 1305 | CE1 | TYR | A | 397 | 22.508 | 30.341 | 29.118 | 1.00121.22 | C |
| ATOM | 1306 | CZ | TYR | A | 397 | 22.739 | -30.044 | -30.456 | 1.00119.78 | C |
| ATOM | 1307 | OH | TYR | A | 397 | 23.892 | -30.531 | -31.055 | 1.00101.40 | O |
| ATOM | 1308 | CE2 | TYR | A | 397 | 21.815 | -29.273 | -31.169 | 1.00121.69 | C |
| ATOM | 1309 | CD2 | TYR | A | 397 | 20.662 | -28.804 | -30.533 | 1.00109.75 | C |
| ATOM | 1310 | C | TYR | A | 397 | 17.852 | 28.769 | 26.309 | 1.00 82.64 | C |
| ATOM | 1311 | O | TYR | A | 397 | 18.410 | -27.953 | -25.573 | 1.00 88.62 | O |
| ATOM | 1312 | N | ILE | A | 398 | 16.561 | -29.055 | -26.197 | 1.00 81.15 | N |
| ATOM | 1313 | CA | ILE | A | 398 | 15.767 | -28.549 | -25.065 | 1.00 76.03 | C |
| ATOM | 1314 | CB | ILE | A | 398 | 14.305 | -29.011 | -25.139 | 1.00 73.57 | C |
| ATOM | 1315 | CG1 | ILE | A | 398 | 13.665 | -28.557 | -26.454 | 1.00 67.67 | C |

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| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 1316 | CD1 | ILE | A | 398 | 13.880 | -27.094 | -26.773 | 1.00 | 68.20 | C |
| ATOM | 1317 | CG2 | ILE | A | 398 | 13.533 | 28.530 | 23.915 | 1.00 | 72.57 | C |
| ATOM | 1318 | C | ILE | A | 398 | 16.338 | -29.016 | -23.736 | 1.00 | 65.41 | C |
| ATOM | 1319 | O | ILE | A | 398 | 16.814 | -30.128 | -23.635 | 1.00 | 62.01 | O |
| ATOM | 1320 | N | LYS | A | 399 | 16.302 | -28.146 | -22.738 | 1.00 | 66.74 | N |
| ATOM | 1321 | CA | LYS | A | 399 | 16.827 | -28.454 | -21.412 | 1.00 | 70.30 | C |
| ATOM | 1322 | CB | LYS | A | 399 | 17.733 | -27.317 | -20.915 | 1.00 | 69.27 | C |
| ATOM | 1323 | CG | LYS | A | 399 | 19.083 | -27.237 | -21.625 | 1.00 | 73.08 | C |
| ATOM | 1324 | CD | LYS | A | 399 | 19.920 | -26.044 | -21.176 | 1.00 | 78.10 | C |
| ATOM | 1325 | CE | LYS | A | 399 | 19.149 | -24.728 | -21.303 | 1.00 | 88.41 | C |
| ATOM | 1326 | NZ | LYS | A | 399 | 19.834 | -23.539 | -20.707 | 1.00 | 94.82 | N |
| ATOM | 1327 | C | LYS | A | 399 | 15.691 | -28.697 | -20.421 | 1.00 | 72.45 | C |
| ATOM | 1328 | O | LYS | A | 399 | 15.790 | -29.541 | -19.526 | 1.00 | 76.55 | O |
| ATOM | 1329 | N | ASP | A | 400 | 14.601 | -27.966 | -20.608 | 1.00 | 68.26 | N |
| ATOM | 1330 | CA | ASP | A | 400 | 13.505 | -27.981 | -19.683 | 1.00 | 66.01 | C |
| ATOM | 1331 | CB | ASP | A | 400 | 13.416 | 26.604 | 19.040 | 1.00 | 76.11 | C |
| ATOM | 1332 | CG | ASP | A | 400 | 12.632 | -26.591 | -17.745 | 1.00 | 79.20 | C |
| ATOM | 1333 | OD1 | ASP | A | 400 | 11.683 | -27.394 | -17.553 | 1.00 | 89.45 | O |
| ATOM | 1334 | OD2 | ASP | A | 400 | 12.956 | -25.717 | -16.927 | 1.00 | 84.83 | O |
| ATOM | 1335 | C | ASP | A | 400 | 12.224 | -28.360 | -20.432 | 1.00 | 65.85 | C |
| ATOM | 1336 | O | ASP | A | 400 | 11.349 | 27.526 | 20.705 | 1.00 | 65.84 | O |
| ATOM | 1337 | N | ARG | A | 401 | 12.124 | -29.647 | -20.746 | 1.00 | 62.84 | N |
| ATOM | 1338 | CA | ARG | A | 401 | 11.024 | -30.177 | -21.527 | 1.00 | 56.25 | C |
| ATOM | 1339 | CB | ARG | A | 401 | 11.244 | -31.659 | -21.801 | 1.00 | 51.53 | C |
| ATOM | 1340 | CG | ARG | A | 401 | 12.606 | -31.870 | -22.407 | 1.00 | 49.85 | C |
| ATOM | 1341 | CD | ARG | A | 401 | 12.819 | -33.222 | -23.054 | 1.00 | 54.50 | C |
| ATOM | 1342 | NE | ARG | A | 401 | 14.171 | -33.264 | -23.604 | 1.00 | 52.60 | N |
| ATOM | 1343 | CZ | ARG | A | 401 | 14.515 | -32.827 | -24.812 | 1.00 | 57.93 | C |
| ATOM | 1344 | NH1 | ARG | A | 401 | 13.610 | -32.338 | -25.657 | 1.00 | 64.60 | N |
| ATOM | 1345 | NH2 | ARG | A | 401 | 15.775 | -32.887 | -25.193 | 1.00 | 62.34 | N |
| ATOM | 1346 | C | ARG | A | 401 | 9.685 | -29.894 | -20.866 | 1.00 | 56.34 | C |
| ATOM | 1347 | O | ARG | A | 401 | 8.715 | -29.530 | -21.546 | 1.00 | 58.60 | O |
| ATOM | 1348 | N | GLU | A | 402 | 9.630 | -30.019 | -19.548 | 1.00 | 58.98 | N |
| ATOM | 1349 | CA | GLU | A | 402 | 8.370 | -29.778 | -18.857 | 1.00 | 68.93 | C |
| ATOM | 1350 | CB | GLU | A | 402 | 8.327 | 30.361 | 17.431 | 1.00 | 76.65 | C |
| ATOM | 1351 | CG | GLU | A | 402 | 9.327 | -29.776 | -16.442 | 1.00 | 98.71 | C |
| ATOM | 1352 | CD | GLU | A | 402 | 8.807 | -28.531 | -15.729 | 1.00 | 117.03 | C |
| ATOM | 1353 | OE1 | GLU | A | 402 | 9.657 | -27.711 | -15.303 | 1.00 | 121.28 | O |
| ATOM | 1354 | OE2 | GLU | A | 402 | 7.561 | -28.368 | -15.594 | 1.00 | 112.07 | O |
| ATOM | 1355 | C | GLU | A | 402 | 7.987 | 28.301 | 18.921 | 1.00 | 67.07 | C |
| ATOM | 1356 | O | GLU | A | 402 | 6.789 | -27.964 | -18.913 | 1.00 | 65.84 | O |
| ATOM | 1357 | N | ALA | A | 403 | 8.987 | -27.424 | -19.027 | 1.00 | 60.94 | N |
| ATOM | 1358 | CA | ALA | A | 403 | 8.681 | -26.003 | -19.198 | 1.00 | 61.26 | C |
| ATOM | 1359 | CB | ALA | A | 403 | 9.936 | -25.171 | -19.160 | 1.00 | 52.63 | C |
| ATOM | 1360 | C | ALA | A | 403 | 7.909 | -25.803 | -20.511 | 1.00 | 66.74 | C |
| ATOM | 1361 | O | ALA | A | 403 | 6.930 | -25.021 | -20.562 | 1.00 | 65.40 | O |

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ATOM   1362  N   VAL A 404       8.327 -26.554 -21.544  1.00 59.50           N
ATOM   1363  CA  VAL A 404       7.659 -26.557 -22.845  1.00 55.42           C
ATOM   1364  CB  VAL A 404       8.592 -27.045 -23.967  1.00 53.67           C
ATOM   1365  CG1 VAL A 404       7.868 -27.091 -25.311  1.00 50.11           C
ATOM   1366  CG2 VAL A 404       9.816 -26.144 -24.050  1.00 49.09           C
ATOM   1367  C   VAL A 404       6.345 -27.345 -22.830  1.00 59.48           C
ATOM   1368  O   VAL A 404       5.345 -26.892 -23.399  1.00 58.36           O
ATOM   1369  N   GLU A 405       6.323 -28.503 -22.167  1.00 62.42           N
ATOM   1370  CA  GLU A 405       5.074  29.274  22.104  1.00 59.91           C
ATOM   1371  CB  GLU A 405       5.251 -30.706 -21.564  1.00 61.01           C
ATOM   1372  CG  GLU A 405       5.175 -30.877 -20.069  1.00 73.57           C
