Dr. Eva Petermann

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Eva Petermann qualified in 2001 with an BSc and MSc in Biochemistry at the Martin Luther University Halle-Wittenberg in Germany. She obtained her PhD in 2004 at the Free University of Berlin, where she worked on the biochemistry of DNA base excision repair. She continued with postdoctoral research in the field of DNA repair and replication in the lab of Keith Caldecott at the Sussex Centre for Genome Damage and Stability in Brighton. In her next postdoctoral position she worked with Thomas Helleday at the Gray Institute for Radiation Oncology and Biology at the University of Oxford, where she also was a Junior Research Fellow at Linacre College. Dr Petermann joined the School of Cancer Sciences as a Lecturer in 2010. She received the European Environmental Mutagen Society Young Scientist Prize in 2010.

Her research activities focus on the question how DNA damage response proteins and anti-cancer treatments influence replication fork progression and stability. Out of this topic two major themes take centre of their research:

The role of cell cycle checkpoint signalling in safeguarding replication
The cell cycle checkpoint protein kinase ATR is activated by perturbed replication forks and transmits its signals to the effector kinase Chk1. Chk1 suppresses further initiation of replication and promotes cell cycle arrest and DNA repair. Inhibition or depletion of Chk1 causes replication stress, and mouse models suggest that ATR and Chk1 act as tumour suppressors. ATR and Chk1 play important roles in regulating normal cellular DNA replication, limiting replication initiation and promoting normal speeds of replication fork progression. The former suggests that excessive initiation may be detrimental to cells. Chk1 inhibition increases Cdk2 activity, which promotes initiation. Therefore, excessive initiation can be prevented by simultaneous inhibition of Cdk2. Cdk inhibition can restore normal speeds of replication fork progression in Chk1-inhibited cells. This suggests that increased replication initiation can interfere with replication fork progression, which may cause replication stress.

DNA damage response to replication inhibitors
Several anti-cancer drugs specifically target replicating cells by interfering with DNA replication, thus generating lethal DNA damage. Such treatments exploit the high proliferation rates of cancer cells, and can be further potentiated by cancer-specific defects in DNA repair. Much research in recent years has focused on understanding the mammalian DNA damage response to replication inhibitors. Using the replication inhibitor hydroxyurea, Eva and co-workers have shown that proteins involved in homologous recombination repair (HR) such as Rad51 and XRCC3, and the HR-promoting proteins PARP1, Mre11 and Chk1 promote the efficient restart of stalled replication forks. Prolonged replication inhibition leads to widespread fork collapse and DSB formation, and HR is required for the repair of these DSBs and promotes survival of replication inhibitor treatments. Such findings could be of clinical importance as several types of cancer can display altered levels of HR activity.