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.

BHDSyndrome.org updates

The signalling diagram illustrating the protein and signalling interactions of Folliculin has been updated according to the latest research. Additionally, a new pop-up box showing the protein structure and interacting partners of Folliculin has been added. The diagram is interactive and fully referenced with peer-reviewed publications. To read more about the new diagram, click here.

Fifth BHD and Second HLRCC Symposium

The Fifth BHD and Second HLRCC Symposium will be held at the École de Louvre in Paris on 28th – 29th June, 2013. Hosted by Professor Stéphane Richard, the Symposium will include sessions for researchers on both BHD and HLRCC. For researchers, the abstract deadline is on **Friday 29th March** and the early-bird registration deadline is on **Sunday 31st March**; instructions for abstract submission and registration can be found on the conference website here.

As in previous years, there will also be a patient session, led by genetic counsellors Lindsay Middelton (National Cancer Institute, USA) and Sophie Deveaux (Hôpital de Bicêtre, France), which provides an excellent opportunity for patients to meet one another and talk to experts in a relaxed and informal environment. The early-bird registration deadline does not affect patients, whose registration fee will remain at €50 to attend the patient session or €100 to attend the whole conference.

New Member of the Myrovlytis Trust Scientific Advisory Board

We are pleased to announce that Professor Arnim Pause has agreed to join the Myrovlytis Trust Scientific Advisory Board. Professor Pause is Associate Professor in the Department of Biochemistry and Canada Research Chair in Molecular Oncology at McGill University, Canada. Professor Pause's research interests include the functional characterisation of the Folliculin protein in *C. elegans* and murine models.

Getting to know you

This quarter, meet Gigi from the USA who was diagnosed with BHD in 2011 and Dr Elaine Dunlop, a Post-Doctoral Research Fellow in Dr Andrew Tee's lab at Cardiff University, who is investigating the role of Folliculin in mTOR signalling. The interviews can be found here.

BHD Research Highlights

Noteworthy papers from the last quarter include:

BASIC:

Lu *et al*. Knockdown of Slingshot 2 (SSH2) serine phosphatase induces Caspase3 activation in human carcinoma cell lines with the loss of the Birt-Hogg-Dubé tumour suppressor gene (FLCN). *Oncogene. 2013* [Epub ahead of print]

- Lu *et al.* show that knockdown of the Slingshot 2 (SSH2) gene leads to the induction of apoptosis specifically in FLCN-null cells, suggesting that inhibiting SSH2 may be an effective therapy for BHD-associated tumours.

Kawai et al. Folliculin regulates cyclin D1 expression through cis-acting elements in the 3' untranslated region of cyclin D1 mRNA. Int J Oncol. 2013

- Kawai *et al.* show that *FLCN* knockdown in HeLa cells leads to increased levels of Cyclin D1. The authors found the FLCN exerts post-transcriptional control on Cyclin D1 expression, via the Cyclin D1 3'UTR.

CLINICAL:

Menko *et al*. A *de novo* FLCN mutation in a patient with spontaneous pneumothorax and renal cancer; a clinical and molecular evaluation. *Fam Cancer*. *2012* [Epub ahead of print]

- Menko *et al*. describe the case of a patient with a *de novo FLCN* mutation.

Pimenta *et al*. Birt-Hogg-Dubé syndrome: metalloproteinase activity and response to doxycycline. *Clinics (Sao Paulo). 2012 Dec;67(12):1501-4*. (Free full text)

- Pimenta *et al*. describe the case of a BHD patient who was originally mis-diagnosed with LAM and responded well to doxycycline treatment. The authors also found Matrix metalloprotease 9 (MMP9) to be highly expressed in macrophages and neutrophils in cyst walls.

Jandaghi *et al*. The discovery of a Persian family with a form of Birt-Hogg-Dubé syndrome lacking the typical cutaneous stigmata of the syndrome. *Clin Imaging. 2013 Jan-Feb;37(1):111-5*. (Free full text)

- Jandaghi *et al*. describe a Persian family with BHD who present with spontaneous pneumothorax.

Nishii *et al*. Unique mutation, accelerated mTOR signaling and angiogenesis in the pulmonary cysts of Birt-Hogg-Dubé syndrome. *Pathol Int. 2013 Jan;63(1):45-55*. (Free full text)

- Nishii *et al*. describe the case of a female BHD patient presenting with lung cysts and recurrent pneumothoraces. The authors found components of the mTOR and HIF-1a signalling pathways to be highly expressed, suggesting that these pathways have been dysregulated in the patient's lung cysts.

Pradella *et al*. Where Birt-Hogg-Dubé meets Cowden Syndrome: mirrored genetic defects in two cases of syndromic oncocytic tumours. *Eur J Hum Genet. 2013*. [Epub ahead of print]

- Pradella *et al*. found that oncocytic tumours resected from a BHD and Cowden Syndrome patient both carried compound heterozygous mutations in the *FLCN* and *PTEN* genes. The authors suggest that such compound heterozygosity causes oncocytic tumourigenesis in the context of Mendelian cancer predisposition syndromes, while mutations in mitochondrial genes cause sporadic oncocytic cancers.

Wee *et al*. Familial multiple discoid fibromas: unique histological features and therapeutic response to topical rapamycin. *Br J Dermatol. 2013.* [Epub ahead of print]

- Wee *et al*. describe the case of siblings with multiple papules on the face and pinnae, which developed in childhood. Whilst the patients did not carry a *FLCN* mutation, their skin lesions responded well to topical rapamycin treatment, suggesting that mTOR signalling is dysregulated in FMDF, as it may be in BHD.

***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