ATOM   1373  CD  GLU A 405       3.780 -31.214 -19.595  1.00 88.54           C
ATOM   1374  OE1 GLU A 405       3.283 -30.581 -18.629  1.00 97.08           O
ATOM   1375  OE2 GLU A 405       3.177 -32.116 -20.200  1.00 99.51           O
ATOM   1376  C   GLU A 405       3.961 -28.495 -21.434  1.00 55.89           C
ATOM   1377  O   GLU A 405       2.842  28.505  21.936  1.00 52.83           O
ATOM   1378  N   LYS A 406       4.258 -27.771 -20.349  1.00 57.14           N
ATOM   1379  CA  LYS A 406       3.202 -26.934 -19.733  1.00 58.73           C
ATOM   1380  CB  LYS A 406       3.654 -26.136 -18.491  1.00 49.12           C
ATOM   1381  C   LYS A 406       2.587 -26.033 -20.801  1.00 57.66           C
ATOM   1382  O   LYS A 406       1.383 -25.943 -20.876  1.00 64.58           O
ATOM   1383  N   LEU A 407       3.414 -25.429 -21.658  1.00 59.01           N
ATOM   1384  CA  LEU A 407       2.937 -24.537 -22.736  1.00 56.49           C
ATOM   1385  CB  LEU A 407       4.093 -23.745 -23.327  1.00 58.83           C
ATOM   1386  CG  LEU A 407       4.693  22.629  22.480  1.00 59.07           C
ATOM   1387  CD1 LEU A 407       5.710 -21.851 -23.303  1.00 53.56           C
ATOM   1388  CD2 LEU A 407       3.590 -21.725 -21.958  1.00 55.33           C
ATOM   1389  C   LEU A 407       2.207 -25.197 -23.899  1.00 56.99           C
ATOM   1390  O   LEU A 407       1.297 -24.594 -24.460  1.00 60.16           O
ATOM   1391  N   GLN A 408       2.636 -26.403 -24.288  1.00 55.78           N
ATOM   1392  CA  GLN A 408       2.014 -27.149 -25.390  1.00 46.25           C
ATOM   1393  CB  GLN A 408       2.924 -28.289 -25.860  1.00 43.35           C
ATOM   1394  CG  GLN A 408       2.206 -29.249 -26.800  1.00 50.51           C
ATOM   1395  CD  GLN A 408       3.100 -30.243 -27.499  1.00 52.91           C
ATOM   1396  OE1 GLN A 408       3.573 -31.189 -26.891  1.00 57.63           O
ATOM   1397  NE2 GLN A 408       3.317 -30.048 -28.803  1.00 55.80           N
ATOM   1398  C   GLN A 408       0.667 -27.717 -24.971  1.00 48.70           C
ATOM   1399  O   GLN A 408      -0.253 -27.836 -25.790  1.00 47.93           O
ATOM   1400  N   GLU A 409       0.553 -28.044 -23.682  1.00 52.95           N
ATOM   1401  CA  GLU A 409      -0.548 -28.845 -23.166  1.00 55.81           C
ATOM   1402  CB  GLU A 409       0.383  29.020  21.679  1.00 62.24           C
ATOM   1403  CG  GLU A 409      -0.810 -30.362 -21.141  1.00 74.06           C
ATOM   1404  CD  GLU A 409      -0.007 -30.744 -19.900  1.00 89.68           C
ATOM   1405  OE1 GLU A 409       0.142 -29.904 -18.967  1.00 93.22           O
ATOM   1406  OE2 GLU A 409       0.486 -31.893 -19.860  1.00 98.84           O
ATOM   1407  C   GLU A 409      -1.903 -28.218 -23.461  1.00 57.56           C
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ATOM   1408  O   GLU A 409      -2.726 -28.841 -24.145  1.00 56.45           O
ATOM   1409  N   PRO A 410      -2.122 -26.963 -22.986  1.00 58.17           N
ATOM   1410  CA  PRO A 410      -3.419 -26.303 -23.135  1.00 51.28           C
ATOM   1411  CB  PRO A 410      -3.165 -24.897 -22.578  1.00 46.19           C
ATOM   1412  CG  PRO A 410      -1.962 -25.040 -21.687  1.00 47.71           C
ATOM   1413  CD  PRO A 410       1.118  26.015  22.448  1.00 55.96           C
ATOM   1414  C   PRO A 410      -3.863 -26.224 -24.582  1.00 49.99           C
ATOM   1415  O   PRO A 410      -5.065 -26.353 -24.835  1.00 55.00           O
ATOM   1416  N   LEU A 411      -2.916 -26.029 -25.507  1.00 45.60           N
ATOM   1417  CA  LEU A 411      -3.209 -25.968 -26.935  1.00 48.64           C
ATOM   1418  CB  LEU A 411       2.012  25.438  27.710  1.00 49.55           C
ATOM   1419  CG  LEU A 411      -1.476 -24.032 -27.506  1.00 52.73           C
ATOM   1420  CD1 LEU A 411      -0.033 -23.982 -27.984  1.00 58.81           C
ATOM   1421  CD2 LEU A 411      -2.275 -23.011 -28.263  1.00 49.99           C
ATOM   1422  C   LEU A 411      -3.636 -27.342 -27.517  1.00 53.47           C
ATOM   1423  O   LEU A 411      -4.574 -27.419 -28.331  1.00 50.37           O
ATOM   1424  N   LEU A 412      -2.964 -28.427 -27.116  1.00 52.80           N
ATOM   1425  CA  LEU A 412      -3.510 -29.774 -27.391  1.00 49.51           C
ATOM   1426  CB  LEU A 412      -2.614 -30.873 -26.856  1.00 46.07           C
ATOM   1427  CG  LEU A 412      -1.355 -31.075 -27.676  1.00 47.72           C
ATOM   1428  CD1 LEU A 412      -0.267 -31.693 -26.812  1.00 46.79           C
ATOM   1429  CD2 LEU A 412      -1.636 -31.879 -28.938  1.00 46.85           C
ATOM   1430  C   LEU A 412      -4.901 -29.950 -26.804  1.00 47.38           C
ATOM   1431  O   LEU A 412       5.797  30.467  27.465  1.00 46.89           O
ATOM   1432  N   ASP A 413      -5.080 -29.491 -25.572  1.00 50.02           N
ATOM   1433  CA  ASP A 413      -6.387 -29.555 -24.925  1.00 60.48           C
ATOM   1434  CB  ASP A 413      -6.325 -29.039 -23.484  1.00 70.74           C
ATOM   1435  CG  ASP A 413      -5.833 -30.111 -22.478  1.00 83.93           C
ATOM   1436  OD1 ASP A 413      -4.898 -30.896 -22.778  1.00 85.17           O
ATOM   1437  OD2 ASP A 413      -6.383 -30.154 -21.356  1.00100.73           O
ATOM   1438  C   ASP A 413      -7.505 -28.884 -25.741  1.00 62.80           C
ATOM   1439  O   ASP A 413      -8.573 -29.502 -25.968  1.00 61.06           O
ATOM   1440  N   VAL A 414      -7.257 -27.659 -26.213  1.00 58.87           N
ATOM   1441  CA  VAL A 414      -8.264 -26.949 -27.009  1.00 59.45           C
ATOM   1442  CB  VAL A 414      -7.884 -25.488 -27.368  1.00 60.02           C
ATOM   1443  CG1 VAL A 414      -9.076 -24.792 -27.968  1.00 59.79           C
ATOM   1444  CG2 VAL A 414       7.453  24.693  26.154  1.00 62.81           C
ATOM   1445  C   VAL A 414      -8.536 -27.699 -28.306  1.00 58.99           C
ATOM   1446  O   VAL A 414      -9.680 -27.788 -28.743  1.00 61.10           O
