2023年第九届华南结构生物学论坛暨医药合成生物产业创新大会

The 9th South China Structural Biology Symposium 2023 & Medicine Synthetic Biology Industry Innovation Convention

会议手册

2023年11月17日-19日

王雅凡

澳门大学 副教授

王雅凡教授现为澳门大学健康科学学院副教授、及澳门大学通识教育课程统筹人（科学于科技范畴）。她在加州大学圣迭戈分校获得学士、硕士及博士学位，后在纽约哥伦比亚大学从事博士后研究工作。在美期间，先后师从Gourisankar Ghosh教授（加州大学圣迭戈分校终身教授）和童亮教授（哥伦比亚大学William R. Kenan，Jr. Professor，美国科学促进会院士AAAS Fellow）。研究领域主要涉及核转录因子NF-κB介导的信号通路;该核转录因子参与免疫和炎症反应，细胞生长和凋亡等重要生命活动。其研究成果发表在世界一流同行评审杂志，如Molecular Cell, Cell Reports, eLife, Nucleic Acid Research 等。王教授还积极参与多项科普活动，现任澳门中小学生科技实践基地（STEM Center）科普联络教授、澳门科技发展基金中学生潜能拓展计划指定导师；并获澳门特区政府推荐为全国青少年科技创新大赛评审专家。

黄林

中山大学孙逸仙纪念医院 副研究员

黄林，中山大学孙逸仙纪念医院PI、分子医学专业博士生导师，中山大学“百人计划”引进中青年杰出人才。黄林博士长期从事非编码RNA结构与功能的研究。研究成果（共同）通讯/第一作者身份发表SCI论文20篇，17篇发表于2016年至2022年。包括Nature Chemical Biology1篇（最后通讯）、Nucleic Acids Research 8篇、Cell chemical biology 2篇等，其中六项研究成果被选为RNA杂志封面。

研究方向：1. 非编码RNA的结构与功能（核糖开关、核酶、致病微生物中未知功能非编码RNA）2. 非编码RNA在特定疾病的发生和发展过程中的作用及分子机制3. 生物信息RNA结构预测。

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B8 Structures of NF-κB p52-DNA complexes rationalize binding mechanisms and transcription activation

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Abstract:

The mammalian NF-κB p52:p52 homodimer together with its cofactor Bcl3 activates transcription of κB sites with a central G/C base pair (bp), while it is inactive toward κB sites with a central A/T bp. To understand the molecular basis for this unique property of p52, we have determined its structure in complex with a P-selectin(PSel)-κB DNA (5'-GGGGTGACCCC-3') (central bp is underlined) and variants changing the central bp to A/T or swapping the flanking bp. The structures reveal a nearly two-fold widened minor groove in the central region of the DNA as compared to all other currently available NF-κB-DNA complex structures, which have a central A/T bp. Microsecond molecular dynamics (MD) simulations of free DNAs and p52 bound complexes reveal that free DNAs exhibit distinct preferred conformations, and p52:p52 homodimer induces the least amount of DNA conformational changes when bound to the more transcriptionally active natural G/C-centric PSel-κB, but adopts closed conformation when bound to the mutant A/T and swap DNAs due to their narrowed minor grooves. Our binding assays further demonstrate that the fast kinetics favored by entropy is correlated with higher transcriptional activity. Overall, our studies have revealed a novel conformation for κB DNA in complex with NF-κB and pinpoint the importance of binding kinetics, dictated by DNA conformational and dynamic states, in controlling transcriptional activation for NF-κB.