Open Ph.D. projects

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Title of the research topic: ADP-ribosylation in DNA repair, cell division and cellular senescence

Description of the research topic: Poly-ADP-ribosylation (PARylation) is a posttranslational modification of proteins which may modify their activity, interactions, and subcellular localization. It is most intensive upon DNA damage: the poly (ADP-ribose) polymerase 1 (PARP1) is rapidly recruited to and activated by DNA strand breaks, and by PARylating itself and a variety of target proteins it initiates the DNA repair pathways. In addition, ADP-ribosylation is involved in various cellular processes, such as cell division and survival, or even exit from the cell cycle and promoting cell death. Our research goal is to characterize novel molecular pathways that are regulated by ADP-ribosylation and to understand their role in DNA replication and repair. Our current research focuses on a protein pair called POLE3 and POLE4, which are accessory subunits of DNA polymerase epsilon. Their absence sensitises human cancer cells to PARP1 inhibitors (PARPi), leading to cell cycle arrest, cell death or cellular senescence. Revealing the underlying molecular mechanisms improves our knowledge about the role of PARP1 in fundamental biological processes and may help expanding the of clinical use of PARPi.?