

论文

Bcl-2蛋白抑制剂结合腔的性质分析

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摘要:

采用多重拷贝同时搜寻(MCSS)等方法对Bcl-2蛋白抑制剂结合腔进行分析. 结果显示, 结合腔可分成P1, L1, P2, P3和P4等5个区域, 其底部呈疏水性, 而P3部位不适合芳香性大基团的结合. 结合腔侧面和边缘处分布有可与配体形成除疏水以外作用的多个重要残基. MCSS计算得到的各种性质官能团在结合腔内的能量优势位置和取向能与已知结合模式的高活性抑制剂的重要基团位置吻合得较好.

关键词: Bcl-2蛋白 多重拷贝同时搜寻 抑制剂 合理设计

Property Analysis of Inhibitors-binding Site of Bcl-2 Protein

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Abstract:

Bcl-2 protein is a new target of anticancer drugs with a bright prospect now. The multiple copy simultaneous search(MCSS) methodology was used to analyze the inhibitors-binding site of Bcl-2. The results show that the inhibitors-binding site can be divided into five subsites(P1, L1, P2, P3, P4), the bottom of which is hydrophobic. And several important residues which can form interactions other than hydrophobic interactions distribute on the side and edge of the inhibitors-binding site. Energetically favorable positions and orientations of various functional groups determined by MCSS computing are

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consistent with these of important groups in high potent inhibitors, which can reversely guide the structure modification and novel design of inhibitors effectively.

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