University of Birmingham

Dr Eva Petermann PhD

Senior Lecturer

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

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About

Eva Petermann is a Senior 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 25 research papers and review articles in the field of DNA replication and the DNA damage response.

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

Her lab has received research funding from Cancer Research UK, the Royal Society, the Wellcome Trust, the MRC and Worldwide Cancer Research.

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"
- BMedSc – year 2 "Advanced Molecular and Experimental Genetics
- 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

DNA Replication, DNA Damage and Repair, Cancer Genetics and DNA damage, Genome Biology

Research Activity

DNA replication is the copying of genetic information during cell division. If progression of the DNA replication machinery is impaired e.g. by obstacles on the DNA, forks can stall or collapse into DNA double strand breaks (DSBs). This is called replication stress and it can promote genomic instability or cell death. My group investigates molecular mechanisms of endogenous and therapy-induced replication stress in cancer.

DNA damage caused by replication inhibitors

Many cytotoxic chemotherapy drugs specifically target cancer cells by interfering with DNA replication, which is essential for cancer proliferation (examples: gemcitabine, 5-fluorouracil, cisplatin). These replication inhibitors stall replication fork progression, which causes toxic double-strand breaks (DSBs). Their therapeutic action can be potentiated by cancer-specific defects in DNA repair, e.g. mutation in the homologous recombination (HR) genes BRCA1 and BRCA2.

BRCA2-mutated cells are generally more sensitive to replication inhibitors than normal cells. Strangely however, they are less sensitive to gemcitabine. We have found that gemcitabine efficiently causes DSBs in normal cells, but leads to fewer DSBs in BRCA2-mutant cells. This suggests that sometimes, DNA repair can promote rather than prevent DSB formation during replication stalling (**http://mct.aacrjournals.org/content/13/10/2412.long (http://mct.aacrjournals.org/content/13/10/2412.long)**).

To better understand this, we are now investigating the cellular pathways that promote DSB formation during replication inhibitor treatments in more detail. DNA replication is an important target for cancer therapy. Uncovering the molecular mechanisms by which replication inhibition kills cells may help to exploit this target much more effectively in the future.

Endogenous replication stress in cancer

Faithful and complete replication of the genome is essential to maintain genomic stability and prevent cancer-promoting mutations. It has been shown that cancer cells can exhibit elevated DNA damage as a result of faulty chromosome replication, which is also known as replication stress. Replication stress may be a major cause of cancer-driving genomic instability.

De-regulation of proliferation by oncogenes is thought to be the cause of replication stress in cancer. However, very little is known about the mechanisms by which hyper-proliferation in cancer may cause replication stress. My lab is interested in finding such mechanisms. Firstly, we have shown that overexpression of the oncogene Cyclin E causes increased levels of replication initiation, which slows down of replication fork progression, thus promoting replication-associated DNA damage. Secondly, we also observed that a considerable portion of Cyclin E-induced replication stress results from interference between replication forks and the transcription machinery (**http://www.nature.com/onc/journal/v32/n32/full/onc2012387a.html (http://www.nature.com/onc/journal/v32/n32/full/onc2012387a.html)**).

We are now further investigating transcription-replication interference as a potential mechanism of replication stress in cancer cells. Knowing which cellular pathways can cause replication stress will help to properly detect and exploit replication stress for cancer therapy.

Publications

Jones RM, Kotsantis P, Stewart GS, Groth P, **Petermann E** (2014) BRCA2 and RAD51 promote double-strand break formation and cell death in response to Gemcitabine. *Mol Cancer Ther* **13**: 2412-2421

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

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