University of Birmingham

Dr Aga Gambus

MRC Career Development Award Fellow and Birmingham Fellow

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

Contact details

Telephone +44(0) 121 414 9165 (tel:+44 121 414 9165)

Email a.gambus@bham.ac.uk (mailto:a.gambus@bham.ac.uk)

Chromosomal Replication Laboratory
School of Cancer Sciences
University of Birmingham
Edgbaston
Birmingham
B15 2TT
UK

About

Aga has moved to Cancer Sciences in 2011 to start her independent research. She was awarded MRC Career Development Award and Birmingham Fellowship supporting her research.

The main focus of Aga's research is on understanding the role of small molecule modifiers: ubiquitin and SUMO, during chromosomal DNA replication.

Qualifications

- PhD in Cancer Research, University of Manchester, 2006
- MSc in Biotechnology, Jagiellonian University, Krakow, Poland, 2002

Biography

Aga Gambus graduated with MSci from Jagiellonian University, Krakow, Poland. She undertook her Master's project with Prof Wolfhard Bandlow at LMU, Munich, (2000-2002). This work, focusing on sister chromatid cohesion, started her interest of cell cycle processes.

Aga joined Dr Karim Labib's laboratory at Paterson Institute for Cancer Research, Manchester, for a PhD project (2002-2006). She identified and characterized a large protein complex built around the eukaryotic replicative helicase at DNA replication forks, named the Replisome Progression Complex (RPC). This work shed light onto the way in which the eukaryotic replisome is organized at the replication forks. During a short post-doctoral position, she also showed that one of the components of the RPC: Ctf4, is responsible for connecting the helicase complex to DNA polymerase alpha at the lagging strand of replication forks.

Aga was awarded the CR-UK Pontecorvo prize in 2007 for the best PhD thesis from CR-UK-funded students and received the Michael Dexter Young Investigator award presented by the Director of the Paterson Institute in December 2006.

Following her PhD work, Aga was awarded a Sir Henry Wellcome Fellowship to continue the research towards understanding the architecture of replication machinery. She joined Prof Julian Blow's laboratory at the Wellcome Trust Centre for Gene Regulation and Expression, Dundee (2007-2011). Using *Xenopus laevis* egg extract system, she showed that inactive core of replicative helicase (Mcm2-7 complex) is loaded onto origins of replication in the form of double hexamers, in agreement with data from a budding yeast *in vitro* reconstitution system. These results suggest that an Mcm2-7 double hexamer can initiate a bidirectional pair of forks during S phase, explaining one of the fundamental rules of DNA replication.

Aga joined School of Cancer Sciences in 2011 where she started her independent research. In 2012 she was awarded MRC Career Development Award Fellowship to study the roles of ubiquitin and SUMO during chromosomal DNA replication. She was also awarded Birmingham Fellowship by University of Birmingham.

Teaching

Part of "Essentials, Ideas, and Techniques of Biology" module, MSc Mathematics and Computation in Biology and Medicine, University of Birmingham.

Tutor on "Genetic basis of cancer" within MBChB module 'Cancer: Causes to Cures'.

Postgraduate supervision

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

- Regulation of eukaryotic DNA replication
- DNA replication and tumor development
- Novel anticancer therapy targets essential for DNA replication

If you are interested in studying any of these subject areas please contact Aga 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. or call +44 (0)121 414 5005.

Research

The role of ubiquitin and SUMO in chromosomal DNA replication

Cell division is the basis for the propagation of life. This involves the precise duplication of genetic information, which is called DNA replication. This process must be, and is, precisely regulated. Any mistakes that are not subsequently repaired can change the way the cell behaves and result in conditions such as genetic diseases, cancer and ageing.

The post-translational modification of proteins by members of the ubiquitin family: specifically ubiquitin and SUMO, is essential to maintain genome stability after DNA damage. Less is known about its role in maintaining genome stability during unperturbed cell cycle: the initiation stage of DNA replication depends on ubiquitin-mediated proteolysis but a growing body of evidence suggests that the further stages of DNA replication are also regulated by these modifications. There are indications that ubiquitin/SUMO ligases play an important role during unperturbed DNA replication, but the proteins they modify are mostly unknown.

