New functions of UHRF1 in DNA methylation

Summary

DNA methylation is a key epigenetic mark involved in transcriptional regulation and genome stability in many eukaryotic species. This mark is essential for mammalian development and cellular survival, and is altered in many prevalent human diseases as well as during aging.

DNA methylation patterns are initially set up by "de novo" DNA methyltransferases. Then, at every subsequent cell division, the replicated DNA undergoes "maintenance" DNA methylation, involving the proteins DNMT1 and UHRF1. Despite their importance, the mechanisms of DNA methylation establishment and maintenance, and the underlying machinery, are still incompletely understood.

To elucidate the biological functions of UHRF1 and DNMT1 in DNA methylation and beyond, we have used the auxin-inducible degron (AID) system, which allows the rapid degradation of tagged proteins. As will be explained in the talk, this system has allowed us to show that UHRF1 has roles in DNA methylation besides stimulating DNMT1, and it has also helped us delineate the cellular response to loss of UHRF1 and/or DNMT1, with implications for cancer.