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About

Paul Badenhorst is a Senior Lecture in the School of Immunity and Infection.

Paul's field of expertise is in Epigenetics and Development. Paul uses both the Drosophila model system and human cells to investigate how chromatin modifying complexes regulate gene expression to control developmental pathways. He has received major grant funding from Cancer Research UK, the Biotechnology and Biological Sciences Research Council and the Medical Research Council.

Qualifications

- PhD, MRC Laboratory of Molecular Biology, University of Cambridge 1997
- MSc Molecular Biology, 1993
- BSc(Hons) Cell Biology, 1991
- BSc Cell Biology and Chemistry, 1990

Biography

Paul Badenhorst qualified with a BSc in Cell Biology and Chemistry from the University of Natal (South Africa) in 1990. He went on to complete a BSc(Hons) and MSc in Molecular Biology at Natal before moving to study for a PhD at the MRC Laboratory of Molecular Biology (Cambridge). While at Cambridge Paul was both a Cambridge Livingstone Scholar and Emanuel Bradlow Overseas Scholar. Following the award of his PhD in 1997, Paul performed post-doctoral research at the National Cancer Institute NIH (Bethesda, USA). As a Wellcome Trust International Prize Traveling Fellow, Paul initiated research into the biological functions of chromatin remodelling enzymes. In 2003, Paul moved to Birmingham where he has continued research into chromatin remodelling and modifying complexes. Paul is currently a Senior Lecturer in the School of Immunity and Infection.

Teaching

Teaching Programmes

- **BMedSci (/undergraduate/courses/med/medical-sci.aspx)** Embryology and Developmental Biology
- **MRes (/postgraduate/courses/combined/med/health-research.aspx)** Research Skills

Postgraduate supervision

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

- Regulation and function of chromatin remodelling enzymes.
- Transcriptional regulation of immune cell differentiation and development

If you are interesting in studying any of these subject areas please contact Paul on the contact deatils 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 (http://www.bham.findaphd.com/?es=y&apl=y&aplt=&show)** .

Research

RESEARCH THEMES

Epigenetics, Gene regulation, Development and Disease.

RESEARCH ACTIVITY

We study how transcription is regulated to control cell identity and function. Our research focuses on two related questions. Firstly, what are the targets of gene-specific transcription factors and how is their activity regulated. Secondly, how do transcription factors function in the context of chromatin to control gene expression. A key element in this is to identify and characterize the accessory chromatin remodeling and modifying complexes that transcription factors recruit. We use *Drosophila* and human cells to investigate these questions.

The main focus of our research has been the function of the conserved ATP-dependent chromatin remodeling enzyme NURF. NURF catalyzes energy-dependent nucleosome sliding *in vitro* and we have shown that it is required for both transcription activation and repression *in vivo*. Using a series of mutant *Drosophila* strains that lack NURF, and whole genome expression profiling (microarrays), we were able to identify gene targets of NURF. In work supported by the Wellcome Trust, we showed that NURF is a co-activator of the *Drosophila* Ecdysone Receptor and that it is required for steroid signaling. In BBSRC and CRUK-funded research we have shown that NURF can binds the amino terminal tail of histone H3 trimethylated at lysine position 4 ($H3K4(Me)_3$). This work revealed that NURF can be recruited to sites of $H3K4(Me)_3$ and is an important effector this epigenetic mark.

We have also shown that *Drosophila* NURF is required for normal leukocyte development. In animals lacking NURF, large numbers of an otherwise rare leukocyte type, the lamellocyte, are produced. Lamellocytes are key mediators of the cellular innate immune response in *Drosophila*. However, as we have shown in our NURF studies, uncontrolled differentiation of lamellocytes leads to an inflammatory syndrome in flies. We have identified transcriptional targets of NURF in leukocytes and have shown that NURF is a co-repressor of JAK/STAT target genes. Loss of NURF leads to precocious activation of STAT responders and lamellocyte differentiation. This is an important result as NURF is conserved between *Drosophila* and humans suggesting that human NURF may also function to hold inflammatory signalling pathways in check. In humans chronic immune-mediated inflammatory conditions often result from the abnormal or continued episodic activation of these pathways leading to disease.

To uncover additional regulators of lamellocyte differentiation that may play a role in inflammatory responses, we have performed a gain-of-function genetic screen and have identified 101 candidate regulators. Amongst these we identified a *Drosophila* homologue of the mammalian transcription repressor REST/NSRF. In our future research we will investigate how REST/NSRF and its associated co-repressor partners ensures correct regulation of lamellocyte differentiation controls inflammatory signalling.

Other activities

- Member of the Genetics Society (UK)
- Member of the Genetics Society of America

Publications

Stofanko M, Kwon SY, Badenhorst P. (2010). Lineage tracing of lamellocytes demonstrates Drosophila macrophage plasticity. PLOS One: 5(11):e14051.

Kwon SY, Xiao H, Wu C, Badenhorst P. (2009). Alternative splicing of NURF301 generates distinct NURF chromatin remodeling complexes with altered modified histone binding specificities. PLOS Genetics: 5(7):e1000574.

Stofanko, M., Kwon S.Y., Badenhorst, P. (2008). A misexpression screen to identify regulators of Drosophila larval hemocyte development. Genetics: 180, 253-267.

Kwon, S.Y., Xiao, H., Glover, B., Tjian, R., Wu, C., Badenhorst, P. (2008) The nucleosome remodelling factor (NURF) regulates genes involved in Drosophila innate immunity. Developmental Biology: 316: 538-547.

Bai, X., Larschan, E., Kwon, S.Y., Badenhorst, P., Kuroda, M.I. (2007) Regional control of chromatin organization by noncoding roX RNAs and the NURF remodeling complex in Drosophila melanogaster. Genetics: 176:1491-1499.

Wysocka, J., Swigut, T., Xiao, H., Milne, T.A., Kwon, S.Y., Landry, J., Kauer, M., Tackett, A.J., Chait, B.T., Badenhorst, P., Wu, C., Allis, C.D. (2006). A PHD finger of NURF couples histone H3 lysine 4 trimethylation with chromatin remodelling. Nature: 442, 86-90.

Badenhorst, P., Xiao, H., Cherbas, L., Kwon, S.Y., Voas, M., Rebay, I., Cherbas, P. and Wu, C. (2005). The Drosophila nucleosome remodeling factor NURF is required for Ecdysteroid signaling and metamorphosis. Genes and Development:19, 2540-2545.

Badenhorst, P., Voas, M., Rebay, I., and Wu, C. (2002). Biological functions of the ISWI chromatin remodeling complex NURF. Genes and Development, 16, 3186-3198.