University of Birmingham

Dr Jonathan Wolf Mueller PhD DSc

Senior Research Fellow

Endocrinology, Diabetes and Metabolism

Contact details

Telephone +44 (0)121 4142764 (tel:+44 121 4142764)

Email j.w.mueller@bham.ac.uk (mailto:j.w.mueller@bham.ac.uk)

School of Clinical and Experimental Medicine
Institute of Biomedical Research, Room 208
University of Birmingham
Edgbaston
Birmingham
B15 2TT
UK

About

Jonathan Mueller is a Senior Research Fellow at the Centre for Endocrinology, Diabetes and Metabolism at the University of Birmingham. Jon is a protein biochemist by training who now applies his profound knowledge in the context of endocrinology.

Being an enthusiastic scientist, Jon has authored more than 15 research papers and received various fellowships (e.g. EMBO ASTF and Wellcome ISSF). In the past, Jon has studied folding-helper enzymes from the parvulin class using biophysical, cell biological and biochemical methodology. More recently, he became interested in the enzymatic activation of sulfate studying so-called PAPS synthases. Having presented this work in an invited seminar in Birmingham, he soon decided to come over to join CEDAM where a special interest exists in this topic due to its severe impact on steroid hormone regulation.

As a lay person, Jon is interested in antibiotics research as well as invasive animal and plant species. Outside of science, Jon is a photographer and has presented his work at various public exhibitions.

Qualifications

- Habilitation (DSc equivalent) and Venia legendi in Biochemistry/Molecular Biology, Univ. Duisburg-Essen, Germany, 2012
- PhD in Biochemistry, Univ. Halle (Salle), Germany, 2004
- Diploma (MA equivalent) in Biochemistry, Univ. Halle (Salle), Germany, 2001

Biography

Jonathan has studied Biochemistry at the Universities of Halle (Saale), Germany, and Kingston upon Hull, UK, with special focus on protein chemistry and molecular biology. He undertook his diploma thesis research project with Lorenz Mayr at Bayer AG, Wuppertal, Germany, benefiting from exposure to an industry-academia collaborative project between the Bayer AG research centre in Wuppertal and the Institute for Technical Biochemistry in Halle, Germany.

Jonathan undertook further training in Biochemistry in his PhD studies with Peter Bayer at Max Planck Institute for Molecular Physiology, Dortmund, which gave him the opportunity to acquire advanced skills in biophysics and analytical spectroscopy including NMR. When Peter was then appointed Head of the Department of Biochemistry at the University of Duisburg-Essen in 2004, Jonathan followed him and took up a fixed-term assistant lecturer position (C1), which provided him with the responsibility for a number of research projects and early leadership experience.

Jon reached scientific independence, when he was able to secure two highly competitive short-term fellowships in 2007 and 2011 from the European Molecular Biology Organisation (EMBO) to visit Annalisa Pastore at the MRC National Institute for Medical Research in London, UK for studying various aspects of PAPS synthase biology. In 2012, Jon joined CEDAM to advance his research on steroid sulfation and PAPS synthases within this unparalleled biomedical translational context.

Teaching

Jonathan has collected significant teaching experience since 2004. At the University of Duisburg-Essen, he has given lectures, seminars and practical courses in biochemistry, structural biology, biophysics and molecular biology for medicinal and biology under-graduate and graduate students. Moreover, he has supervised bachelor thesis projects as primary supervisor and served as secondary supervisor to a number of bachelor projects. Only in 2012, his teaching portfolio was even more enriched by teaching appointments with the Universities for Applied Sciences Bonn-Rhein-Sieg in Rheinbach and Cologne, Campus Leverkusen. There, Jonathan has taught bioinformatics for bachelor students in pharmaceutical chemistry (Leverkusen) as well as virology for master students and microbiology for bachelor students in biomedical sciences (Rheinbach).

Now at UoB, Jonathan participates in small group teaching in Molecular Endocrinology to medical students, supervises various student research projects and is involved in research taster classes to medical students.

Postgraduate supervision

Jonathan is always interested in recruiting talented new students and postdoctoral associates. Please feel free to contact him for further information on current opportunities. If you are interested in furthering your studying any endocrine-related cancers please contact Jon 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

Sulfation processes are a vital element of human physiology. For example, thyroid hormones and various steroid hormones are sulfated as a mechanism of reversible inactivation and to increase solubility facilitating renal excretion. All human sulfation processes are catalysed by various sulfotransferases that generally rely on provision

of active sulfate in the form of the molecule PAPS, which is provided by the two PAPS synthase isoforms, PAPSS1 and PAPSS2. Defects in PAPSS genes will therefore compromise a large number of sulfation processes.

Our group has reported a female patient with PAPSS2 mutations who presented with strikingly disturbed androgen metabolism. Severely impaired sulfation of the principal androgen precursor DHEA to inactive DHEAS resulted in increased conversion of DHEA to active androgen, resulting in androgen excess. Intriguingly, both PAPSS isoforms are expressed in the adrenal cortex; hence, it is an open question why intact PAPSS1 could not functionally compensate for PAPSS2-loss in this patient.