ATOM   1447  N   LEU A 415      -7.488 -28.234 -28.923  1.00 59.50           N
ATOM   1448  CA  LEU A 415      -7.654 -28.854 -30.230  1.00 60.81           C
ATOM   1449  CB  LEU A 415      -6.327 -29.231 -30.875  1.00 59.84           C
ATOM   1450  CG  LEU A 415      -6.424 -29.812 -32.289  1.00 50.72           C
ATOM   1451  CD1 LEU A 415      -7.227 -28.945 -33.246  1.00 48.88           C
ATOM   1452  CD2 LEU A 415      -5.014 -29.949 -32.783  1.00 49.83           C
ATOM   1453  C   LEU A 415      -8.520 -30.073 -30.116  1.00 62.84           C
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ATOM   1454  O   LEU A 415     -9.449 -30.257 -30.911  1.00 68.74           O
ATOM   1455  N   GLN A 416     -8.233 -30.899 -29.119  1.00 65.22           N
ATOM   1456  CA  GLN A 416     -9.096 -32.043 -28.855  1.00 66.79           C
ATOM   1457  CB  GLN A 416     -8.706 -32.762 -27.571  1.00 65.76           C
ATOM   1458  CG  GLN A 416     -9.459 -34.062 -27.355  1.00 67.80           C
ATOM   1459  CD  GLN A 416     -8.674 -35.018 -26.484  1.00 73.78           C
ATOM   1460  OE1 GLN A 416     -8.110 -34.621 -25.467  1.00 86.43           O
ATOM   1461  NE2 GLN A 416     -8.613 -36.280 -26.886  1.00 76.04           N
ATOM   1462  C   GLN A 416    -10.565 -31.604 -28.855  1.00 62.03           C
ATOM   1463  O   GLN A 416     11.308  32.026  29.724  1.00 65.46           O
ATOM   1464  N   LYS A 417    -10.953 -30.718 -27.934  1.00 61.20           N
ATOM   1465  CA  LYS A 417    -12.319 -30.168 -27.899  1.00 57.88           C
ATOM   1466  CB  LYS A 417    -12.389 -28.954 -26.984  1.00 56.75           C
ATOM   1467  CG  LYS A 417    -12.055 -29.241 -25.531  1.00 58.63           C
ATOM   1468  CD  LYS A 417    -13.242 -28.976 -24.616  1.00 59.71           C
ATOM   1469  CE  LYS A 417    -12.794 -28.766 -23.169  1.00 62.16           C
ATOM   1470  NZ  LYS A 417    -13.894 -28.272 -22.282  1.00 61.95           N
ATOM   1471  C   LYS A 417    -12.893 -29.800 -29.276  1.00 54.47           C
ATOM   1472  O   LYS A 417    -13.982 -30.284 -29.639  1.00 48.54           O
ATOM   1481  N   CYS A 419    -12.242 -30.614 -32.209  1.00 64.55           N
ATOM   1482  CA  CYS A 419     12.508  31.828  32.945  1.00 63.36           C
ATOM   1483  CB  CYS A 419     11.340  32.770  32.791  1.00 66.64           C
ATOM   1484  SG  CYS A 419     -9.910 -32.161 -33.685  1.00 73.04           S
ATOM   1485  C   CYS A 419    -13.757 -32.474 -32.429  1.00 66.21           C
ATOM   1486  O   CYS A 419    -14.667 -32.754 -33.194  1.00 74.12           O
ATOM   1487  N   LYS A 420    -13.795 -32.667 -31.114  1.00 73.78           N
ATOM   1488  CA  LYS A 420    -14.904 -33.289 -30.393  1.00 75.38           C
ATOM   1489  CB  LYS A 420    -14.486 -33.493 -28.936  1.00 76.69           C
ATOM   1490  CG  LYS A 420    -15.019 -34.748 -28.272  1.00 80.41           C
ATOM   1491  CD  LYS A 420    -14.106 -35.177 -27.125  1.00 90.64           C
ATOM   1492  CE  LYS A 420    -14.232 -36.669 -26.810  1.00 93.41           C
ATOM   1493  NZ  LYS A 420    -13.202 -37.105 -25.823  1.00 89.08           N
ATOM   1494  C   LYS A 420     16.189  32.456  30.441  1.00 79.70           C
ATOM   1495  O   LYS A 420    -17.206 -32.851 -29.861  1.00 85.34           O
ATOM   1496  N   ILE A 421    -16.136 -31.308 -31.119  1.00 71.31           N
ATOM   1497  CA  ILE A 421    -17.297 -30.446 -31.276  1.00 69.53           C
ATOM   1498  CB  ILE A 421    -17.021 -29.028 -30.730  1.00 63.55           C
ATOM   1499  CG1 ILE A 421    -17.218 -29.003 -29.216  1.00 67.12           C
ATOM   1500  CD1 ILE A 421    -16.534 -27.831 -28.529  1.00 72.24           C
ATOM   1501  CG2 ILE A 421    -17.906 -27.987 -31.396  1.00 59.06           C
ATOM   1502  C   ILE A 421    -17.715 -30.380 -32.737  1.00 80.37           C
ATOM   1503  O   ILE A 421    -18.868 -30.645 -33.052  1.00 92.14           O
ATOM   1504  N   HIS A 422    -16.764 -30.039 -33.611  1.00 87.06           N
ATOM   1505  CA  HIS A 422    -17.006 -29.738 -35.032  1.00 88.20           C
ATOM   1506  CB  HIS A 422     15.856  28.894  35.581  1.00 88.80           C
ATOM   1507  CG  HIS A 422    -15.994 -27.408 -35.325  1.00 93.84           C
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ATOM   1508  ND1 HIS A 422     -15.746 -26.481 -36.282  1.00103.34           N
ATOM   1509  CE1 HIS A 422     -15.937 -25.248 -35.775  1.00 96.73           C
ATOM   1510  NE2 HIS A 422     -16.311 -25.383 -34.487  1.00 94.67           N
ATOM   1511  CD2 HIS A 422     -16.354 -26.700 -34.179  1.00 93.11           C
ATOM   1512  C   HIS A 422     -17.155 -30.976 -35.882  1.00 87.14           C
ATOM   1513  O   HIS A 422     -17.463 -30.890 -37.071  1.00 83.68           O
ATOM   1514  N   GLN A 423     -16.902 -32.135 -35.286  1.00 87.95           N
ATOM   1515  CA  GLN A 423     -17.031 -33.432 -35.963  1.00 97.55           C
ATOM   1516  CB  GLN A 423     -15.963 -33.632 -37.080  1.00 90.40           C
ATOM   1517  CG  GLN A 423     -14.597 -32.984 -36.816  1.00 98.93           C
ATOM   1518  CD  GLN A 423     -13.860 -32.494 -38.073  1.00101.26           C
ATOM   1519  OE1 GLN A 423      13.589  31.288  38.222  1.00 91.60           O
ATOM   1520  NE2 GLN A 423     -13.506 -33.427 -38.967  1.00 92.59           N
ATOM   1521  C   GLN A 423     -17.036 -34.557 -34.906  1.00100.38           C
ATOM   1522  O   GLN A 423     -16.002 -35.197 -34.661  1.00 91.43           O
ATOM   1523  N   PRO A 424     -18.198 -34.771 -34.243  1.00100.72           N
ATOM   1524  CA  PRO A 424     -18.288 -35.854 -33.264  1.00102.59           C
ATOM   1525  CB  PRO A 424     -19.430 -35.413 -32.341  1.00 93.52           C
ATOM   1526  CG  PRO A 424     -20.214 -34.396 -33.113  1.00 97.36           C
ATOM   1527  CD  PRO A 424     -19.477 -34.048 -34.379  1.00 99.11           C
