DBMR Research Conference

Seminar room EG050
Murtenstrasse 24, 3008 Bern

Date: **Friday, February 7, 2025, 11am – 12pm**

Title: **Processing of replication lesions during mitosis by the CIP2A-TOPBP1 complex**

Speaker: **Prof. Marcel van Vugt, University Medical Center, Department of Medical Oncology, University of Groningen, NL**

Bio: Marcel van Vugt trained in Medical Biology at the University of Utrecht (MSc, 2000) and did PhD training with René Medema on cell cycle regulation at the Netherlands Cancer Institute (Amsterdam, the Netherlands (2005). Subsequently, he performed post-doctoral training with Michael Yaffe at MIT, Cambridge, USA. Here, he studied DNA damage signalling in cancer and developed methods to predict novel kinase-substrate interactions based on mass-spectrometry data. After setting up an independent research group at the department of Medical Oncology of the UMCG (Groningen, the Netherlands) in 2009, he engaged in studying the cellular effects of genome damage and its underlying genetic defects, aiming to better understand these mechanisms and to improve cancer therapy. Since 2018, Marcel van Vugt is Professor of Molecular Oncology at the University of Groningen, and currently serves as the scientific director of the Comprehensive Cancer Center Groningen. Research in the lab focuses on the following main research questions:

- How is DNA re-wired during the cell cycle, and specifically during mitosis?
- How does DNA damage affect the behavior and cell fate of (cancer) cells, including inflammatory responses and genomic scars?

Abstract: Cells are equipped with DNA repair pathways that in conjunction with cell cycle checkpoint maintain genome integrity. Specifically, cell cycle checkpoints prevent entry into mitosis when DNA is not completely replicated DNA or when DNA lesions remain unrepaired. Preventing mitotic DNA damage is relevant because the canonical DNA repair pathways HR and NHEJ are inactivated during mitosis.

In contrast to untransformed cells, cancer cells frequently enter mitosis with persistent DNA lesions, and apparently have pathways to deal with these DNA lesions. Indeed, mitotic cells appear to have dedicated pathways to process DNA damage, although the mechanistic wiring and the players involved remain largely elusive.

We have recently used proteomic analyses to identify factors that respond to mitotic DNA damage. Using genetic approaches and 'stimulated emission depletion microscopy (STED)' microscopy approaches, we demonstrate how the TOPBP1-CIP2A complex is organized during progression through mitosis and how it recruits DNA repair factors, particularly the SMX nuclease complex in mitosis to process genomic regions of under-replicated DNA. Finally, we show how TOPBP1-CIP2A-mediated recruitment of the SMX complex determines viability in BRCA1/2 mutant cells.

Host: Prof. Dr. Sven Rottenberg, Cancer Therapy Resistance Cluster, Department for BioMedical Research and Institute of Animal Pathology, Vetsuisse, University of Bern

Next DBMR Research Conference: Monday, March 3, 2025, 5pm-6pm
Speaker and title: tba