Dr Eva Petermann PhD

Lecturer

School of Cancer Sciences (/schools/cancer/index.aspx)

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About

Eva Petermann is a Lecturer and Research Group Leader at the School of Cancer Sciences.

http://www.birmingham.ac.uk/dna-replication-petermann (http://www.birmingham.ac.uk/dna-replication-petermann)

Dr Petermann has published more than 20 research papers and review articles in the field of DNA replication and the DNA damage response. Her lab has received research funding from Cancer Research UK, the Royal Society, the Wellcome Trust and the MRC.

Lab Members: Dr Rebecca M Jones (postdoc), Dr Panagiotis Kotsantis (postdoc)

Qualifications

- PhD in Biochemistry, 2004
- BSc/MSc in Biochemistry, 2001

Biography

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.

Teaching

- **Medicine and Surgery MBChB (/undergraduate/courses/med/medicine.aspx)** - BMS year 2 "Cancer - Causes to Cures"
- Biosciences - BIO387 Cancer Biology

Postgraduate supervision

Dr Petermann is interested in supervising doctoral research students in the following areas:

- Deregulation of DNA replication and genomic instability
- The DNA damage response to replication inhibitors

If you are interested in studying any of these subject areas please contact Dr Petermann on the contact details above, or for any general doctoral research enquiries, please email: **dr@contacts.bham.ac.uk (mailto:dr@contacts.bham.ac.uk)** or call +44 (0)121 414 5005.

For a full list of available Doctoral Research opportunities, please visit our Doctoral Research programme listings.

Research

Research Themes

Cancer Genetics, Cancer Cell Biology

Research Activity

If replication fork progression is impaired, forks can stall or collapse into DNA double strand breaks (DSBs), a situation termed replication stress. Endogenous replication stress may be an important driving factor of tumourigenesis. Consequently, cellular pathways responding to replication stress can be expected to act as tumour suppressors, while pathways promoting replication stress may be tumour promoting. On the other hand, many DNA-damaging anti-cancer drugs act by interfering with

DNA replication. Eva's group investigates how DNA damage response proteins and anti-cancer treatments influence replication fork progression and stability.

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.

Publications

Zimmerman KM, Jones RM, **Petermann E**, Jeggo PA (2013) Diminished origin licensing capacity specifically sensitises tumour cells to replication stress.*Mol Cancer Res* **4**:370-380

Jones RM, Mortusewicz O, Afzal I, Lorvellec M, Garcia P, Helleday T, **Petermann E** (2013) Increased replication initiation and conflicts with transcription underlie Cyclin E-induced replication stress. *Oncogene* **32**:3744-3753

Jones RM, **Petermann E** (2012) Replication fork dynamics and the DNA damage response. *Biochem J* **443**:13-26

Petermann E, Helleday T (2010) Pathways of mammalian replication fork restart. *Nat Rev Mol Cell Biol* **11**: 683-687

Petermann E, Woodcock M, Helleday T (2010) Chk1 promotes replication fork progression by controlling replication initiation. *Proc Natl Acad Sci U S A* **107**: 16090-16095

Petermann E, Orta ML, Issaeva N, Schultz N, Helleday T (2010) Hydroxyurea-stalled replication forks become progressively inactivated and require two different RAD51-mediated pathways for restart and repair. *Mol Cell* **37**: 492-502

Bryant HE, **Petermann E**, Schultz N, Jemth AS, Loseva O, Issaeva N, Johansson F, Fernandez S, McGlynn P, Helleday T (2009) PARP is activated at stalled forks to mediate Mre11-dependent replication restart and recombination. *Embo J* **28**: 2601-2615

Wilsker D, **Petermann E**, Helleday T, Bunz F (2008) Essential function of Chk1 can be uncoupled from DNA damage checkpoint and replication control. *Proc Natl Acad Sci U S A* **105**: 20752-20757

Maya-Mendoza A, **Petermann E**, Gillespie DA, Caldecott KW, Jackson DA (2007) Chk1 regulates the density of active replication origins during the vertebrate S phase. *Embo J* **26**:2719-31.

Petermann E, Maya-Mendoza A, Zachos G, Gillespie DA, Jackson DA, Caldecott K (2006) Chk1 Requirement for High Global Rates of Replication Fork Progression during Normal Vertebrate S Phase. *Mol Cell Biol* **26**:3319-26