Previously, Jon could show that PAPSS2 is an unstable protein being partially unfolded at physiological temperature. Moreover, the PAPS biosynthesis intermediate APS stabilised PAPSS2 notably. Functional divergence may also relate to differential subcellular localisation of PAPSS isoforms. Therefore, Jon developed protein variants that had either nuclear localisation or export signals disrupted by point mutation resulting in cytoplasmic and nuclear protein variants, respectively. These variants can now be tested in a DHEA/DHEAS conversion assay, say in a larger functional context. Besides, Jon is interested in understanding the disease-causing mutations within the gene for PAPSS2 on a molecular and cellular level employing a rich portfolio of experimental techniques ranging from steroid conversion assays over state-of-the-art protein chemical and molecular biological methods till newly developed LC-MS/MS-based bioanalytical techniques.

Other activities

Ad hoc referee for the following bodies

International journals

- Analytical Biochemistry
- Biological Chemistry
- Evolutionary Bioinformatics
- Journal of Biological Chemistry
- Perspectives in Medicinal Chemistry
- PLoS ONE
- Proteomics Insights

Other bodies

- Medical Research Council (MRC), UK
- Deutscher Akademischer Austauschdienst (DAAD)
- Swiss Prot – Protein-Datenbank

Membership in Professional Societies

- Society for Endocrinology, UK; Biochemical Society, UK; The Endocrine Society, USA
- Deutsche Gesellschaft für Biophysik (DGfB); Deutscher Hochschulverband (DHV); FES-Ehemalige e.V. der Friedrich-Ebert-Stiftung (FES); Gesellschaft für Biochemie und Molekularbiologie (GBM), Mitglied in den Studiengruppen Protein Engineering und Biophysikalische Chemie

Publications

Matena A, Sinnen C, van den Boom J, Wilms C, Dybowski JN, Maltaner R, Mueller JW, Link NM, Hoffmann D and Bayer P (2013) **Transient Domain Interactions Enhance the Affinity of the Mitotic Regulator Pin1 toward Phosphorylated Peptide Ligands (doi:pii: S0969-2126(13)00266-9. 10.1016/j.str.2013.07.016.)** . *Structure* [Epub ahead of print]

ORCID: 0000-0003-1212-189X; ResearcherID: D-1632-2010; Scopus Author ID: 7402829417

Mueller JW and Shafqat N (2013) **Adenosine-5'-phosphosulfate - a multifaceted modulator of bifunctional 3'-phospho-adenosine-5'-phosphosulfate synthases and related enzymes (http://onlinelibrary.wiley.com/doi/10.1111/febs.12252/abstract;jsessionid=2748ED5F8C4C3F54F54418D35EF372F0.d01t01)** . *FEBS Journal* 280(13):3050-7

van den Boom J, Heider D, Martin SR, Pastore A, and Mueller JW (2012) **PAPS synthases – naturally fragile enzymes specifically stabilised by nucleotide binding (http://www.jbc.org/content/287/21/17645.long)** . *J Biol Chem* 287(21):17645-55

Schröder E, Gebel L, Eremeev AA, Morgner J, Grum D, Knauer SK, Bayer P and Mueller JW (2012) **Human PAPS synthase isoforms are dynamically regulated enzymes with access to nucleus and cytoplasm (http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0029559)** . *PLoS ONE* 7(1) e29559

Mueller JW, Link NM, Matena A, Hoppstock L, Rüppel A, Bayer P, Blankenfeldt W. (2011), Crystallographic proof for an extended hydrogen-bonding network in small prolyl isomerases. **J Am. Chem. Soc**., 133:20096–20099

Ehrentraut S, Hassler M, Oppikofer M, Kueng S, Weber JM, Mueller JW, Gasser SM, Ladurner AG and Ehrenhofer-Murray AE (2011) **Structural basis for the role of the Sir3 AAA+ domain in silencing: interaction with Sir4 and unmethylated histone H3K79 (http://genesdev.cshlp.org/content/25/17/1835.long)** . *Genes and Development* 25(17):1835-46

Grum D, van den Boom J, Neumann D, Matena A, Link NM and Mueller JW (2010) A heterodimer of human 3'-phospho-adenosine-5'-phosphosulphate (PAPS) synthases is a new sulphate activating complex. *Biochem Biophys Res Commun* 395(3):420-5

Kessler D, Papatheodorou P, Stratmann T, Dian EA, Rassow J, Hartmann-Fatu C, Bayer P and Mueller JW (2007) **The DNA Binding Parvulin Par17 is Targeted to the Mitochondrial Matrix by a Recently Evolved Prepeptide Uniquely Present in Hominidae (http://www.biomedcentral.com/1741-7007/5/37)** . *BMC Biol* 5:37