



ISM Lunchtime Seminar Series

The ISM Lunchtime Seminars are online bi-monthly events, which take place on Thursdays, 13:00-13:30h, and are open to all interested colleagues and students. ISM researchers and guest speakers present their work during a 15 min seminar, in the English language, followed by a brief Q&A session.

We are happy to announce our next speaker: Deeksha Malhan, PhD, from the research group of Prof. Dr. Angela Relógio.

Title: Rucaparib-Induced Circadian Disruption and Adverse Events in Ovarian Cancer: Findings from the MAMOC Trial

Abstract:

Ovarian cancer (OC) is a leading cause of gynaecologic cancer mortality, with most cases diagnosed at an advanced stage. Standard treatment includes cytoreductive surgery, chemotherapy, and PARP inhibitors (PARPi) for maintenance in high-grade OC. PARP1, a key target of PARPi, interacts with the CLOCK-BMAL1 complex, regulating circadian rhythms. This study examines circadian disruptions in BRCA wild-type OC patients receiving rucaparib vs. placebo and their impact on patient-reported outcomes. As part of the Phase III MAMOC trial, 42 patients with advanced OC were randomized to rucaparib (n=28) or placebo (n=14). Patient-reported outcomes (EORTC-QLQ-C30/OV28, FSI) and daily activity data were collected. A subset of 15 patients underwent molecular circadian clock analysis via qPCR and NanoString. Mathematical modelling assessed 24-hour toxicity profiles of patients. Rucaparib significantly disrupted circadian gene expression, notably *BMAL1* and *PER2*, correlating with fatigue severity. Rucaparib-induced phase shifts and amplitude changes in clock and cancer-related genes (*CRY2*, *RORC*, *TP53*) were linked to increased adverse effects. Mathematical modelling revealed toxicity variability based on individual circadian rhythms. These findings highlight circadian rhythm dysregulation in PARPi toxicity. Aligning drug administration with circadian rhythms may optimize treatment by reducing side effects while enhancing efficacy.

When: 20th March 2025 at 13:00h

Where: MS-Teams (to join, please click [here](#))

Please follow the rules below to make these seminars a success:

- Please use your real name while entering the meeting. Participants with cryptic names will not be given access to the seminar.
- Please turn off your microphone while the seminar is taking place.
- Please feel free to ask questions!

Contact information: Please contact [Dr. Annakarina Mundorf](#) or [Dr. Deeksha Malhan](#) for further information.