ATOM   1528  C   PRO A 424     -18.616 -37.163 -33.977  1.00107.48           C
ATOM   1529  O   PRO A 424     -18.546 -38.258 -33.383  1.00 99.01           O
ATOM   1530  N   GLU A 425     -18.948 -37.033 -35.259  1.00107.88           N
ATOM   1531  CA  GLU A 425      19.209  38.181  36.110  1.00115.14           C
ATOM   1532  CB  GLU A 425     -19.649 -37.738 -37.511  1.00115.00           C
ATOM   1533  CG  GLU A 425     -21.035 -37.087 -37.553  1.00116.54           C
ATOM   1534  CD  GLU A 425     -21.987 -37.568 -36.451  1.00113.17           C
ATOM   1535  OE1 GLU A 425     -22.635 -36.709 -35.819  1.00103.23           O
ATOM   1536  OE2 GLU A 425     -22.098 -38.793 -36.204  1.00112.87           O
ATOM   1537  C   GLU A 425     -18.020 -39.138 -36.153  1.00109.54           C
ATOM   1538  O   GLU A 425     -18.173 -40.334 -35.895  1.00118.69           O
ATOM   1539  N   ASN A 426     -16.839 -38.602 -36.442  1.00 99.12           N
ATOM   1540  CA  ASN A 426     -15.620 -39.397 -36.413  1.00 93.27           C
ATOM   1541  CB  ASN A 426     -14.882 -39.337 -37.758  1.00 95.06           C
ATOM   1542  CG  ASN A 426      15.046  38.005  38.467  1.00 99.63           C
ATOM   1543  OD1 ASN A 426     -15.329 -37.960 -39.669  1.00101.37           O
ATOM   1544  ND2 ASN A 426     -14.856 -36.913 -37.733  1.00 96.63           N
ATOM   1545  C   ASN A 426     -14.698 -39.056 -35.244  1.00 81.44           C
ATOM   1546  O   ASN A 426     -13.941 -38.093 -35.323  1.00 80.55           O
ATOM   1547  N   PRO A 427     -14.737 -39.878 -34.170  1.00 78.48           N
ATOM   1548  CA  PRO A 427     -13.974 -39.641 -32.933  1.00 73.80           C
ATOM   1549  CB  PRO A 427     -14.477 -40.736 -31.982  1.00 75.15           C
ATOM   1550  CG  PRO A 427     -14.900 -41.839 -32.894  1.00 86.15           C
ATOM   1551  CD  PRO A 427     -15.453 -41.171 -34.128  1.00 80.35           C
ATOM   1552  C   PRO A 427     -12.490 -39.802 -33.105  1.00 69.45           C
ATOM   1553  O   PRO A 427     -11.765 -39.769 -32.115  1.00 72.63           O
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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 1554 | N | GLN | A | 428 | 12.042 | 39.984 | 34.345 | 1.00 | 75.00 | N |
| ATOM | 1555 | CA | GLN | A | 428 | -10.621 | -40.196 | -34.636 | 1.00 | 73.25 | C |
| ATOM | 1556 | CB | GLN | A | 428 | -10.379 | -41.553 | -35.296 | 1.00 | 80.26 | C |
| ATOM | 1557 | CG | GLN | A | 428 | -10.496 | -41.544 | -36.819 | 1.00 | 78.26 | C |
| ATOM | 1558 | CD | GLN | A | 428 | -11.927 | -41.651 | -37.314 | 1.00 | 75.72 | C |
| ATOM | 1559 | OE1 | GLN | A | 428 | -12.722 | -42.394 | -36.752 | 1.00 | 70.39 | O |
| ATOM | 1560 | NE2 | GLN | A | 428 | -12.252 | -40.927 | -38.387 | 1.00 | 71.60 | N |
| ATOM | 1561 | C | GLN | A | 428 | -10.109 | -39.113 | -35.539 | 1.00 | 66.96 | C |
| ATOM | 1562 | O | GLN | A | 428 | -9.324 | -39.365 | -36.441 | 1.00 | 72.66 | O |
| ATOM | 1563 | N | HIS | A | 429 | 10.551 | 37.894 | 35.295 | 1.00 | 66.17 | N |
| ATOM | 1564 | CA | HIS | A | 429 | -10.038 | -36.771 | -36.038 | 1.00 | 64.78 | C |
| ATOM | 1565 | CB | HIS | A | 429 | -11.100 | -35.700 | -36.120 | 1.00 | 64.36 | C |
| ATOM | 1566 | CG | HIS | A | 429 | -10.805 | -34.643 | -37.131 | 1.00 | 60.62 | C |
| ATOM | 1567 | ND1 | HIS | A | 429 | -10.406 | -34.935 | -38.379 | 1.00 | 64.02 | N |
| ATOM | 1568 | CE1 | HIS | A | 429 | -10.227 | -33.801 | -39.060 | 1.00 | 69.88 | C |
| ATOM | 1569 | NE2 | HIS | A | 429 | -10.526 | -32.774 | -38.242 | 1.00 | 70.69 | N |
| ATOM | 1570 | CD2 | HIS | A | 429 | -10.888 | -33.267 | -37.049 | 1.00 | 60.34 | C |
| ATOM | 1571 | C | HIS | A | 429 | -8.789 | -36.225 | -35.404 | 1.00 | 63.01 | C |
| ATOM | 1572 | O | HIS | A | 429 | -7.789 | -35.934 | -36.101 | 1.00 | 58.11 | O |
| ATOM | 1573 | N | PHE | A | 430 | -8.838 | -36.072 | -34.080 | 1.00 | 52.42 | N |
| ATOM | 1574 | CA | PHE | A | 430 | -7.743 | -35.432 | -33.358 | 1.00 | 56.65 | C |
| ATOM | 1575 | CB | PHE | A | 430 | -8.112 | -35.208 | -31.877 | 1.00 | 53.08 | C |
| ATOM | 1576 | CG | PHE | A | 430 | -7.005 | -34.638 | -31.028 | 1.00 | 45.34 | C |
| ATOM | 1577 | CD1 | PHE | A | 430 | -6.377 | -33.432 | -31.365 | 1.00 | 46.47 | C |
| ATOM | 1578 | CE1 | PHE | A | 430 | -5.362 | -32.913 | -30.569 | 1.00 | 41.31 | C |
| ATOM | 1579 | CZ | PHE | A | 430 | 4.978 | 33.597 | 29.416 | 1.00 | 41.25 | C |
| ATOM | 1580 | CE2 | PHE | A | 430 | -5.613 | -34.780 | -29.068 | 1.00 | 38.72 | C |
| ATOM | 1581 | CD2 | PHE | A | 430 | -6.615 | -35.289 | -29.873 | 1.00 | 40.49 | C |
| ATOM | 1582 | C | PHE | A | 430 | -6.517 | -36.301 | -33.553 | 1.00 | 57.09 | C |
| ATOM | 1583 | O | PHE | A | 430 | -5.465 | -35.835 | -33.982 | 1.00 | 62.69 | O |
| ATOM | 1584 | N | ALA | A | 431 | -6.684 | -37.591 | -33.322 | 1.00 | 63.48 | N |
| ATOM | 1585 | CA | ALA | A | 431 | -5.625 | -38.549 | -33.620 | 1.00 | 62.18 | C |
| ATOM | 1586 | CB | ALA | A | 431 | -6.153 | -39.960 | -33.433 | 1.00 | 55.42 | C |
| ATOM | 1587 | C | ALA | A | 431 | -4.999 | -38.348 | -35.033 | 1.00 | 56.11 | C |
| ATOM | 1588 | O | ALA | A | 431 | 3.786 | 38.443 | 35.218 | 1.00 | 49.59 | O |
| ATOM | 1589 | N | CYS | A | 432 | -5.810 | -38.035 | -36.028 | 1.00 | 56.05 | N |
| ATOM | 1590 | CA | CYS | A | 432 | -5.226 | -37.831 | -37.347 | 1.00 | 59.54 | C |
| ATOM | 1591 | CB | CYS | A | 432 | -6.289 | -37.840 | -38.432 | 1.00 | 64.93 | C |
| ATOM | 1592 | SG | CYS | A | 432 | -7.009 | -39.472 | -38.697 | 1.00 | 70.90 | S |
| ATOM | 1593 | C | CYS | A | 432 | -4.404 | -36.561 | -37.404 | 1.00 | 55.56 | C |
| ATOM | 1594 | O | CYS | A | 432 | -3.349 | -36.532 | -38.024 | 1.00 | 59.39 | O |
| ATOM | 1595 | N | LEU | A | 433 | -4.866 | -35.516 | -36.736 | 1.00 | 50.72 | N |
| ATOM | 1596 | CA | LEU | A | 433 | -4.103 | -34.291 | -36.715 | 1.00 | 47.48 | C |
