武汉物数所理论交叉学术交流系列报告

第二一八期

报告题目：Key residues in TLR4-MD2 tetramer formation identified by free energy simulations

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报告内容： Toll-like receptors (TLRs) play a central role in both the innate and adaptive immune systems by recognizing pathogen-associated molecular patterns and inducing the release of the effector molecules of the immune system. The dysregulation of the TLR system may cause various autoimmune diseases and septic shock. A series of molecular dynamics simulations and free energy calculations were performed to investigate the ligand-free, lipopolysaccharide (LPS)-bound, and neoseptin3-bound $(TLR4\text{-}MD2)_2$ tetramers. Compared to earlier simulations done by others, our simulations showed that TLR4 structure was well maintained with stable interfaces. Free energy decomposition by molecular mechanics Poisson-Boltzmann surface area (MM-PBSA) method suggests critical roles that two hydrophobic clusters I85-L87-P88 and I124-L125-P127 of MD2, together with LPS and neoseptin3, may play in TLR4 activation. We propose that 1) direct contacts between TLR4 convex surface and LPS and neoseptin3 at the region around L442 significantly increase the binding and 2) binding of LPS and neoseptin3 in the central hydrophobic cavity of MD2 triggers burial of F126 and exposure of I85-L87-P88 that facilitate formation of $(TLR4\text{-}MD2)_2$ tetramer and activation of TLR4 system.

报告人简介： 段勇教授，美国加州大学戴维斯分校生物医学系教授。段勇教授的研究重点为理论与计算生物物理学和生物信息学等紧密联系的跨学科领域。主要包括：蛋白质折叠机制的计算机模拟研究；发展精确的描述分子体系动力学模拟的力场；与人类疾病相关的蛋白聚合研究；蛋白和配体的相互作用，G 蛋白偶连受体的动力学模拟等。作为AMBER分子力场的负责人，段勇教授领导多个校所研究小组发展和完善新一代分子力场。段勇教授已授在Science，PNAS及J. Am. Chem. Soc上发表论文100余篇，累计被引用超过13000次，H-index超过41.

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