Chinese Academy of Sciences

Key Lab for Biomedical Effects of Nanomaterials and Nanosafety

中科院纳米生物效应与安全性重点实验室

Nanosafety Lab. CAS

学术报告通知

CAS NS Forum (NO. 351)

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题　目：Tc toxin: a versatile weapon targeting mammals

时　间：2022 年 3月 10日 (星期四), 下午2：00

地　点：国家纳米科学中心，科研楼阶梯教室

主 持人：梁兴杰 研究员

摘要：

Toxin complex (also referred to as Tc toxin) is first identified in entomopathogenic bacteria. Typical Tc toxins are hetero-multimeric exotoxins composed of TcA, TcB and TcC subunits. High-resolution structures of example Tc toxins have been well documented, while the pathogenic roles and distribution of Tc toxins among different bacterial genera remain unclear.

We have performed a comprehensive genome-wide analysis, and established a database that includes 1,608 identified Tc loci. We found that TcCs conform to the architecture of typical polymorphic toxins, with C-terminal hypervariable regions encoding various toxic domains. Based on further analysis of Tc loci, a “two-level” evolutionary dynamics scenario is proposed for TcC homologues. TcA can form homopentamer that mediates the binding with receptors, thus contributing to the host tropism of Tc toxin. We therefore performed genome-wide CRISPR-Cas9 screens, and have validated glycans and sulfated glycosaminoglycans as Tc toxin receptors.

Based on these study, we further investigate the pathogenic role of Tc toxin with uncharacterized toxic domain as well as the different binding receptors of Tc toxin. In the present study, we found that PTC2, Tc toxin from P. luminescens W14, can induce ribotoxic stress response in various types of cells, which is mediated by the acetyltransferase activity. By systematically genome-wide screenings, we found that different TcAs can be recognized by different host factors. These results demonstrate that Tc toxins not only encode various toxic domains, but also harbor versatile host tropisms, implying that that Tc toxins represent an important versatile toxin superfamily with diverse pathogenic mechanisms.

个人简介：

宋楠，博士，副教授，特聘博导。2006年获山东大学学士学位，2012年取得清华大学博士学位，2012至2018年在军事医学研究院从事博士后研究，现任职于首都医科大学附属北京友谊医院。

长期从事病原微生物感染相关研究，近五年围绕细菌毒素自身性质及毒力作用等取得重要进展，包括:发现细菌毒素等通过翻译后修饰调控宿主固有免疫的作用机制；针对多种细菌毒素Tc toxin及eCIS的分布、进化机制进行分析，并建立开源数据库；发现多型性细菌毒素Tc toxin靶向宿主细胞的作用机制。以第一或通讯作者发表SCI论文 13 篇，包括Molecular Cell、Cell Reports、PLOS Pathogens等期刊，总影响因子超过90，单篇最高引用超200次。先后承担国家自然科学基金青年、面上项目等，并入选北京市医管中心“青苗”计划。

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