| ATOM | 1597 | CB | LEU | A | 433 | -4.816 | -33.183 | -35.920 | 1.00 | 50.56 | C |
| ATOM | 1598 | CG | LEU | A | 433 | -6.136 | -32.737 | -36.594 | 1.00 | 46.45 | C |
| ATOM | 1599 | CD1 | LEU | A | 433 | -6.989 | -31.822 | -35.741 | 1.00 | 40.50 | C |

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 1600 | CD2 | LEU | A | 433 | -5.837 | -32.093 | -37.938 | 1.00 47.93 | C |
| ATOM | 1601 | C | LEU | A | 433 | -2.747 | -34.614 | -36.167 | 1.00 43.21 | C |
| ATOM | 1602 | O | LEU | A | 433 | -1.741 | -34.333 | -36.821 | 1.00 48.74 | O |
| ATOM | 1603 | N | LEU | A | 434 | 2.708 | 35.253 | 35.009 | 1.00 39.41 | N |
| ATOM | 1604 | CA | LEU | A | 434 | -1.411 | -35.670 | -34.439 | 1.00 47.95 | C |
| ATOM | 1605 | CB | LEU | A | 434 | -1.572 | -36.447 | -33.129 | 1.00 50.42 | C |
| ATOM | 1606 | CG | LEU | A | 434 | -2.021 | -35.611 | -31.919 | 1.00 51.41 | C |
| ATOM | 1607 | CD1 | LEU | A | 434 | -1.840 | -36.409 | -30.638 | 1.00 52.36 | C |
| ATOM | 1608 | CD2 | LEU | A | 434 | -1.263 | -34.285 | -31.840 | 1.00 48.27 | C |
| ATOM | 1609 | C | LEU | A | 434 | -0.596 | -36.486 | -35.412 | 1.00 50.07 | C |
| ATOM | 1610 | O | LEU | A | 434 | 0.561 | -36.171 | -35.670 | 1.00 55.51 | O |
| ATOM | 1611 | N | GLY | A | 435 | -1.221 | -37.527 | -35.957 | 1.00 53.60 | N |
| ATOM | 1612 | CA | GLY | A | 435 | -0.631 | -38.377 | -36.985 | 1.00 53.10 | C |
| ATOM | 1613 | C | GLY | A | 435 | 0.151 | -37.674 | -38.073 | 1.00 48.76 | C |
| ATOM | 1614 | O | GLY | A | 435 | 1.165 | -38.179 | -38.527 | 1.00 52.55 | O |
| ATOM | 1615 | N | ARG | A | 436 | -0.317 | -36.506 | -38.473 | 1.00 48.94 | N |
| ATOM | 1616 | CA | ARG | A | 436 | 0.363 | -35.708 | -39.475 | 1.00 54.03 | C |
| ATOM | 1617 | CB | ARG | A | 436 | 0.629 | 34.735 | 40.100 | 1.00 59.23 | C |
| ATOM | 1618 | CG | ARG | A | 436 | -1.859 | -35.430 | -40.694 | 1.00 66.51 | C |
| ATOM | 1619 | CD | ARG | A | 436 | -1.544 | -36.651 | -41.566 | 1.00 68.91 | C |
| ATOM | 1620 | NE | ARG | A | 436 | -2.705 | -37.537 | -41.713 | 1.00 83.28 | N |
| ATOM | 1621 | CZ | ARG | A | 436 | -2.848 | -38.723 | -41.106 | 1.00102.33 | C |
| ATOM | 1622 | NH1 | ARG | A | 436 | 1.887 | 39.187 | 40.300 | 1.00117.35 | N |
| ATOM | 1623 | NH2 | ARG | A | 436 | -3.948 | -39.461 | -41.307 | 1.00 88.32 | N |
| ATOM | 1624 | C | ARG | A | 436 | 1.654 | -35.008 | -39.023 | 1.00 57.04 | C |
| ATOM | 1625 | O | ARG | A | 436 | 2.587 | -34.874 | -39.817 | 1.00 64.38 | O |
| ATOM | 1626 | N | LEU | A | 437 | 1.732 | -34.567 | -37.766 | 1.00 57.29 | N |
| ATOM | 1627 | CA | LEU | A | 437 | 2.990 | -34.020 | -37.219 | 1.00 54.51 | C |
| ATOM | 1628 | CB | LEU | A | 437 | 2.867 | -33.643 | -35.743 | 1.00 48.04 | C |
| ATOM | 1629 | CG | LEU | A | 437 | 1.580 | -32.888 | -35.373 | 1.00 52.90 | C |
| ATOM | 1630 | CD1 | LEU | A | 437 | 1.504 | -32.711 | -33.877 | 1.00 49.56 | C |
| ATOM | 1631 | CD2 | LEU | A | 437 | 1.422 | -31.551 | -36.085 | 1.00 49.13 | C |
| ATOM | 1632 | C | LEU | A | 437 | 4.134 | -35.001 | -37.379 | 1.00 60.72 | C |
| ATOM | 1633 | O | LEU | A | 437 | 5.306 | -34.641 | -37.229 | 1.00 74.06 | O |
| ATOM | 1634 | N | THR | A | 438 | 3.796 | -36.245 | -37.682 | 1.00 57.18 | N |
| ATOM | 1635 | CA | THR | A | 438 | 4.793 | -37.272 | -37.813 | 1.00 53.65 | C |
| ATOM | 1636 | CB | THR | A | 438 | 4.211 | 38.637 | 37.456 | 1.00 62.06 | C |
| ATOM | 1637 | OG1 | THR | A | 438 | 3.432 | -38.526 | -36.256 | 1.00 64.51 | O |
| ATOM | 1638 | CG2 | THR | A | 438 | 5.311 | -39.603 | -37.190 | 1.00 67.52 | C |
| ATOM | 1639 | C | THR | A | 438 | 5.382 | -37.268 | -39.214 | 1.00 55.70 | C |
| ATOM | 1640 | O | THR | A | 438 | 6.607 | -37.314 | -39.381 | 1.00 62.54 | O |
| ATOM | 1641 | N | GLU | A | 439 | 4.531 | 37.201 | 40.230 | 1.00 58.80 | N |
| ATOM | 1642 | CA | GLU | A | 439 | 5.025 | -36.972 | -41.595 | 1.00 58.26 | C |
| ATOM | 1643 | CB | GLU | A | 439 | 3.883 | -36.852 | -42.591 | 1.00 60.07 | C |
| ATOM | 1644 | CG | GLU | A | 439 | 3.358 | -38.193 | -43.067 | 1.00 68.73 | C |
| ATOM | 1645 | CD | GLU | A | 439 | 2.142 | -38.045 | -43.942 | 1.00 73.41 | C |

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ATOM   1646  OE1 GLU A 439       2.305 -37.861 -45.186  1.00 70.86           O
ATOM   1647  OE2 GLU A 439       1.027 -38.109 -43.365  1.00 73.97           O
ATOM   1648  C   GLU A 439       5.878 -35.728 -41.623  1.00 59.04           C
ATOM   1649  O   GLU A 439       6.817 -35.646 -42.406  1.00 60.59           O
ATOM   1650  N   LEU A 440       5.546 -34.770 -40.749  1.00 63.30           N
ATOM   1651  CA  LEU A 440       6.360 -33.577 -40.550  1.00 65.21           C
ATOM   1652  CB  LEU A 440       5.616  32.565  39.684  1.00 66.60           C
ATOM   1653  CG  LEU A 440       4.981 -31.330 -40.334  1.00 64.16           C
ATOM   1654  CD1 LEU A 440       4.945 -31.373 -41.860  1.00 59.95           C
ATOM   1655  CD2 LEU A 440       3.592 -31.107 -39.749  1.00 69.64           C
ATOM   1656  C   LEU A 440       7.753 -33.917 -40.003  1.00 65.04           C
ATOM   1657  O   LEU A 440       8.742 -33.689 -40.688  1.00 75.49           O
ATOM   1658  N   ARG A 441       7.837 -34.514 -38.816  1.00 61.14           N
ATOM   1659  CA  ARG A 441       9.137 -34.940 -38.286  1.00 62.28           C
ATOM   1660  CB  ARG A 441       9.016 -35.823 -37.043  1.00 56.38           C
ATOM   1661  CG  ARG A 441       8.140 -35.244 -35.961  1.00 59.09           C
ATOM   1662  CD  ARG A 441       8.701 -33.998 -35.295  1.00 54.25           C
ATOM   1663  NE  ARG A 441       7.984  33.868  34.036  1.00 54.02           N
ATOM   1664  CZ  ARG A 441       8.517 -34.168 -32.862  1.00 50.03           C
ATOM   1665  NH1 ARG A 441       7.804 -34.096 -31.765  1.00 46.11           N
ATOM   1666  NH2 ARG A 441       9.777 -34.542 -32.798  1.00 55.41           N
ATOM   1667  C   ARG A 441       9.942 -35.684 -39.310  1.00 61.22           C
