第 1184 回生物科学セミナー

日時：平成 30 年 2 月 9 日（金）18：00-19：00　理学部 3 号館 326 号室

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演題: CRISPR-associated nucleases: structures and mechanisms of genome defenders and editors.

In bacteria, CRISPR-Cas systems function as an adaptive genome defense pathway to provide resistance against molecular parasites such as viruses and other mobile genetic elements. Guided by short RNA molecules, these systems deploy CRISPR-associated nucleases to recognize and degrade invading nucleic acid elements. CRISPR-Cas systems are highly diverse and six major types have been identified thus far, each having a distinct mechanism of RNA-guided nucleic acid interference.

Our work focuses on studying the molecular mechanisms of CRISPR-associated nucleases. To this end, we previously determined the three-dimensional structures of the type II CRISPR-associated nuclease Cas9 in complex with a guide RNA and target DNA, revealing the atomic details of its DNA binding and cutting mechanisms. More recently, we have also studied the type V-specific DNA nuclease Cas12. Our studies provide a mechanistic framework for understanding the biological function of the enzymes and for the ongoing development of CRISPR-Cas genome editing technologies.

In contrast to type II and type V systems, type III CRISPR-Cas systems detect and degrade invasive genetic elements by an RNA-guided, RNA-targeting multisubunit interference complex that possesses dual RNase and DNase activities. The type III CRISPR-associated protein Csm6 additionally contributes to interference by functioning as a standalone ribonuclease. We recently showed that Csm6 proteins are activated through a cyclic oligoadenylate second messenger generated by the type III interference complex. These results point to a hitherto unprecedented mechanism for regulation of CRISPR interference that bears striking conceptual similarity to mammalian innate immune signaling.

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