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 redesign

The BHD Syndrome website has been redesigned. The objectives of the new design were aesthetics, facilitating the navigation and having a responsive layout for all platforms: desktops, phones and tablets. It also includes an updated and more interactive FLCN signalling pathway. Explore the site and let us know what you think. Your feedback is most welcome!

New PhD thesis on BHD Syndrome

Dr Paul Johannesma from the VU University Medical Centre of Amsterdam has recently published his PhD thesis: "Renal and Pulmonary Aspects of Birt-Hogg-Dube syndrome". An online version of the thesis is available here.

Getting to know you

This quarter meet Sabina from Spain who was diagnosed with BHD in 2013 and Dr Masaya Baba who is based at the Kumamoto University in Japan. Dr Baba is interested in the molecular mechanisms of kidney cancer development in BHD Syndrome and in the molecular functions of FLCN in murine disease models. The interviews can be found here.

BHD Research Highlights

Noteworthy papers from the last quarter include:

Basic:

Furuya *et al*., 2016. Establishment and characterization of BHD-F59RSVT, an immortalized cell line derived from a renal cell carcinoma in a patient with Birt-Hogg-Dubé syndrome. Lab Invest. 2016 Dec 19.

- Furuya *et al.* established a new cell line from a BHD patient's chromophobe RCC. The authors investigated FLCN mutations, chromosome profiles, and cytopathologic characteristics of the cell line to confirm its suitability for functional analysis of the typical phenotype of BHD-associated RCC with impaired FLCN.

Wada *et al*., 2016. The tumor suppressor FLCN mediates an alternate mTOR pathway to regulate browning of adipose tissue. Genes Dev. 2016 Nov 15: 30(22)

- Wada *et al.* showed that FLCN regulates the browning of adipose tissue via a non-canonical mTOR pathway. The adipose-specific deletion of FLCN allows TFE3 to migrate to the nucleus where it induces PGC-1, which drives mitochondrial biogenesis and the browning program.

Hoshika *et al*., 2016. Haploinsufficiency of the folliculin gene leads to impaired functions of lung fibroblasts in patients with Birt–Hogg–Dubé syndrome. Physiol Rep. 2016 Nov: 4(21)

- Hoshika *et al.* report that FLCN is associated with chemotaxis in lung fibroblasts and that, together reduced TGF-β1 expression by lung fibroblasts from BHD patients, *FLCN* haploinsufficiency seems to cause lung fibroblast dysfunction, impairing tissue repair.

Clinical:

Gunji-Niitsu *et al*., 2016. Benign clear cell "sugar" tumor of the lung in a patient with Birt-Hogg-Dubé syndrome: a case report. BMC Med Genet. 2016 Nov 21;17(1):85.

- Gunji-Niitsu *et al.* reported for the first time, a patient with BHD syndrome associated with a clear cell "sugar" tumour (CCST) of the lung. In BHD, the established propensity for cancer is limited to the renal tumours. Whether BHD syndrome confers the risk of developing other types of cancer remains unknown.

Matsutani *et al*., 2016. Birt-Hogg-Dube syndrome accompanied by pulmonary arteriovenous malformation. J Thorac Dis. 2016 Oct; 8(10):E1187-E1189.

- Matsutani *et al.* reported for the first time a case of BHD syndrome accompanied by pulmonary arteriovenous malformation. It is unknown if there is a relationship between the two.

Yukawa *et al*., 2016. A Case of Birt-Hogg-Dubé (BHD) Syndrome Harboring a Novel Folliculin (FLCN) Gene Mutation. Am J Case Rep. 2016 Oct 26;17:788-792.

- Yukawa *et al.* reported a novel deletion mutation (c.57_58delCT) in exon 4 of the *FLCN* gene in a patient presenting with multiple lung cysts, skin papules and an history of pneumothorax.

Furuya *et al*., 2016. Genetic, epidemiologic and clinicopathologic studies of Japanese Asian patients with Birt-Hogg-Dubé syndrome. Clin Genet. 2016 Nov; 90(5):403-412.

- Furuya *et al.* presented a new study describing genetic, epidemiologic and clinicopathologic features of 312 Asian individuals with BHD manifestations based on data from 120 probands from different families. Their results show that recurrent pneumothorax are the major symptoms suggestive of a BHD diagnosis. Lung and kidney manifestations are more informative as diagnostic criteria for BHD in the Japanese population as the cutaneous manifestations are very subtle.

Gupta *et al*., 2016. Chest Computed Tomographic Image Screening for Cystic Lung Diseases in Patients with Spontaneous Pneumothorax is Cost-effective. Ann Am Thorac Soc. 2016 Oct 13.

- Gupta *et al.* presented a new study evaluating the cost-effectiveness of high resolution computed tomographic (HRCT) chest imaging for early diagnosis of LAM, BHD, and PLCH in patients presenting with an apparent primary spontaneous pneumothorax (SP). In their analysis, the authors show that HRCT image screening for BHD, LAM and PLCH in patients with apparent primary SP is cost-effective and suggest that clinicians should consider performing a screening HRCT in these patients.

Review:

Schmidt *et al*., 2016. Genetic predisposition to kidney cancer. Semin Oncol. 2016 Oct;43(5):566-574.

- Schmidt *et al.* reviewed the clinical characteristics and the causative genes inherited for renal cell carcinoma syndromes, such as BHD. The authors also summarized the pathways that are dysregulated when the inherited genes are mutated, and recommended clinical management of patients with these inherited renal cancer syndromes.

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