University of Birmingham

Professor Ferenc Mueller

Professor in Developmental Genetics

Reproduction, Genes and Development

Contact details

Telephone +44 (0) 12141 42895 (tel:+44 12141 42895)

Email f.mueller@bham.ac.uk (mailto:f.mueller@bham.ac.uk)

School of Clinical and Experimental Medicine
College of Medical and Dental Sciences
University of Birmingham
Edgbaston
Birmingham
B15 2TT
UK

About

Dr Ferenc Mueller leads a research group in the Centre for Rare Diseases and Personalised Medicine. His group studies transcription regulation in embryo development. Their research projects include the function of promoter recognition proteins in regulating differential gene expression during vertebrate embryo development and comparative/functional genomic analysis of cis-regulatory elements. They develop high throughput approaches to study transcriptional regulators in the zebrafish embryo model system. They exploit the advantages of zebrafish in search for non-coding mutations causing human disease and study the in vivo roles of orthologs of human genes that have been associated with disease causing mutations. His group currently consists of 4 post docs, 1 technician and 3 PhD Students. Their research is funded by various projects of the 7th Framework programme of the European Union and the Myrovlytis Trust.

Qualifications

- PhD, 1997, Hungarian Academy of Sciences PhD programme,
- MSc (equivalent 5 year degree) 1993, University of Gödöllö, Hungary, Biotechnology

Biography

Ferenc Mueller joined the University of Birmingham in 2007 as Senior Lecturer, he was appointed as Reader in 2010 before being awarded his Chair in March 2014. He was research group leader in the institute of Toxicology and Genetics at the Forschungszentrum Karlsruhe (currently Karlsruhe Institute of Technology) in Germany (2001-2007). He was postdoctoral fellow at the IGBMC Strasbourg, France (EMBO and FRM fellowships 1997-2001) and research fellow at the University of Southampton UK (1995-1997).

Teaching

- Director of Postgraduate Research in the School of Clinical and Experimental Medicine
- MRes, Genes and Hormones, module coordinator
- BMed Sci, Molecular Biology, 2nd year, lecturing,
- BMed Sci, Genes to Therapy, 3rd year course, course coordinator

Postgraduate supervision

Ferenc is interested in supervising doctoral research students in the following areas:

- Transcription regulation in embryo development
- High throughout screening with zebrafish embryos
- In vivo modelling of the genetic basis of human disease in zebrafish

Current PhD students: Irene Miguel, Sundeep Dhillon, Rhiannon Mary Hurst

Research

1. Transcription regulation in development

The Mueller group investigates transcriptional regulation processes that regulate protein coding and non-coding gene activities during and after the transition from a pluripotent cell mass of the blastula into a highly complex, differentiated vertebrate embryo. They combine comparative genomics and *in vivo* functional analysis of gene regulation exploiting the capabilities offered by the zebrafish model system. They have developed new techniques for high throughput *in vivo* analysis of cis-regulatory modules (CRMs) aiding in the identification of a large number of transcriptional enhancer elements in developmental genes. Their research contributed to the understanding of the complexity of promoter regulation by the characterisation of novel members of the TATA binding protein family and the functional characterisation of vertebrate promoter recognition proteins. They established novel *in vivo* assays of studying general transcription factors in the complexity of the embryo using embryo manipulation tools and modern genomics techniques (RNA, CAGE and ChIP sequencing). Lab members working on the topic: Dr Yavor Hadzhiev, Dr Nan Li, Dr Padma Putta, Ms Jennifer Roberts.

2. Zebrafish as a vertebrate model for human genetics / disease

i) *Non-coding mutations in disease*

CRMs and other non-coding functional elements of developmental regulator genes are mutated in numerous congenital disorders. The aberration of gene expression regulation can also lead to multifactorial diseases. The identification of non-coding functional elements will greatly enhance efforts in mapping non-coding mutations responsible for congenital and multifactorial disorders. Mueller and collaborators (U. Liebel and M. Reischl at KIT, Karlsruhe) pioneered the automation of imaging of tens of thousands of transgenic zebrafish embryos in order to initiate high throughput screens for mutation carrying cis-regulatory elements. To complement the technology development they apply bioinformatics (comparative genomics) and biochemical prediction of cis-regulatory modules (ChIP sequencing). They collaborate with B. Lenhard (Uni Bergen) E. Stupka (UCL), P. Carninci (RIKEN) and U. Straehle (KIT, Karlsruhe) in a concerted effort to map the functional CRMs of zebrafish. Ultimately, this work will aid in their effort to develop the transparent and fast developing fish embryo as a high throughput transgenic sensor for efficient screening of functionally conserved cis-regulatory elements relevant in human diseases. Lab members working on the topic: Dr Yavor Hadzhiev, Ms Irene Miguel.

<start_ii>ii) Zebrafish models for genetic disorders

The Mueller group utilises their functional genomic experience with the fish model and collaborate with clinical and non-clinical investigators in their search for the in vivo function of disease causing genes. In the last 3 years they made progress by establishing a new zebrafish model for the Birt-Hogg-Dube syndrome (with E. Maher). They have been studying the biological function of genes with newly discovered disease causing mutations and demonstrated essential organogenesis functions for genes causing familial syndromes such as ARC and Warburg Micro syndromes (collaborations with E. Maher, P. Gissen, I. Alianidis). Lab members working on the topic: Dr Emma Kenyon, Dr Nan Li, Harmeet Gill.

<start_iii>iii) Phenotype detection for drug screening

Based on their experience with high throughput screening of zebrafish embryos, the Mueller group is exploiting automated imaging to screen gene expression phenotypes and develop novel methods for physiological phenotype detection to screen for drug effects in zebrafish embryos (collaboration with U. Liebel, Karlsruhe and A. Sik, Bham). Lab members working on the topic: Dr Yavor Hadzhiev, Mr Sundeep Dhillon.

Publications

Andersson R, Gebhard C, Miguel -Escalada I, Hoof I, Bornholdt J, Boyd M, Chen Y, Zhao X, Schmidl C, Suzuki T, Ntini E, Arner E, Valen E, Li K, Schwarzfischer L, Glatz D, Raithel J, Lilje B, Rapin N, Bagger FO, Jørgensen M, Andersen PR, Bertin N, Rackham O, Burroughs AM, Baillie JK, Ishizu Y, Shimizu Y, Furuhata E, Maeda S, Negishi Y, Mungall CJ, Meehan TF, Lassmann T, Itoh M, Kawaji H, Kondo N, Kawai J, Lennartsson A, Daub CO, Heutink P, Hume DA Jensen TH, Suzuki H, Hayashizaki Y, Müller F, Fantom Consortium, Forrest AR, Carninci P, Rehli M and Sandelin A (2014) **An atlas of active enhancers across human cell types and tissues (http://www.ncbi.nlm.nih.gov/pubmed/24670763)** . *Nature* 507(7493):455-61

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Lindeman LC, Andersen IS, Reiner AH, Li N, Aanes H, Ostrup O, Winata C, Mathavan S, Müller F, Alestrom P and Collas P (2011) **Prepatterning of Developmental Gene Expression by Modified Histones before Zygotic Genome Activation (http://www.ncbi.nlm.nih.gov/pubmed/22137762)** . *Dev Cell*21(6):993-1004

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Gehrig J, Reischl M, Kalmar E, Ferg M, Hadzhiev Y, Zaucker A, Song C, Schindler S, Liebel U and Müller F (2009) **Automated high throughput mapping of promoter-enhancer interactions in zebrafish embryos (http://www.ncbi.nlm.nih.gov/pubmed/19898487)** . *Nature Methods*6(12):911-6