Oral presentation

Human PLD3 structure reveals insight into 5' exonuclease-mediated nucleic acid degradation

Yvette Roske

Max Delbrueck Centrum, Germany
yroske@mdc-berlin.de

While the mechanism of PLD phospholipase activity has been extensively characterized, not much is known about how PLDs bind and hydrolyze nucleic acids. Here, we determined the high-resolution crystal structure of the luminal N-glycosylated domain of human PLD3 in its apo- and single-stranded DNA-bound forms. PLD3 has a typical phospholipase fold and forms homodimers with two independent catalytic centers via a newly identified dimerization interface. The structure of PLD3 in complex with an ssDNA-derived thymidine product in the catalytic center provides insights into the substrate binding mode of nucleic acids in the PLD family. Our structural data suggest a mechanism for substrate binding and nuclease activity in the PLD family and provide the structural basis to design immunomodulatory drugs targeting PLD3.