Birt-Hogg-Dubé Newsletter

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You are receiving this email because you have expressed an interest in BHD. We hope you will enjoy this and future editions. If you do not wish to receive this newsletter, please see the end of the email for instructions.

Save the Date! Third International BHD Symposium, Maastricht, 11th and 12th May, 2011

The Third International BHD Symposium will be held in Maastricht, the Netherlands, on 11th and 12th May 2011. We are delighted to announce already that Dr. Bin Teh of Van Andel Institute, Dr. Kuniaki Seyama of Juntendo University, and Dr. Sunil Sudarshan of the University of Texas Health Science Center at San Antonio have accepted to come as keynote speakers. Further details will be available soon. We hope to see many of you there!

New Research Funding

The Myrovlytis Trust is pleased to award a number of two-year grants:

A grant to Dr Seung-Beom Hong, recently Research Fellow at the National Cancer Institute, will allow for investigation of the functional relationships among folliculin and its interacting proteins.

Dr Kyle Furge of the Van Andel Institute in Michigan will be supported to test potential therapies for the renal tumours associated with BHD syndrome.

Dr Andrew Tee of Cardiff University has received a grant in order to examine the roles of reactive oxygen species and hypoxia-inducible factor (HIF) in BHD syndrome.

An award to Dr Ferenc Mueller, at the University of Birmingham, will provide for the development of a zebrafish model for BHD syndrome to study the function of the folliculin gene.

Website Updates

BHDSyndrome.org will be undergoing a large scale re-design in the new year. If there are any aspects of the site which you particularly like or which you consider need changing, please do email your thoughts to: contact@bhdsyndrome.org.

One exciting new feature will be video interviews with researchers, providing an opportunity to hear straight from the front lines of current research, learn about future prospects and have a chance to get to know the scientists endeavouring to understand and treat BHD.

Getting to know you!

The next instalment of 'Getting to know you' presents Dr Justin Roth, researcher at the University of Alabama at Birmingham who is working on renal gene therapy, and Mary from the United States, who was diagnosed with BHD Syndrome in 2004. The interviews can be found here.

BHD Research Highlights

In the last quarter several important BHD research papers have been published. These include:

BASIC SCIENCE:

Hong *et al,* 2010. Inactivation of the FLCN Tumor Suppressor Gene Induces TFE3 Transcriptional Activity by Increasing Its Nuclear Localization. *PLoS ONE* 5(12): e15793. Epublished ahead of print. (Full text available in the BHD Article Library)

- Presented a novel mechanism for inducing oncogenic transcription factor TFE3. Found that inactivation of the folliculin gene *FLCN* correlated with increased levels of TFE3 and affected post-translational modification of TFE3, localizing TFE3 to the nucleus. *FLCN* inactivation also increased GPNMB expression, regulated by the MiTF/TFE transcription family. Hong *et al.* have elucidated another aspect of the regulatory activity of FLCN.

Klomp *et al,* 2010. Birt-Hogg-Dubé renal tumors are genetically distinct from other renal neoplasias and are associated with up-regulation of mitochondrial gene expression. *BMC Med Genomics*. 2010 Dec 16;3(1):59. Epublished ahead of print. (Full text available in the BHD Article Library)

- Demonstrated that BHD-associated renal tumours exhibit distinct gene expression profiles when compared with those of other renal tumours. The differences detected in molecular activity add further evidence that folliculin may regulate mitochondrial function and so place new emphasis on the role of folliculin in the AMPK pathway.

Preston *et al,* 2010. Absence of the Birt-Hogg-Dubé gene product is associated with increased hypoxia-inducible factor transcriptional activity and a loss of metabolic flexibility. *Oncogene.* Nov 8. Epublished ahead of print.

- Suggested that hypoxia-inducible factor (HIF) signalling is involved in tumour formation of renal cell carcinomas in Birt-Hogg-Dubé syndrome, and proposed that folliculin may affect HIF through the AMPK, mTOR and Akt pathways.
- As the cells lacking folliculin appeared to exhibit the 'Warburg effect', favouring glycolytic over lipid metabolism, the authors indicated that glycolytic metabolism may offer an attractive target in the therapy of renal tumours implicated in BHD syndrome.

CLINICAL:

Cocciolone *et al,* 2010. Multiple desmoplastic melanomas in Birt-Hogg-Dubé syndrome and a proposed signaling link between folliculin, the mTOR pathway, and melanoma susceptibility. *Arch Dermatol*. 2010 Nov;146(11):1316-8.

- Examined possible links between Birt-Hogg-Dubé syndrome and the genesis of melanomas.

Hayashi *et al,* 2010. Birt-Hogg-Dubé Syndrome with Multiple Cysts and Recurrent Pneumothorax: Pathological Findings. *Internal Medicine.* Vol. 49 (2010). No. 19 pp.2137-2142. (Full text available in the BHD Article Library)

- This case study of a 39-year-old woman presenting with right-sided pneumothorax demonstrated that BHD syndrome should be considered in patients presenting with multiple pulmonary cysts with or without skin eruption, or kidney tumour.

If you would like to participate in our 'Getting to know you!' feature, please contact us at contact@BHDSyndrome.org

If you would like to submit information or suggest a topic for the next newsletter, please contact the editor at info@BHDsyndrome.org