ATOM   1668  O   ARG A 441      11.156 -35.543 -39.364  1.00 70.19           O
ATOM   1669  N   THR A 442       9.277 -36.499 -40.110  1.00 62.64           N
ATOM   1670  CA  THR A 442      10.004 -37.257 -41.119  1.00 70.69           C
ATOM   1671  CB  THR A 442       9.131 -38.313 -41.822  1.00 71.74           C
ATOM   1672  OG1 THR A 442       7.764 -38.112 -41.455  1.00 80.59           O
ATOM   1673  CG2 THR A 442       9.526 -39.687 -41.371  1.00 74.92           C
ATOM   1674  C   THR A 442      10.718  36.343  42.118  1.00 67.80           C
ATOM   1675  O   THR A 442      11.923 -36.466 -42.280  1.00 75.79           O
ATOM   1676  N   ALA A 443      10.002 -35.406 -42.739  1.00 61.80           N
ATOM   1677  CA  ALA A 443      10.593 -34.563 -43.776  1.00 65.25           C
ATOM   1678  CB  ALA A 443       9.565 -33.579 -44.325  1.00 72.69           C
ATOM   1679  C   ALA A 443      11.850 -33.832 -43.290  1.00 66.39           C
ATOM   1680  O   ALA A 443      12.665 -33.371 -44.096  1.00 66.41           O
ATOM   1681  N   ASN A 444      11.997 -33.746 -41.970  1.00 63.69           N
ATOM   1682  CA  ASN A 444      13.191 -33.204 -41.338  1.00 63.80           C
ATOM   1683  CB  ASN A 444      12.952 -33.003 -39.837  1.00 66.70           C
ATOM   1684  CG  ASN A 444      12.706 -31.549 -39.468  1.00 69.12           C
ATOM   1685  OD1 ASN A 444      12.919  30.642  40.267  1.00 78.39           O
ATOM   1686  ND2 ASN A 444      12.278 -31.322 -38.247  1.00 72.52           N
ATOM   1687  C   ASN A 444      14.477 -33.996 -41.557  1.00 65.88           C
ATOM   1688  O   ASN A 444      15.489 -33.689 -40.943  1.00 71.85           O
ATOM   1689  N   HIS A 445      14.442 -35.002 -42.428  1.00 74.09           N
ATOM   1690  CA  HIS A 445      15.634 -35.760 -42.777  1.00 78.71           C
ATOM   1691  CB  HIS A 445      15.456 -37.216 -42.379  1.00 90.40           C
```

[1919]

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| ATOM | 1692 | CG | HIS | A | 445 | 14.916 | -38.102 | -43.486 | 1.00 99.18 | C |
| ATOM | 1693 | ND1 | HIS | A | 445 | 15.596 | -39.164 | -43.958 | 1.00100.65 | N |
| ATOM | 1694 | CE1 | HIS | A | 445 | 14.882 | -39.752 | -44.937 | 1.00112.37 | C |
| ATOM | 1695 | NE2 | HIS | A | 445 | 13.736 | -39.063 | -45.092 | 1.00105.91 | N |
| ATOM | 1696 | CD2 | HIS | A | 445 | 13.724 | 38.043 | 44.213 | 1.00106.09 | C |
| ATOM | 1697 | C | HIS | A | 445 | 15.954 | -35.621 | -44.243 | 1.00 87.44 | C |
| ATOM | 1698 | O | HIS | A | 445 | 17.120 | -35.468 | -44.617 | 1.00 97.42 | O |
| ATOM | 1699 | N | HIS | A | 446 | 14.917 | -35.672 | -45.082 | 1.00 92.78 | N |
| ATOM | 1700 | CA | HIS | A | 446 | 15.026 | -35.477 | -46.538 | 1.00 95.68 | C |
| ATOM | 1701 | CB | HIS | A | 446 | 13.779 | 35.991 | 47.248 | 1.00 93.64 | C |
| ATOM | 1702 | C | HIS | A | 446 | 15.252 | -34.034 | -46.898 | 1.00 93.63 | C |
| ATOM | 1703 | O | HIS | A | 446 | 15.743 | -33.731 | -47.980 | 1.00 97.93 | O |
| ATOM | 1704 | N | HIS | A | 447 | 14.848 | -33.135 | -46.004 | 1.00 97.08 | N |
| ATOM | 1705 | CA | HIS | A | 447 | 15.281 | -31.743 | -46.026 | 1.00 99.16 | C |
| ATOM | 1706 | CB | HIS | A | 447 | 14.078 | -30.780 | -45.818 | 1.00100.70 | C |
| ATOM | 1707 | CG | HIS | A | 447 | 14.336 | -29.293 | -46.174 | 1.00 97.57 | C |
| ATOM | 1708 | ND1 | HIS | A | 447 | 15.459 | -28.625 | -45.827 | 1.00100.29 | N |
| ATOM | 1709 | CE1 | HIS | A | 447 | 15.369 | -27.339 | -46.243 | 1.00 95.32 | C |
| ATOM | 1710 | NE2 | HIS | A | 447 | 14.172 | -27.170 | -46.830 | 1.00 88.39 | N |
| ATOM | 1711 | CD2 | HIS | A | 447 | 13.503 | -28.344 | -46.795 | 1.00 97.92 | C |
| ATOM | 1712 | C | HIS | A | 447 | 16.236 | -31.750 | -44.870 | 1.00 96.88 | C |
| ATOM | 1713 | O | HIS | A | 447 | 16.042 | -31.045 | -43.885 | 1.00102.68 | O |
| ATOM | 1714 | N | ALA | A | 448 | 17.259 | 32.602 | 44.966 | 1.00100.72 | N |
| ATOM | 1715 | CA | ALA | A | 448 | 18.356 | -32.646 | -43.988 | 1.00106.39 | C |
| ATOM | 1716 | CB | ALA | A | 448 | 19.713 | -32.625 | -44.697 | 1.00107.12 | C |
| ATOM | 1717 | C | ALA | A | 448 | 18.241 | -31.484 | -43.008 | 1.00106.92 | C |
| ATOM | 1718 | O | ALA | A | 448 | 17.702 | -31.658 | -41.903 | 1.00 94.38 | O |
| ATOM | 1719 | N | GLU | A | 449 | 18.740 | -30.313 | -43.431 | 1.00105.12 | N |
| ATOM | 1720 | CA | GLU | A | 449 | 18.495 | -29.044 | -42.748 | 1.00100.79 | C |
| ATOM | 1721 | CB | GLU | A | 449 | 19.456 | -28.884 | -41.554 | 1.00 94.59 | C |
| ATOM | 1722 | CG | GLU | A | 449 | 18.991 | -29.609 | -40.282 | 1.00101.78 | C |
| ATOM | 1723 | CD | GLU | A | 449 | 19.497 | -29.013 | -38.963 | 1.00109.32 | C |
| ATOM | 1724 | OE1 | GLU | A | 449 | 19.711 | -27.787 | -38.875 | 1.00104.34 | O |
| ATOM | 1725 | OE2 | GLU | A | 449 | 19.658 | -29.780 | -37.983 | 1.00112.57 | O |
| ATOM | 1726 | C | GLU | A | 449 | 18.505 | -27.813 | -43.702 | 1.00104.05 | C |
| ATOM | 1727 | O | GLU | A | 449 | 19.300 | 27.761 | 44.649 | 1.00106.57 | O |
| ATOM | 1728 | N | MET | A | 450 | 17.601 | -26.851 | -43.467 | 1.00 89.32 | N |
| ATOM | 1729 | CA | MET | A | 450 | 17.652 | -25.542 | -44.136 | 1.00 93.70 | C |
| ATOM | 1730 | CB | MET | A | 450 | 16.246 | -25.030 | -44.401 | 1.00 94.11 | C |
| ATOM | 1731 | CG | MET | A | 450 | 16.138 | -23.549 | -44.762 | 1.00 91.31 | C |
| ATOM | 1732 | SD | MET | A | 450 | 14.782 | -22.780 | -43.826 | 1.00 99.00 | S |
| ATOM | 1733 | CE | MET | A | 450 | 14.249 | -21.524 | -44.978 | 1.00104.95 | C |
| ATOM | 1734 | C | MET | A | 450 | 18.450 | -24.487 | -43.337 | 1.00100.86 | C |
| ATOM | 1735 | O | MET | A | 450 | 17.912 | -23.428 | -42.955 | 1.00 82.40 | O |
| ATOM | 1736 | N | LEU | A | 451 | 19.730 | -24.771 | -43.077 | 1.00103.14 | N |
| ATOM | 1737 | CA | LEU | A | 451 | 20.589 | -23.777 | -42.424 | 1.00103.77 | C |

[1965]

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ATOM   1738  CB  LEU A 451      21.541 -24.393 -41.396  1.00 89.77           C
