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.

Sixth BHD Symposium and First International Upstate Kidney Cancer Symposium 2015

We are delighted to announce that the Sixth BHD Symposium and First International Upstate Kidney Cancer Symposium will be hosted by Dr Mehdi Mollapour and Professor Gennady Bratslavsky at the Upstate Medical University in Syracuse, New York, on 23rd-26th September 2015. We would be delighted to see as many of you there as possible.

BHDSyndrome.org updates

We have a developed a new "Finding a Doctor" page in our patient information section. An interactive map provides the location and contact details for VHL alliance specialist Clinical Care Centres for kidney treatments around the world and the LAM pulmonary care centres in the USA.

We have also reviewed our Advanced Information pamphlets and Clinical Introduction to BHD guide to ensure they contain the most up to date information on symptoms and treatments.

Cancer in our Genes International Patient Databank

The Cancer in Our Genes International Patient (CGIP) Databank aims to identify similarities and differences between BHD, VHL, HLRCC, SDH and related conditions to improve treatments. You can read more about the importance of this project here. Please consider participating in this important clinical research by going to www.vhl.org/databank.

Getting to know you

This quarter, meet Anna from the Sweden who was diagnosed with BHD in 2008, and Mitsuko Furuya who is a clinician and researcher in Yokohama City University. Mitsuko is part of the BHD-NET team working to increase the understanding of pulmonary and renal pathologies in BHD and raise awareness in Japan. The interviews can be found here.

BHD Research Highlights

Noteworthy papers from the last quarter include:

Basic:

Reyes *et al.,* Fnip1 regulates skeletal muscle fiber type specification, fatigue resistance, and susceptibility to muscular dystrophy. Proc Natl Acad Sci USA. 2015 Jan 13;112(2):424-9.

- Using a *Fnip1* null mouse model Reyes *et al.* reported a role for Fnip1 in skeletal muscle fibre specification. The increase in type 1 fibre specification was linked to increased AMPK activation and increased expression of the AMPK-target and coactivator PGC1α.

Hasumi *et al.,* Folliculin-interacting proteins Fnip1 and Fnip2 play critical roles in kidney tumour suppression in cooperation with Flcn. Proc Natl Acad Sci USA. 2015 Mar 16. [Epub ahead of print]

- Hasumi *et al.*, report that loss of the folliculin interacting proteins Fnip1 and Fnip2 in mouse kidney cells is sufficient to induce tumour formation. The molecular hallmarks of this tumourigenesis are the same as those seen after homozygous loss of folliculin suggesting activation of the same pathways and a shared function in normal tissue.

Clinical:

Johannesma *et al.,* Prevalence of Birt-Hogg-Dubé syndrome in patients with apparently primary spontaneous pneumothorax. Eur Respir J. 2014 Dec 23. [Epub ahead of print]

- Johannesma *et al.* present cohort data that suggests 5-10% of patients diagnosed with PSP could in fact be undiagnosed BHD patients. They recommend that history of PSP and location of pulmonary cysts should be used to identify prime candidates for genetic analysis.

Furuya *et al* Distinctive expression patterns of glycoprotein non-metastatic B and folliculin in renal tumours in patients with Birt-Hogg-Dubé syndrome. Cancer Sci. 2015 Jan 8. [Epub ahead of print]

- Furuya *et al.* report the divergent expression on FLCN and GPNMB in sporadic and BHD renal tumours. Loss of FLCN expression in combination with a gain of GPNMB expression in BHD chromophobe tumours and HOCTs can distinguish them from sporadic chromophobe tumours and oncocytomas. It is not sufficient however to distinguish between sporadic and FLCN-associated forms of ccRCC.

Iribe *et al*., Immunohistochemical characterization of renal tumours in patients with Birt-Hogg-Dubé Syndrome. Pathol Int. 2015 Mar; 65(3):126-32.

- Iribe *et al.*, report on immunohistochemical characterisation of RCCs from BHD patients; differential expression of CK7, Ksp-cadherin and CD82 can distinguish sporadic chromophobe RCC and oncocytomas from BHD-HOCTs, but cannot distinguish sporadic and BHD-associated forms of chromophobe RCC and ccRCC.

Review:

Dal Sasso *et al.,* Birt-Hogg-Dubé syndrome. State-of-the-art review with emphasis on pulmonary involvement. Respir Med. 2014 Dec 9 [Epub ahead of print]

- A concise and succinct review of current BHD literature covering genetics, pathology, clinical manifestation, diagnosis and treatment. There is some focus on pulmonary pathology development and Dal Sasso *et al.,* support recently suggested guidelines for BHD genetic testing based on initial pulmonary imaging.

Schmidt and Linehan Clinical features, genetics and potential therapeutic approaches for Birt–Hogg–Dubé syndrome Expert Opinion on Orphan Drugs. 2015 Jan, 3(1): 15-29.

- A detailed review covering the clinical manifestations, genetics, diagnostic criteria and clinical management of BHD, the known functions of folliculin and the molecular consequences of its loss. Schmidt and Linehan also comment on current treatments and future developments.

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