BİLKENT UNIVERSITY

MOLECULAR BIOLOGY AND GENETICS

DEPARTMENTAL SEMINAR

"Open and closed conformations of DNA methyltransferase-1 (Dnmt1) controls the maintenance DNA methylation in mammals"

Dr. Ahmet Can Berkyürek

Institute for Protein Research, Osaka University

The main objective of this study is to elucidate mechanistic aspects of the maintenance DNA methylation in mammals by using mouse proteins as a model. DNA methylation plays an essential role in development through regulating gene expression. DNA methyltransferase-1 (Dnmt1) faithfully propagates DNA methylation patterns to next generations during replication and is recruited to replicating region by its "replication foci targeting sequence" (RFTS). Interestingly, three-dimensional structure of Dnmt1 solved by our group exhibited that the RFTS was plugging the catalytic pocket and stabilized by four hydrogen bonds. For this, DNA cannot access the catalytic center, and thus the RFTS should be removed from the catalytic pocket for the active DNA methylation. To this end, we have analyzed biochemical and biophysical features of the maintenance DNA methylation and discovered two distinct mechanisms mediating the removal of the RFTS domain of Dnmt1 from the catalytic pocket.

Firstly, we have found that Dnmt1 with the RFTS domain exhibited a DNA length dependent methylation activity that might facilitate the initial loading of Dnmt1 to replication foci. Even though exact mechanism for DNA-length dependent function is not clear yet, we speculate that Dnmt1 might wrap the long DNA around itself. Additionally, the SRA domain of Uhrf1, which is a prerequisite factor for maintenance DNA methylation and selectively binds to hemi-methylated DNA, stimulated DNA methylation activity of Dnmt1 by interacting with the RFTS domain. Also, the interaction between the SRA and RFTS domains facilitated DNA accession to the catalytic center. From these results we propose that the SRA domain removes the RFTS domain from the catalytic pocket and handovers the DNA to the catalytic center of Dnmt1.

Date-Time : Friday, October 2, 2015 – at 13:40
Place : SBZ-14
Host : Serkan Göktuna