高等学校化学学报 2008, 29(7) 1432-1437 DOI: ISSN: 0251-0790 CN: 22-1131/O6

论文

用分子对接方法研究HIV-1整合酶与病毒DNA的结合模式

胡建平[1,2], 柯国涛[1], 常珊[1], 陈慰祖[1], 王存新[1]

1. 北京工业大学生命科学与生物工程学院, 北京 100124;
2. 乐山师范学院化学与生命科学系, 乐山 614004

摘要:

用分子对接方法研究了HIV-1整合酶(Integrase, IN)二聚体与3' 端加工(3' Processing, 3'-P)前的8 bp及27 bp病毒DNA的相互作用, 并获得IN与27 bp病毒DNA的特异性结合模式. 模拟结果表明, IN有特异性DNA结合区和非特异性DNA结合区; IN二聚体B链的K14, R20, K156, K159, K160, K186, K188, R199和A链的K219, W243, K244, R262, R263是IN结合病毒DNA的关键残基; 并从结构上解释了能使IN发挥活性的病毒DNA的最小长度是15 bp. 通过分析结合能发现, IN与DNA稳定结合的主要因素是非极性相互作用, 而关键残基与病毒DNA相互识别主要依赖于极性相互作用. 模拟结果与实验数据较吻合.

关键词: HIV-1整合酶 病毒DNA 分子对接 结合模式 药物分子设计

Studies on the Binding Modes of HIV-1 Integrase with Viral DNA *via* Molecular Docking Method

HU Jian-Ping[1,2], KE Guo-Tao[1], CHANG Shan[1], CHEN Wei-Zu[1], WANG Cun-Xin[1]*

1. College of Life Science and Biological Bioengineering, Beijing University of Technology, Beijing 100022, China;
2. Department of Chemistry and Life Science, Leshan Normal University, Leshan 614004, China

Abstract:

HIV-1 integrase(IN) integrates the viral DNA into the host cell chromosome, however, the binding mode of IN with the viral DNA and the integration mechanism remain unclear. In this paper, molecular docking method was used to investigate the interactions of HIV-1 IN dimer with the 8 bp and 27 bp segments of viral DNA before the 3' processing(3'-P) reaction, and the specific binding mode between IN and its substrate 27 bp segments of viral DNA was obtained. The results show that IN has one specific DNA-binding region and another non-specific DNA-binding region. The key residues for IN dimer binding with viral DNA are K14, R20, K156, K159, K160, K186, K188, R199 residues in chain B and K219, W243, K244, R262, R263 residues in chain A. The explanation for the minimum length of 15 bp viral DNA to activate IN was given on the basis of the docked complex structure. Through the analysis of the binding energy, it was found that non-polar interactions are the principal factor favoring the binding between IN and DNA; whereas, the stable association of viral DNA with the key residues are mainly driven by polar interactions. The simulation results basically agree with the experimental data, which provide us with some structural information for the drug design on the basis of the structure of HIV-1 IN.

Keywords: HIV-1 integrase Viral DNA Molecular docking Binding mode Drug molecule design

收稿日期 2007-09-21 修回日期 1900-01-01 网络版发布日期

DOI:

基金项目:

通讯作者: 王存新

作者简介:

参考文献：

1. Engelman A., Mizuuchi K., Craigie R.. Cell[J], 1991, 67: 1211—1221
2. Chow S. A.. Methods[J], 1997, 12: 306—317
3. Gallay P., Swingler S., Song J., *et al*.. Cell[J], 1995, 83: 569—576
4. Chen J. C., Krucinski J., Miercke L. J., *et al*.. Proc. Nat.l Acad. Sci.[J], 2000, 97: 8233—8238
5. Luca L. D., Pedretti A., Vistoli G., *et al*.. Biochem. Biophys. Res. Commun.[J], 2003, 310: 1083—1088
6. Esposito D., Craigie R.. EMBO J.[J], 1998, 17: 5832—5843
7. Espeseth A. S., Felock P., Wolfe A.. Proc. Natl. Acad. Sci.[J], 2000, 97: 11244—11249
8. Lee S. P., Kim H. G., Censullo M. L., *et al*.. Biochemistry[J], 1995, 34: 10205—10214
9. Vink C., van Gent D. C., Elgersma Y., *et al*.. J. Virol.[J], 1991, 65: 4636—4644
10. Petrey D., Xiang Z. X., Tang C. L., *et al*.. Protein-Struct. Funct. Genet.[J], 2003, 53: 430—435
11. Goldgur Y., Craigie R., Cohen G. H., *et al*.. Proc. Natl. Acad. Sci.[J], 1996, 96: 13040—13043
12. Goldgur Y., Dyda F., Hickman A. B., *et al*.. Proc. Natl. Acad. Sci.[J], 1998, 95: 9150—9154
13. Bujacz G., Jaskolski M., Alexandratos J., *et al*.. Structure[J], 1996, 4: 89—96
14. Wang J. Y., Ling H., Yang W., *et al*.. EMBO J.[J], 2001, 20: 7333—7343
15. Cai M., Zheng R., Caffrey M., *et al*.. Nat. Struct. Biol.[J], 1997, 4: 567—577
16. SYBYL 6.5[CP], St. Louis: Tripos Inc., 1699 South Hanley, 1999
17. Mandell J. G., Roberts V. A., Pique M. E., *et al*.. Prot. Eng.[J], 2001, 14(2): 105—113
18. Baker N. A., Sept D., Joseph S., *et al*.. Proc. Natl. Acad. Sci.[J], 2001, 98: 10037—10041
19. Kollman P. A., Massova I., Reyes C., *et al*.. Acc. Chem. Res.[J], 2000, 33: 889—897
20. Wang W., Donini O., Reyes C., *et al*.. Annu. Rev. Biophys. Biomol. Struct.[J], 2001, 30: 211—243
21. Tsui V., Case D. A.. Biopolymers[J], 2001, 56: 275—291
22. Simonson T.. Curr. Opin. Struct. Biol.[J], 2001, 11: 243—252
23. Bashford D., Case D. A.. Ann. Rev. Phys. Chem.[J], 2000, 51: 129—152
24. Still W. C., Tempczyk A., Hawley R. C., *et al*.. J. Am. Chem. Soc.[J], 1990, 112: 6127—6129
25. Weiser J., Shenkin P. S., Still W. C.. J. Comput. Chem.[J], 1999, 20: 217—230
26. Eijkelenboom A. P., Sprangers R., Hard K., *et al*.. Proteins[J], 1999, 36: 556—564
27. Zhu H. M., Chen W. Z., Wang C. X.. Bioorg. Medicinal Chem. Letter.[J], 2005, 15: 475—477
28. Karki R. G., Tang Y., Burke T. R. Jr., *et al*.. J. Comput.-Aided Mol. Design[J], 2004, 18(12): 739—760
29. Wang J. M., Cieplak P., Kollman P. A.. J. Comput. Chem.[J], 2000, 21: 1049—1074
30. Wang J., Wolf R. M., Caldwell J. W., *et al*.. J. Comput. Chem.[J], 2004, 25: 1157—1174
31. Wang C. X., Shi Y. Y., Zhou F., *et al*.. Proteins[J], 1993, 15: 5—9

本刊中的类似文章

1． 许伟,蔡萍,严明,许琳,欧阳平凯 .*Thermus thermophilus* 木糖异构酶与木糖醇的分子对接及模型分析[J]. 高等学校化学学报, 2007,28(5): 971-973
2．郑喜亮; 张红星; 孙家锺.双金属存在下整合酶和抑制剂5CITEP的分子对接研究[J]. 高等学校化学学报, 2006,27(7): 1298-1302
3． 肖勇军, 王建国, 刘幸海, 李永红, 李正名 .基于受体结构的AHAS抑制剂的设计、合成及生物活性[J]. 高等学校化学学报, 2007,28(7): 1280-
4．楚慧郢, 郑清川, 赵勇山, 张红星.人类2-氨基3-羧基粘康酸6-半醛脱羧酶(ACMSD)与底物及抑制剂作用模型的理论研究
[J]. 高等学校化学学报, 2008,29(12): 2398-2402
5．郑清川,吕绍武,赵勇山,牟颖,罗贵民,孙家锺 .GSH对两种谷胱甘肽过氧化物酶模拟物活性影响的研究[J]. 高等学校化学学报, 2008,29(12): 2337-2340
6．朱艳艳, 苏延伟, 漆遥, 谭宏伟, 王艳, 陈光巨.金属核酸酶及寡聚酰胺与双链DNA分子对接模式的理论研究[J]. 高等学校化学学报, 2009,30(4): 781-785

文章评论

序号	时间	反馈人	邮箱	标题	内容

1	2009-	reviewups	edfwen@163.com	sdweue

boots ugg 5825
shoes sale ugg su