The main aim of work carried out in Dr Aga Gambus's lab is therefore to use the experience in studying protein complexes assembled during DNA replication to investigate their regulation by ubiquitin and SUMO.

Two model systems used in Aga's laboratory are: cell free *Xenopus laevis* egg extract system and human cell lines.

Other activities

- Member of the EMBO Expert Women in Life Sciences (WiLS)
- Member of the British Society for Cell Biology (BSCB)
- Reviewer for grant funding bodies and journals.

Publications

- Moreno SP, Bailey R, Campion N, Herron S, Gambus A. **Polyubiquitylation drives replisome disassembly at the termination of DNA replication (http://www.ncbi.nlm.nih.gov/pubmed/25342805)** . Science. 2014 Oct 24;346(6208):477-81. doi: 10.1126/science.1253585.

This manuscript has been made available as open access by Science:

Abstract:
http://www.sciencemag.org/cgi/content/abstract/346/6208/477?ijkey=bgdl23CCdRDz6&keytype=ref&siteid=sci (http://www.sciencemag.org/cgi/content/abstract/346/6208/477?ijkey=bgdl23CCdRDz6&keytype=ref&siteid=sci)

Reprint:
http://www.sciencemag.org/cgi/rapidpdf/346/6208/477?ijkey=bgdl23CCdRDz6&keytype=ref&siteid=sci (http://www.sciencemag.org/cgi/rapidpdf/346/6208/477?ijkey=bgdl23CCdRDz6&keytype=ref&siteid=sci)

Full Text:
http://www.sciencemag.org/cgi/content/full/346/6208/477?ijkey=bgdl23CCdRDz6&keytype=ref&siteid=sci (http://www.sciencemag.org/cgi/content/full/346/6208/477?ijkey=bgdl23CCdRDz6&keytype=ref&siteid=sci)

- Gambus A, Blow JJ. Mcm8 and Mcm9 form a dimeric complex in Xenopus laevis egg extract that is not essential for DNA replication initiation.**Cell Cycle**. 2013 Mar 21;12(8).
- Park J, Long DT, Lee KY, Abbas T, Shibata E, Negishi M, Luo Y, Schimenti JC, Gambus A, Walter JC, Dutta A. The MCM8-MCM9 Complex Promotes RAD51 Recruitment at DNA Damage Sites To Facilitate Homologous Recombination.**Mol Cell Biol**. 2013 Apr;33(8):1632-44. doi: 10.1128/MCB.01503-12.
- Gillespie PJ*, Gambus A*, Blow JJ (2012)Preparation and use of Xenopus egg extracts to study DNA replication and chromatin associated proteins. **Methods**, Apr 19. PMID: 22521908
- ^Gambus A, Khoudoli GA, Jones RC, Blow JJ (2011) Mcm2-7 Form Double Hexamers At Licensed Origins In Xenopus Egg Extract **J Biol Chem**. Apr 1;286(13):11855-64. Epub 2011 Jan 31. PMID: 21282109
- ^Gambus A*, van Deursen F*, Polychronopoulos D, Foltman M, Jones RC, Edmondson RD, Calzada A, Labib K (2009) A key role for Ctf4 in coupling the MCM2-7 helicase to DNA polymerase alpha within the eukaryotic replisome. **EMBO J**. Oct 7;28(19):2992-3004. Epub 2009 Aug 6. PMID: 19661920
- Labib, K. and Gambus, A. (2007) A key role for the GINS complex at DNA replication forks. **Trends Cell Biol**17: 271-278. PMID: 17467990
- Gambus A, Jones R, Sanchez-Diaz A, Kanemaki M, van Deursen F, Edmondson R, Labib K. (2006) GINS maintains association of Cdc45 with MCM in replisome progression complexes at eukaryotic DNA replication forks. **Nature Cell Biology**Apr;8(4):358-66. Epub 2006 Mar 12. PMID: 16531994
- Kanemaki M, Sanchez-Diaz A, Gambus A, Labib K. (2003) Functional proteomic identification of DNA replication proteins by induced proteolysis in vivo. **Nature**. Jun 12;423(6941):720-4. Epub 2003 May 25. PMID: 12768207