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研究论文

Tobramycin与16S rRNA A位点复合物的分子动力学模拟

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摘要 采用分子动力学方法(Molecular dynamics, MD)对托普霉素(Tobramycin)与16S rRNA的A位点复合物的特异性识别机制进行了理论模拟研究, 模拟时间为3.6 ns. 结果表明, A位点中波动最大的部位是两个环外碱基A1492和A1493; tobramycin的环Ⅰ和环Ⅱ是其最保守的结构单元, 可能参与了Tobramycin与16S rRNA的A位点之间的特异性识别. 另外, 发现一个残存时间为3.6 ns的“结构化”水分子, 它桥接了Tobramycin环Ⅱ的N3与环Ⅰ的N6'之间的氢键, 稳定了Tobramycin的结构; Tobramycin周围水合密度较高的位点出现在环Ⅰ和环Ⅱ附近, 这也正是晶体结构中形成较多水媒介氢键及动力学模拟中结构化水分子出现的位置. 动力学模拟证实Tobramycin与16S rRNA间的结合是大量氢键及水分子相互作用的结果, 这有助于设计和开发以Tobramycin为基础, 具有高亲和力及特异性的16S rRNA抑制剂.

关键词 分子动力学 托普霉素 16S rRNA A 位点 水合密度

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Molecular Dynamics Simulation on the Complex of the Tobramycin and 16S rRNA A Site

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Abstract A 3.6 ns molecular dynamics simulation was carried out on the complex system of tobramycin and 16S rRNA in order to understand the speciality recognition mechanism between tobramycin and 16S rRNA at the molecular level. The results demonstrate that two looped out bases(A1492 and A1493) of the A site is the flexible part, while ring Ⅰ and ring Ⅱ of tobramycin are the most conservative elements. Moreover, ring Ⅰ and ring Ⅱ of tobramycin may be function conservative unit which may participate in the specificity recognition for tobramycin binding to the 16S rRNA A site. In addition, a structural water molecule was detected during the whole MD simulation trajectory, which bridged the contacts between ring Ⅱ (N3)and ring Ⅰ (N6') of tobramycin and enhanced the rigid of tobramycin structure. There is one hydration site with the higher water density in the vicinity of ring Ⅰ and ring Ⅱ of tobramycin. This result is consistent with the crystal structure detected that the most water-medial hydrogen bonds were listed in the same situation. Our study illustrates that recognition mechanism between tobramycin and 16S rRNA A site was due to a few hydrogen bond and water molecule interactions, which play a great role in designing high affinity and speciality inhibitors of 16S rRNA A site based on tobramycin.

Key words Molecular dynamics; Tobramycin; 16S rRNA A site; Hydration density

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