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 newsletter for instructions.

Fifth BHD Symposium

We are delighted to announce that the Fifth International BHD Symposium will be held in Paris, France on 28-29th June, 2013. The Symposium will be hosted by Professor Stéphane Richard at the École du Louvre. The programme will include talks on both BHD and HLRCC and, as in previous years, there will be parallel sessions for patients and families.

Registration and abstract submission will be open presently. Please check the Fifth BHD Symposium page regularly for updates.

Getting to know you

This quarter, meet Gloria from the USA, who was diagnosed with BHD earlier this year and Dr Stephen Land, Senior Lecturer at the University of Dundee, who is investigating lung cyst formation in Birt-Hogg-Dubé Syndrome. The interviews can be found here.

BHD Research Highlights

Noteworthy papers from the last quarter include:

BASIC:

Gaur *et al.,* 2012. The Birt-Hogg-Dubé tumor suppressor Folliculin negatively regulates ribosomal RNA synthesis. *Hum Mol Genet. 2012 Oct 24.* [Epub ahead of print]

- Gaur *et al.* report that Regulatory particle triple-A ATPase 4 (Rpt4) interacts with FLCN in the *Drosophila* nucleolus to downregulate rRNA synthesis and that dFLCN inhibits Ras/ERK signalling.

Medvetz *et al.,* 2012. Folliculin, the Product of the Birt-Hogg-Dube Tumor Suppressor Gene, Interacts with the Adherens Junction Protein p0071 to Regulate Cell-Cell Adhesion. *PLoS One. 2012;7(11):e47842.* (free full text)

- Medvetz *et al.* report that FLCN interacts with p0071 (Plakophilin 4) to regulate RhoA signaling and cell-cell adhesion. They also used a conditional FLCN allele to delete FLCN in mouse epidermis. These mice show a similar phenotype to other cell-cell adhesion knock outs, and have a hyper-proliferative epidermal phenotype indicative of Rho signaling defects.

Hasumi *et al.* 2012. Regulation of Mitochondrial Oxidative Metabolism by Tumor Suppressor FLCN. *J Natl Cancer Inst. 2012 Nov 21;104(22):1750-64*

- Hasumi *et al.* used conditional alleles of FLCN and PPARGC1A to investigate their roles in murine mitochondrial function. They show that FLCN inhibits PPARGC1A function, thereby regulating mitochondrial oxidative metabolism.

Reiman *et al.* 2012. Gene Expression and Protein Array Studies of Folliculin-regulated Pathways. *Anticancer Res. 2012 Nov;32(11):4663-70.*

- Reiman *et al.* used microarray analysis to identify novel pathways involving FLCN. They found that the expression of Wnt signaling, Cadherin signaling and apoptosis genes were affected by the loss of FLCN.

By combining their data with previously published data, they showed RAB27B expression to be dysregulated in all three datasets, identifying it as a potential FLCN interactor.

CLINICAL:

Happle 2012. Hornstein-Birt-Hogg-Dubé syndrome: a renaming and reconsideration. *Am J Med Genet A. 2012 Jun;158A(6):1247-51.*

- The author presents the argument that Hornstein and Knickenberg were the first to comprehensively describe BHD in 1976 and consequently the syndrome should be renamed Hornstein-Birt-Hogg-Dubé Syndrome.

Lindor et al., 2012. Birt-Hogg-Dube syndrome presenting as multiple oncocytic parotid tumors. *Hered Cancer Clin Pract. 2012 Oct 10;10(1):13.* (Free full text)

- Lindor *et al.* present the case of a 45 year old woman who presented in clinic with parotid tumours and fibrofolliculomas who was found to have a FLCN mutation. The parotid tumours were oncocytic, a characteristic commonly seen in BHD kidney tumours.

REVIEW:

Tee and Pause, 2012. Birt-Hogg-Dubé: tumour suppressor function and signalling dynamics central to folliculin. *Fam Cancer. 2012 Oct 25.* [Epub ahead of print]

- The authors review the role of FLCN in tumour suppression and numerous cell signalling pathways, including AMPK signalling, energy sensing and transcription regulation.

Schmidt 2012. Birt-Hogg-Dubé syndrome: from gene discovery to molecularly targeted therapies. *Fam Cancer. 2012 Oct 30.* [Epub ahead of print]

- A review of BHD research from the discovery of the FLCN gene to identifying interacting partners and its role in cellular pathways, and how this knowledge may lead to new therapies for the disease.

Middelton 2012. Birt-Hogg-Dubé: beyond the clinical manifestations. *Fam Cancer. 2012 Nov 23.* [Epub ahead of print]

- The author reviews the non-medical effects of having BHD, including psychological and financial, and suggests ways in which these problems can be better addressed in clinic.

Kuroda et al., 2012. Review of renal oncocytosis (multiple oncocytic lesions) with focus on clinical and pathobiological aspects. *Histol Histopathol. 2012 Nov;27(11):1407-12.*

- Kuroda *et al*. review the clinical and biological aspects of renal oncocytosis and suggest that Birt-Hogg-Dubé should be considered in the differential diagnosis of patients with these tumours.

Furuya & Nakatani 2012. Birt-Hogg-Dubé syndrome: clinicopathological features of the lung. *J Clin Pathol. 2012 Dec 8* [Epub ahead of print]

- The authors review the clinical and pathological features of the lung symptoms seen in BHD patients.

To participate in an interview feature, submit information or suggest a topic for the next newsletter, please contact us at contact@BHDSyndrome.org.

BHD foundation