Birt-Hogg-Dubé Newsletter

June 2012 Vol.11, No.2

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 interactions of Folliculin has been updated according to the latest research. The interactive diagram includes a new feature: a pop-up box displaying Folliculin-associated phosphorylation events in greater detail. The diagram is fully referenced with peer-reviewed publications.

Several new interviews filmed at the Fourth BHD Symposium are now online. This series of interviews includes perspectives from a broader range of experts including Dr Ilene Sussman, Director of the VHL Family Alliance, Professor Frank McCormack, a leader in the cystic lung disease field, and Dr Vera Krymskaya, whose lab studies the basic biology of lung diseases. More will be coming soon!

BHD Pulmonary Centres

The LAM Foundation has 24 LAM Clinics across the USA - pulmonary centres of excellence. They also specialise in the lung symptoms of BHD. More information and contact details are available on the BHD Pulmonary Centres page.

New Member of the Myrovlytis Trust Scientific Advisory Board

We are pleased to announce that Dr Andrew Tee has agreed to join the Myrovlytis Trust Scientific Advisory Board. Dr Tee is a Research Lecturer at the Institute of Medical Genetics, Cardiff University School of Medicine, UK and a fellow of the Association for International Cancer Research. Dr Tee leads a research group investigating the cellular mechanisms underlying tuberous sclerosis complex and BHD syndrome, particularly the activity of a key protein called mammalian target of rapamycin (mTOR).

New Research Funding

We are delighted to announce the following grant awards:

Professor Stéphane Richard of the École Pratique des Hautes Études has received a grant for a new project investigating the functions of *Folliculin* variants.

Professor David Kwiatkowski of Harvard Medical School has been awarded a grant to study the genetics of BHD-associated tumours.

Getting to know you

This quarter, meet Sophie from France, who was diagnosed with BHD syndrome this year, as well as Professor Stéphane Richard, Professor at the École Pratique des Hautes Études and director of PREDIR, the French national expert centre for rare renal cancer syndromes funded by the Institut National du Cancer.

BHD Research Highlights

Noteworthy papers from the last quarter include:

BASIC:

Baba *et al*., 2012. The Folliculin-FNIP1 pathway deleted in human Birt-Hogg-Dubé syndrome is required for mouse B cell development. *Blood*. 2012 June 18.

Park *et al*, 2012. Disruption of Fnip1 Reveals a Metabolic Checkpoint Controlling B Lymphocyte Development. *Immunity*. 2012 May 16.

- Both groups have found that knocking out FNIP1 in mice resulted in the arrest of B cell development. Experiments by Park *et al*. suggested that loss of FNIP1 led to dysregulation of homeostasis though mTOR and AMPK pathways. Baba *et al*. showed that arrest resulted from rapid caspase-induced pre-B cell death. Baba *et al.* additionally demonstrated that conditional deletion of *FLCN* also resulted in B cell developmental arrest. Both groups of investigators have indicated an interesting novel role for FNIP1.

Behrends *et al.*, 2010. Network organization of the human autophagy system. *Nature*. 2010 Jul 1;466(7302):68-76. (Free full text)

- While this study is two years old, its findings are relevant in light of the papers above. Behrends *et al.* ran a screen of the proteins involved in autophagy. The results suggest that FNIP1 interacts with the autophagy protein GABARAP.

CLINICAL:

Jandaghi *et al*., 2012. The discovery of a Persian family with a form of Birt-Hogg-Dubé syndrome lacking the typical cutaneous stigmata of the syndrome. *Clinical Imaging*. 2012 Apr 25.

- The authors reported the case of a woman who presented with bilateral renal cell carcinoma and personal and family history of spontaneous pneumothorax. 23 members of her family were tested for BHD; 10 individuals were found to a carry a *FLCN* mutation. 7 of these had presented with no symptoms.

Shuch *et al*., 2012. Targeting the mTOR pathway in Chromophobe Kidney Cancer. *J Cancer*. 2012;3:152-7. (Free full text)

- Shuch *et al.* discussed the potential of mTOR targeted therapies in renal cell carcinoma. The authors presented the case of a patient with metastasis who was placed on temsirolimus and is performing well with five years of ongoing treatment. Shuch *et al.* also reviewed literature on mTOR agents which reported at least partial responses in patients.

Tobino and Seyama, 2012. Birt-Hogg-Dubé syndrome with renal angiomyolipoma. *Intern Med*. 2012; 51(10):1279-80. (Free full text)

Byrne *et al*., 2012. Birt-Hogg-Dubé syndrome with a renal angiomyolipoma: Further evidence of a relationship between Birt-Hogg-Dubé syndrome and tuberous sclerosis complex. *Australas J Dermatol*. 2012 May;53(2):151-4.

- Tobino and Seyama and Bryne *et al*. each reported a case of a patient diagnosed with BHD and found to have a renal angiomyolipoma. The findings of both groups highlight the variability of presentation in BHD syndrome and emphasise careful clinical examination and consideration of family history in making an accurate diagnosis.

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