ATOM   1739  CG  LEU A 451      21.120 -25.506 -40.441  1.00 90.84           C
ATOM   1740  CD1 LEU A 451      19.644  25.498  40.031  1.00 73.62           C
ATOM   1741  CD2 LEU A 451      21.526 -26.816 -41.092  1.00 93.42           C
ATOM   1742  C   LEU A 451      21.387 -22.980 -43.445  1.00114.92           C
ATOM   1743  O   LEU A 451      21.254 -23.187 -44.661  1.00110.68           O
ATOM   1744  N   MET A 452      22.218 -22.074 -42.923  1.00118.46           N
ATOM   1745  CA  MET A 452      22.966 -21.100 -43.717  1.00107.65           C
ATOM   1746  CB  MET A 452      23.969 -21.799 -44.644  1.00111.30           C
ATOM   1747  C   MET A 452      22.014 -20.195 -41.504  1.00106.81           C
ATOM   1748  O   MET A 452      21.446 -19.250 -43.947  1.00105.09           O
ATOM   1749  N   SER A 453      21.819 -20.527 -45.782  1.00117.80           N
ATOM   1750  CA  SER A 453      21.102 -19.685 -46.761  1.00122.52           C
ATOM   1751  CB  SER A 453      21.692 -19.920 -48.162  1.00121.72           C
ATOM   1752  OG  SER A 453      21.628 -21.284 -48.553  1.00114.02           O
ATOM   1753  C   SER A 453      19.573 -19.906 -46.671  1.00118.89           C
ATOM   1754  O   SER A 453      19.138  20.481  45.680  1.00134.67           O
ATOM   1755  N   TRP A 454      18.722 -19.490 -47.621  1.00112.65           N
ATOM   1756  CA  TRP A 454      18.996 -18.924 -48.952  1.00109.31           C
ATOM   1757  CB  TRP A 454      19.733 -17.581 -48.892  1.00106.13           C
ATOM   1758  CG  TRP A 454      19.274 -16.664 -47.784  1.00 96.11           C
ATOM   1759  CD1 TRP A 454      18.169  16.823  46.956  1.00 95.92           C
ATOM   1760  NE1 TRP A 454      18.066 -15.777 -46.075  1.00105.74           N
ATOM   1761  CE2 TRP A 454      19.048 -14.869 -46.281  1.00 92.90           C
ATOM   1762  CD2 TRP A 454      19.872 -15.377 -47.379  1.00 89.99           C
ATOM   1763  CE3 TRP A 454      20.965 -14.631 -47.798  1.00 86.91           C
ATOM   1764  CZ3 TRP A 454      21.246 -13.433 -47.136  1.00 77.69           C
ATOM   1765  CH2 TRP A 454      20.454 -12.970 -46.072  1.00 78.50           C
ATOM   1766  CZ2 TRP A 454      19.332 -13.667 -45.637  1.00 82.13           C
ATOM   1767  C   TRP A 454      19.632 -19.900 -49.922  1.00108.91           C
ATOM   1768  O   TRP A 454      19.559 -21.126 -49.748  1.00 98.17           O
ATOM   3485  O1  FMT X   1      -2.798 -41.152 -25.987  1.00 53.40           O
ATOM   3486  C   FMT X   1      -3.990 -40.894 -26.261  1.00 61.42           C
ATOM   3487  O2  FMT X   1      -4.400 -40.564 -27.518  1.00 65.83           O
ATOM   3488  O1  FMT X   2      -5.245 -44.027 -28.469  1.00 75.04           O
ATOM   3489  C   FMT X   2       4.653  43.216  29.174  1.00 70.78           C
ATOM   3490  O2  FMT X   2      -4.592 -43.444 -30.483  1.00 66.32           O
ATOM   3491  O1  FMT X   3      -7.393 -44.564 -27.272  1.00 89.05           O
ATOM   3492  C   FMT X   3      -7.419 -44.851 -26.079  1.00 95.81           C
ATOM   3493  O2  FMT X   3      -6.347 -44.676 -25.299  1.00 85.52           O
ATOM   3494  O1  FMT X   4       0.104  43.401  27.890  1.00 83.82           O
ATOM   3495  C   FMT X   4      -0.922 -42.820 -27.533  1.00 79.19           C
ATOM   3496  O2  FMT X   4      -1.273 -41.673 -28.109  1.00 73.77           O
ATOM   3509  O   HOH H   1      -0.025 -40.433 -30.245  0.50 53.19           O
ATOM   3511  O   HOH H   2       2.383 -34.329 -59.541  1.00 63.63           O
ATOM   3512  O   HOH H   3      17.876  -8.232 -45.202  1.00 50.92           O
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[2011]

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| ATOM | 3513 | O | HOH H | 4 | 23.564 | -14.407 | -46.075 | 1.00 63.41 | O |
| ATOM | 3514 | O | HOH H | 5 | -12.464 | -36.958 | -23.418 | 1.00 79.65 | O |
| ATOM | 3520 | O | HOH H | 6 | 20.925 | -11.121 | -41.216 | 1.00 53.50 | O |
| ATOM | 3521 | O | HOH H | 7 | 14.694 | -6.599 | -47.111 | 1.00 80.57 | O |
| ATOM | 3522 | O | HOH H | 8 | 20.186 | -9.607 | -44.541 | 1.00 46.88 | O |
| ATOM | 3523 | O | HOH H | 9 | 18.634 | -22.911 | -51.218 | 1.00 56.55 | O |
| ATOM | 3525 | O | HOH H | 10 | 15.435 | 24.628 | 69.491 | 1.00 95.44 | O |
| ATOM | 3526 | O | HOH H | 11 | 17.275 | -17.501 | -43.269 | 1.00 52.94 | O |
| ATOM | 3530 | O | HOH H | 12 | -8.123 | -38.910 | -21.499 | 1.00 72.83 | O |
| ATOM | 3593 | O4 | IVE F | 1 | 5.562 | -23.549 | -57.435 | 1.00 34.73 | O |
| ATOM | 3594 | C30 | IVE F | 1 | 6.253 | -23.361 | -56.483 | 1.00 42.27 | C |
| ATOM | 3595 | C25 | IVE F | 1 | 6.851 | -22.035 | -56.366 | 1.00 41.94 | C |
| ATOM | 3596 | C24 | IVE F | 1 | 5.830 | -21.162 | -57.036 | 1.00 45.13 | C |
| ATOM | 3597 | O6 | IVE F | 1 | 5.960 | -19.849 | -56.530 | 1.00 48.25 | O |
| ATOM | 3598 | C23 | IVE F | 1 | 5.888 | -21.173 | -58.561 | 1.00 41.83 | C |
| ATOM | 3599 | C28 | IVE F | 1 | 6.497 | -22.395 | -59.183 | 1.00 42.70 | C |
| ATOM | 3600 | O3 | IVE F | 1 | 6.887 | -22.052 | -60.508 | 1.00 44.36 | O |
| ATOM | 3601 | C27 | IVE F | 1 | 7.588 | -22.876 | -58.287 | 1.00 46.83 | C |
| ATOM | 3602 | C29 | IVE F | 1 | 8.178 | -24.237 | -58.349 | 1.00 42.29 | C |
| ATOM | 3603 | C26 | IVE F | 1 | 7.967 | 22.092 | 57.317 | 1.00 42.50 | C |
| ATOM | 3604 | C21 | IVE F | 1 | 4.454 | -21.635 | -56.814 | 1.00 47.17 | C |
| ATOM | 3605 | C22 | IVE F | 1 | 3.880 | -22.126 | -58.097 | 1.00 48.41 | C |
| ATOM | 3606 | O2 | IVE F | 1 | 4.564 | -21.300 | -59.018 | 1.00 48.52 | O |
| ATOM | 3607 | C20 | IVE F | 1 | 3.737 | -21.615 | -55.680 | 1.00 52.89 | C |
| ATOM | 3608 | C19 | IVE F | 1 | 4.066 | 21.170 | 54.329 | 1.00 52.54 | C |
| ATOM | 3609 | C18 | IVE F | 1 | 3.070 | -21.492 | -53.519 | 1.00 50.84 | C |
| ATOM | 3610 | C17 | IVE F | 1 | 2.811 | -21.291 | -52.048 | 1.00 46.67 | C |
| ATOM | 3611 | C31 | IVE F | 1 | 1.920 | -22.423 | -51.587 | 1.00 44.91 | C |
| ATOM | 3612 | C16 | IVE F | 1 | 3.931 | -21.428 | -51.088 | 1.00 45.07 | C |
| ATOM | 3613 | C15 | IVE F | 1 | 4.453 | -22.798 | -51.161 | 1.00 43.49 | C |
| ATOM | 3614 | C46 | IVE F | 1 | 5.807 | -23.099 | -50.643 | 1.00 47.11 | C |
| ATOM | 3615 | C14 | IVE F | 1 | 3.759 | -23.799 | -51.649 | 1.00 34.92 | C |
| ATOM | 3616 | C13 | IVE F | 1 | 4.490 | 25.104 | 51.616 | 1.00 40.02 | C |
| ATOM | 3617 | C12 | IVE F | 1 | 5.892 | -24.866 | -52.109 | 1.00 40.15 | C |
| ATOM | 3618 | O1 | IVE F | 1 | 6.440 | -26.057 | -52.591 | 1.00 41.50 | O |
| ATOM | 3619 | C8 | IVE F | 1 | 7.794 | -25.799 | -52.731 | 1.00 41.58 | C |
| ATOM | 3620 | O | IVE F | 1 | 8.512 | -26.984 | -52.915 | 1.00 42.09 | O |
| ATOM | 3621 | C4 | IVE F | 1 | 9.767 | 26.790 | 52.353 | 1.00 38.79 | C |
| ATOM | 3622 | C2 | IVE F | 1 | 9.368 | -26.942 | -50.936 | 1.00 35.80 | C |
| ATOM | 3623 | C1 | IVE F | 1 | 10.587 | -27.145 | -50.096 | 1.00 40.97 | C |
| ATOM | 3624 | C | IVE F | 1 | 11.476 | -25.994 | -50.449 | 1.00 42.24 | C |
| ATOM | 3625 | C3 | IVE F | 1 | 8.424 | -28.113 | -50.913 | 1.00 39.75 | C |
| ATOM | 3626 | C5 | IVE F | 1 | 10.204 | -25.374 | -52.596 | 1.00 35.48 | C |
| ATOM | 3627 | C47 | IVE F | 1 | 11.705 | -25.188 | -52.585 | 1.00 36.77 | C |
| ATOM | 3628 | C6 | IVE F | 1 | 9.586 | -24.572 | -51.505 | 1.00 38.03 | C |
| ATOM | 3629 | C7 | IVE F | 1 | 8.164 | 25.062 | 51.471 | 1.00 36.96 | C |

[2057]

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ATOM   3630  C9  IVE F   1       8.027 -24.961 -53.950  1.00 42.04           C
ATOM   3631  C11 IVE F   1       5.784 -23.950 -53.301  1.00 43.98           C
ATOM   3632  C10 IVE F   1       6.927 -23.989 -54.303  1.00 48.72           C
ATOM   3633  05  IVE F   1       6.450 -24.416 -55.545  1.00 45.48           O
ATOM   3634  07  IVE F   1       3.180 -21.459 -49.920  1.00 44.35           O
ATOM   3635  C32 IVE F   1       3.919 -20.960 -48.865  1.00 44.67           C
ATOM   3636  C33 IVE F   1       5.400 -20.975 -48.789  1.00 36.88           C
ATOM   3637  C34 IVE F   1       5.557 -19.975 -47.667  1.00 47.38           C
ATOM   3638  013 IVE F   1       6.818 -19.417 -47.765  1.00 48.17           O
ATOM   3639  C45 IVE F   1       7.570 -20.231 -48.627  1.00 54.34           C
ATOM   3640  C35 IVE F   1       4.576 -18.865 -47.897  1.00 46.83           C
ATOM   3641  C36 IVE F   1       3.445 -19.589 -48.449  1.00 40.88           C
ATOM   3642  C37 IVE F   1       2.045 -19.107 -48.138  1.00 37.66           C
ATOM   3643  08  IVE F   1       3.367 -20.712 -47.614  1.00 45.84           O
ATOM   3644  09  IVE F   1       4.079 -18.406 -46.691  1.00 56.29           O
ATOM   3645  C38 IVE F   1       5.114 -17.919 -45.898  1.00 44.61           C
ATOM   3646  C39 IVE F   1       4.492 -16.762 -45.173  1.00 42.48           C
ATOM   3647  C40 IVE F   1       4.874 -15.387 -45.689  1.00 50.96           C
ATOM   3648  012 IVE F   1       3.737 -14.578 -45.832  1.00 55.04           O
ATOM   3649  C44 IVE F   1       4.181 -13.391 -46.446  1.00 58.46           C
ATOM   3650  C41 IVE F   1       5.504 -15.371 -47.042  1.00 49.52           C
ATOM   3651  011 IVE F   1       6.895 -15.337 -46.846  1.00 44.10           O
ATOM   3652  C42 IVE F   1       5.266 -16.684 -47.674  1.00 54.85           C
ATOM   3653  010 IVE F   1       6.039 -17.467 -46.827  1.00 39.32           O
ATOM   3654  C43 IVE F   1       5.796 -16.638 -49.094  1.00 59.34           C
END。
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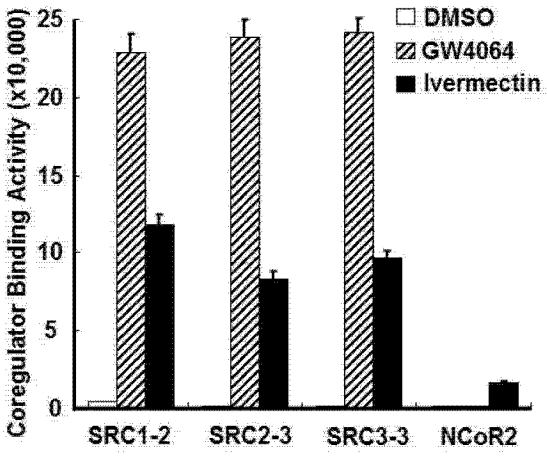
Coregulator Binding Activity (x10,000)
25
20
15
10
5
0
DMSO
GW4064
Ivermectin
SRC1-2
SRC2-3
SRC3-3
NCoR2

图 1

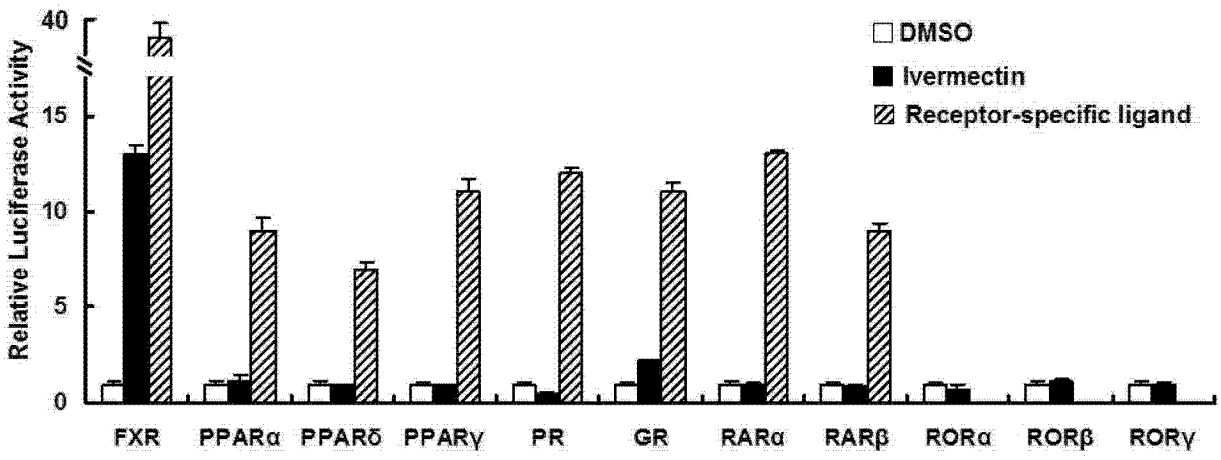
Relative Luciferase Activity
40
15
10
5
0
DMSO
Ivermectin
Receptor-specific ligand
FXR
PPARα
PPARδ
PPARγ
PR
GR
RARα
RARβ
RORα
RORβ
RORγ

图 2

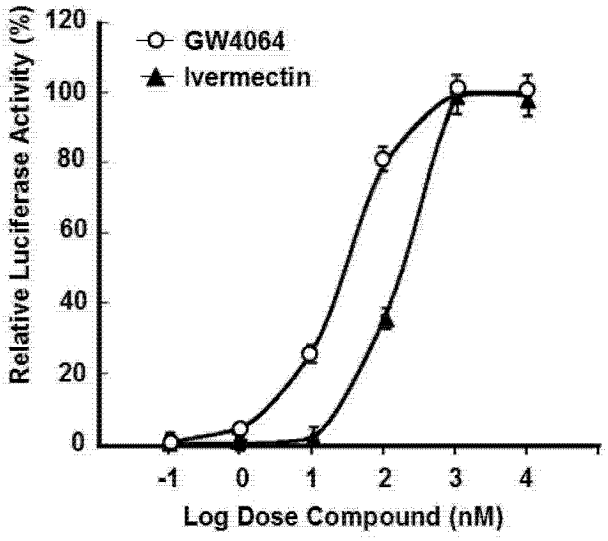
Relative Luciferase Activity (%)
120
100
80
60
40
20
0
GW4064
Ivermectin
-1
0
1
2
3
4
Log Dose Compound (nM)

图 3

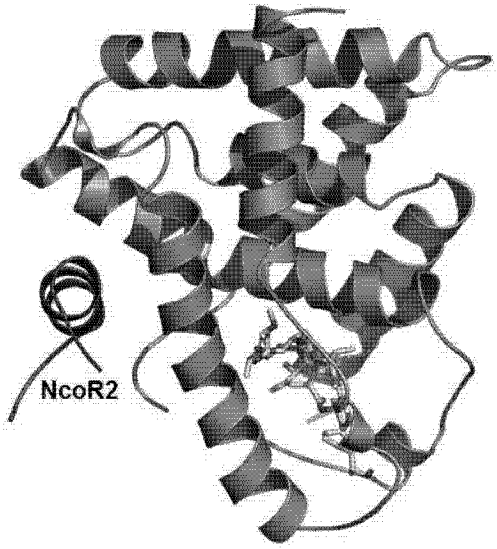
NcoR2

图 4

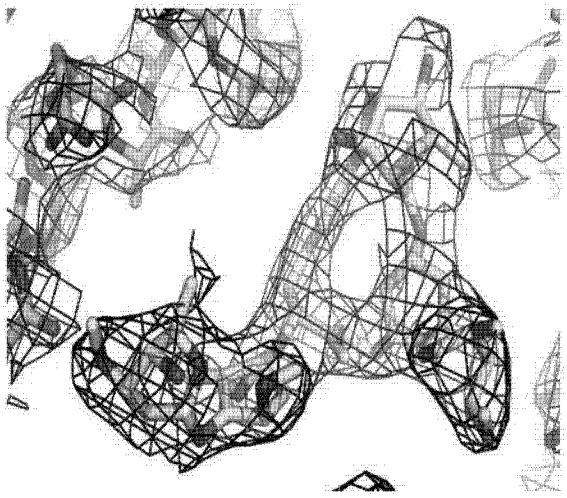

图 5

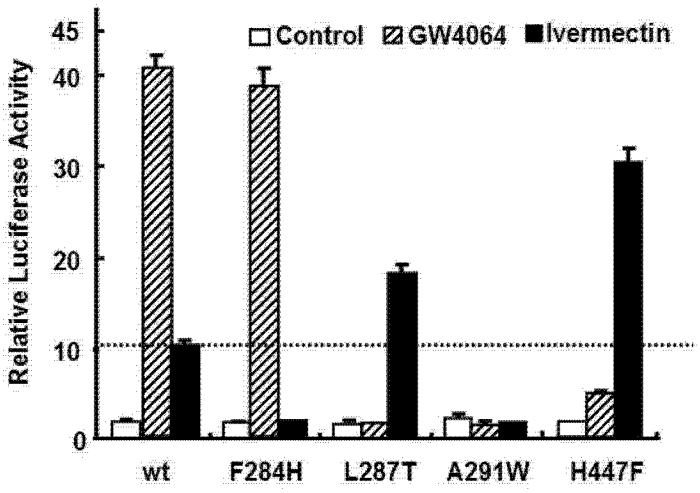


图 6

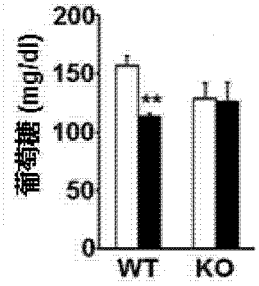


图 7

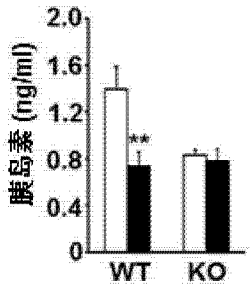


图 8

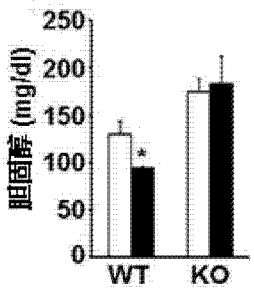


图 9

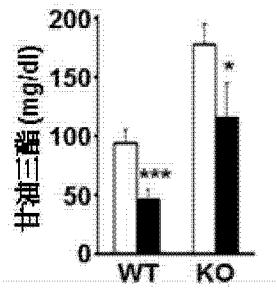


图 10

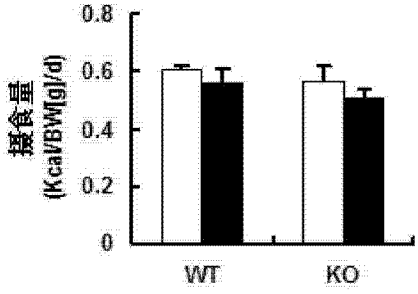


图 11

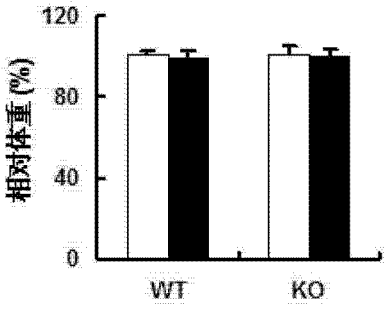


图 12

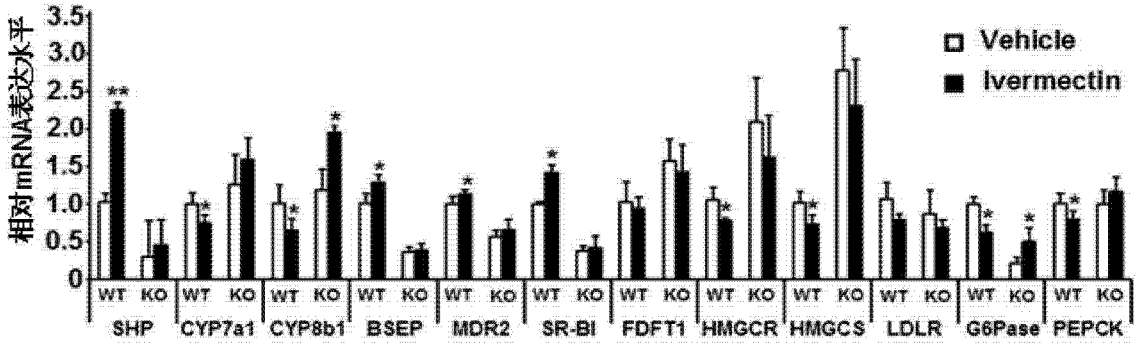


图 13

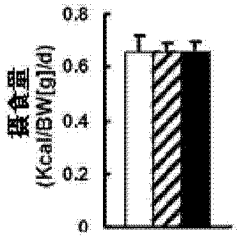


图 14

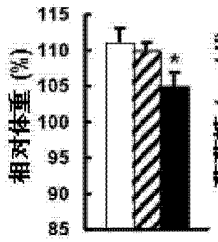


图 15

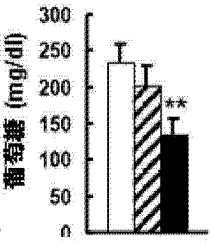


图 16

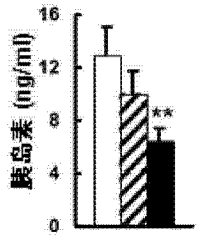


图 17

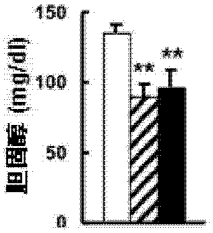


图 18

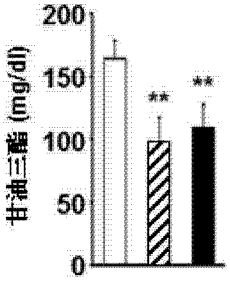


图 19

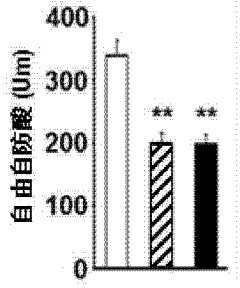


图 20

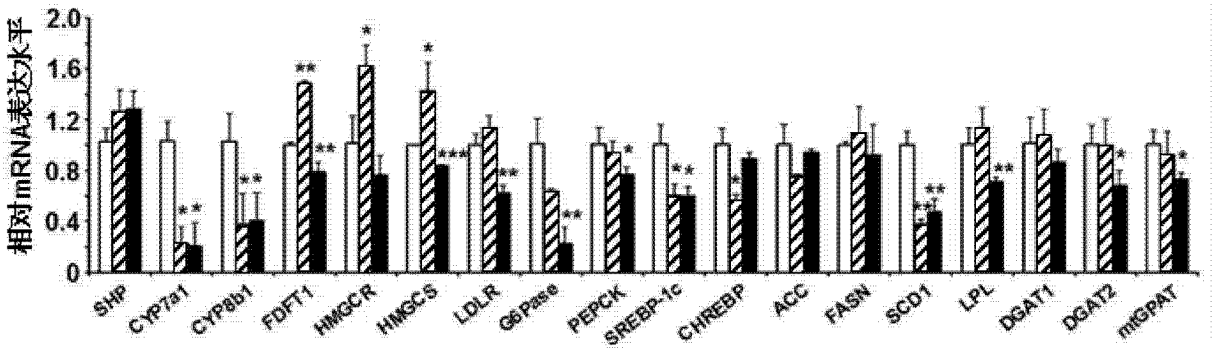


图 21

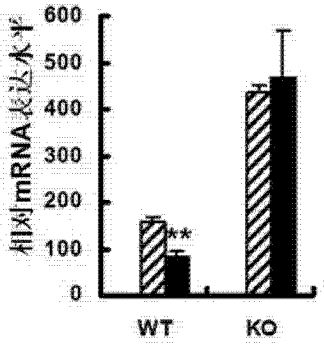


图 22

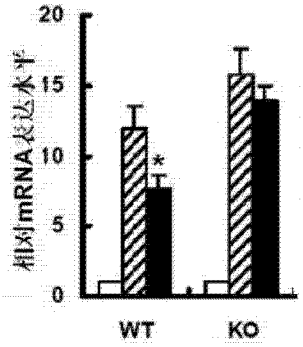


图 23

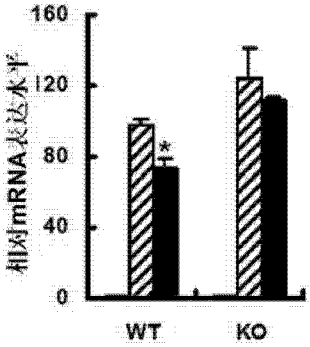


图 24

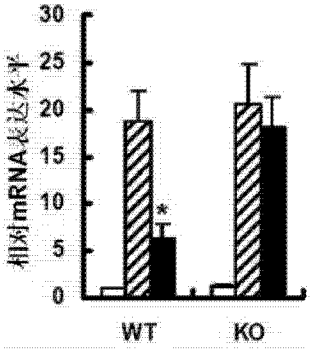


图 25

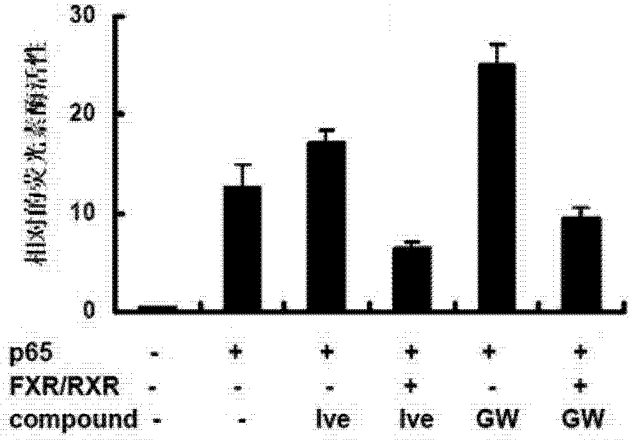


图 26

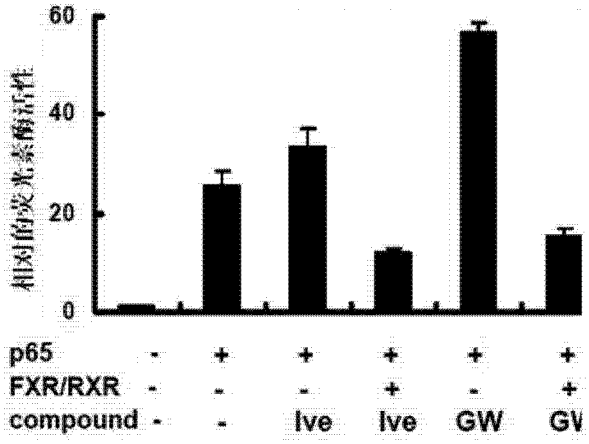
60
40
20
0
相对的荧光素酶活性
p65 - + + + + +
FXR/RXR - - - + - +
compound - - Ive Ive GW GV

图 27

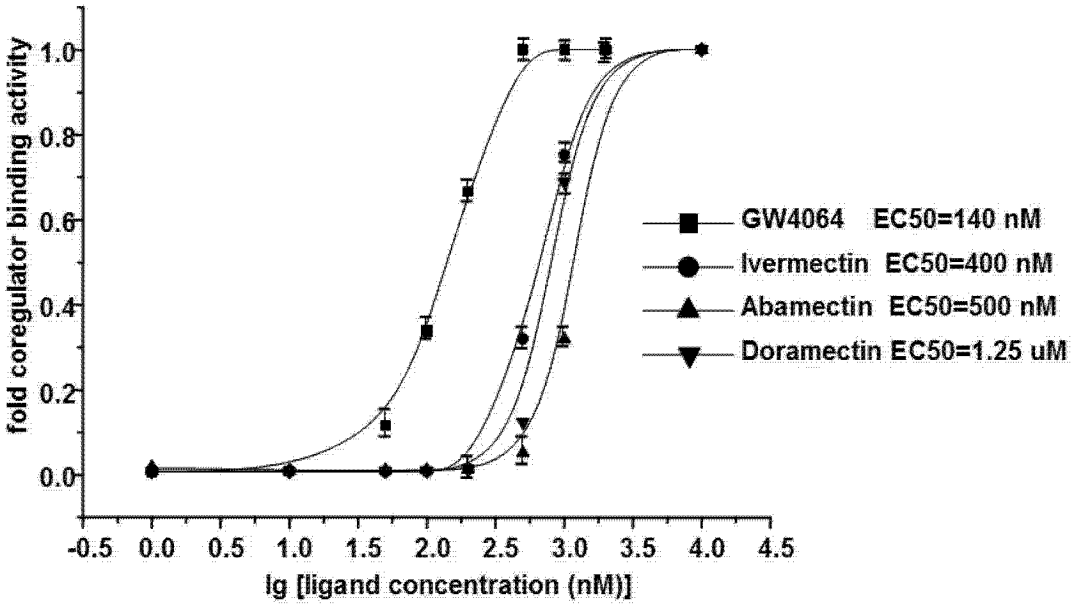
fold coregulator binding activity
1.0
0.8
0.6
0.4
0.2
0.0
-0.5 0.0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5
lg [ligand concentration (nM)]
GW4064 EC50=140 nM
Ivermectin EC50=400 nM
Abamectin EC50=500 nM
Doramectin EC50=1.25 uM

图 28

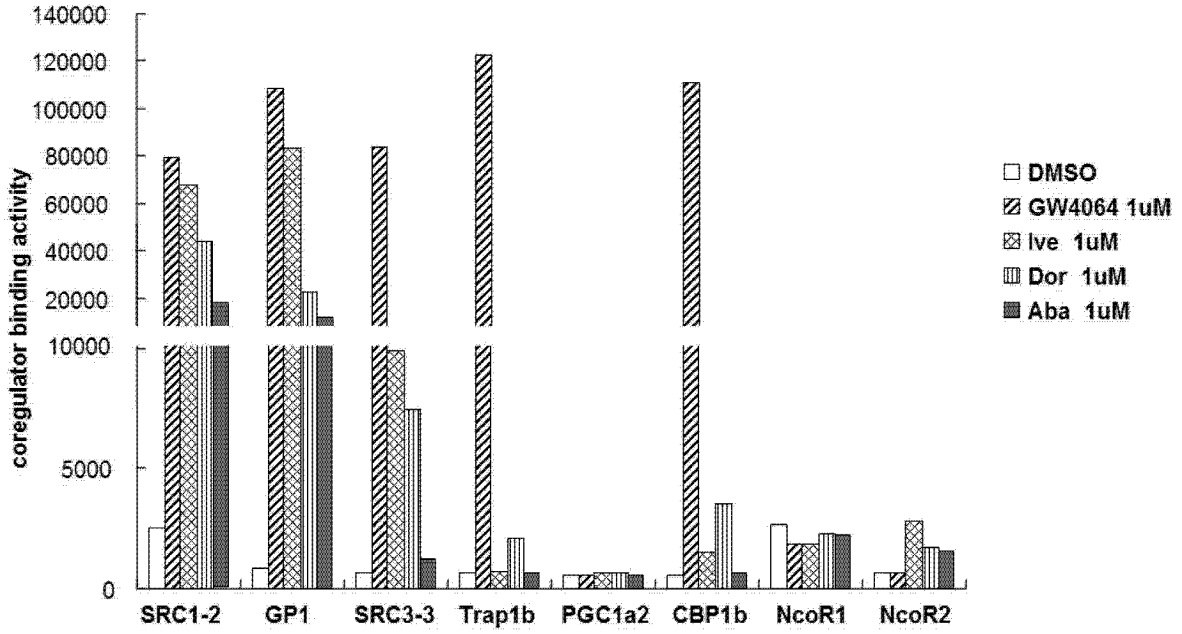
140000
120000
100000
80000
60000
40000
20000
10000
5000
0
coregulator binding activity
SRC1-2
GP1
SRC3-3
Trap1b
PGC1a2
CBP1b
NcoR1
NcoR2
DMSO
GW4064 1uM
Ive 1uM
Dor 1uM
Aba 1uM

图 29