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 email for instructions.

BHD Research Blog

Duncan Azzopardi of the Myrovlytis Trust has started writing a regular blog at www.BHDSyndrome.org. The blog is aimed primarily at researchers within the field interested in an external opinion on current publications, although Duncan hopes it will be relevant to others involved in BHD. As with most other features www.BHDSyndrome.org, interactivity is greatly encouraged and readers can leave comments. Go check it out!

BHD Forum

Thank you to everyone who has contributed so far to the BHD Forum. One of the major aims behind www.BHDSyndrome.org is to encourage and foster a BHD community – a community that includes scientists, clinicians, individuals and families affected by BHD. We look forward to its continued growth and success

BHD Funding News

The Myrovlytis Trust is funding three research projects into renal gene therapy. The projects, which will use a variety of viral and non-viral methods, are being led by: Dr Yosef Haviv (Hadassah-Hebrew University Medical Centre, Israel); Dr Richard Harbottle (Imperial College, London, UK); a collaboration between Professor Andy Baker and Dr Laura Denby (Glasgow, UK) and Professor David Curiel and Dr Justin Roth (University of Alabama, Birmingham, USA) .

The Myrovlytis Trust has awarded a research grant to Dr Vera Krymskaya, Associate Professor at the University of Pennsylvania. The grant, for up to two years, will fund a post-doc to look at the role of Folliculin in cell proliferation, cell-cell contact formation and cell-cell interactions.

Second BHD Symposium – A date for your diary

The next BHD Symposium is currently scheduled for April 22nd 2010 in Washington DC, USA. This will be an excellent occasion for researchers to present their work and share their findings with each other. More details will be available in due course.

BHD Information Pamphlets – Watch this space

We are currently in the process of developing information pamphlets on different aspects of BHD Syndrome. These will include a general overview of the disease and information regarding specific symptoms and their respective treatments. We know that there is no typical BHD patient and that you may only want to learn about the specifics of the symptoms you currently have, without burdening you

with too much detail. They will be available to download off the website and you may wish to share them with family members and health care providers.

New Feature: Getting to know you!

In each issue of the BHD Syndrome newsletter we have encouraged users of our website to interact with each other and share personal stories in order to demystify BHD syndrome. Well, now we've decided to make a feature out of it! Every three months we will interview a BHD Researcher and a BHD patient. We hope you'll find it an interesting way of getting to know the faces behind BHD, both in the lab and at home. For this first issue we have interviewed Dr Laura Schmidt and Mark, a patient from New Zealand: both interviews are available in full in this newsletter, as well as on www.BHDSyndrome.org. Subsequent interviews will be available at www.BHDSyndrome.org/topics/interviews

Click to read:

BHD Researcher Interview: Dr Laura S. Schmidt

Biography: Dr. Schmidt obtained her Ph.D. degree in biochemistry from Vanderbilt University in Nashville. She held postdoctoral fellowships at Indiana University under Dr. Howard Guest, and at Boston College under Dr. Joseph Orlando. She was a Medical Foundation scholar at Tufts University Medical School in Boston in the laboratory of Dr. James T. Park. Dr. Schmidt was employed at the NCI as a member of the Laboratory of Immunobiology from 1990 to 2005, and recently joined the Urologic Oncology Branch, NCI, NIH. Her research is aimed at the identification of renal cancer susceptibility genes through the study of families with inherited renal cell carcinoma.

1. How did you get interested in BHD research?

For the past 20 years my research interests have been focused on the identification of genes that predispose individuals to the development of kidney tumors through the study of families in which kidney cancer is inherited. I have been part of the NCI team that discovered the VHL gene, which causes clear cell kidney cancer associated with the von Hippel Lindau disease, and identified mutations in the MET oncogene that predispose to papillary renal tumors in Hereditary Papillary Renal Carcinoma. In the late 1990's we described 5 families with a rare inherited renal neoplasm, renal oncocytoma, for which the causative gene was unknown. When a careful dermatologic examination revealed fibrofolliculomas, the cutaneous hallmark lesion of Birt-Hogg-Dube´ syndrome, on the faces of some of these patients, we were able to make a clear connection between this rare dermatologic disorder and a risk for developing kidney neoplasms. We recruited additional BHD families with fibrofolliculomas and kidney tumors, which enabled us to localize the BHD locus by linkage to chromosome 17 and identify causative mutations in the FLCN gene.

2. *What are you currently working on?*

Now that the FLCN gene has been identified and the mutation spectrum well documented, our laboratory is focused on understanding the function of the encoded protein, folliculin, in normal cell pathways and how mutations in FLCN can lead to the development of kidney cancer in BHD patients. We have developed a number of mouse models of BHD as well as cell-based systems to help us in our research.

3. What would help current research (equipment, technique etc.)?

The discovery of a biomarker specifically linked to the types of kidney tumors that develop in BHD patients would be useful for diagnostic purposes and for the development of therapeutic treatments. When the function of the FLCN protein is elucidated, the development of a functional assay will be immensely helpful to our research.

4. What recent developments in the field have interested you most?

Emerging data from several labs have supported an interaction of FLCN with the converging PI3K-AKT-mTOR and AMPK-TSC1/2-mTOR pathways that regulate cell growth through nutrient and energy sensing. This is most significant because it links FLCN with other tumor suppressor genes that have been shown to regulate these pathways and which, when mutated, give rise to hamartoma "overgrowth" syndromes like BHD syndrome. Our goal as researchers is to uncover and clarify the details of this most interesting connection.

5. Do you have a favourite research paper?

The two papers describing kidney-targeted FLCN inactivation in the mouse [Baba et al., (2008) J Natl Cancer Inst.100:140-54; Chen et al.,(2008) PLoS One. 3:e3581] have provided exciting in vivo models with which to elucidate FLCN function and for testing therapeutic drug treatments.

6. What are your short/long term goasl?

In the short term, we are following up on data from protein-protein interaction studies and gene expression analyses that suggest novel pathways in which FLCN interaction may be important. Our long-range goal is to develop therapeutic treatments for BHD-associated kidney cancer based upon the results of FLCN functional studies.

7. How do you see the field developing in the next ten years?

Ultimately BHD researchers are united in a common goal to develop therapeutic treatments for the cutaneous lesions and kidney tumors that develop in BHD patients. Our concerted effort to elucidate FLCN function and to understand how loss of FLCN dysregulates the biochemical pathway(s) with which it interacts will provide the basis for targeted therapies to improve the prognosis and quality of life of BHD patients.

8. What's your favourite book/film/music?

I love all musical theater, but I guess my favorite is "West Side Story".

9. What did you want to be when you were younger?

As long as I can remember, I loved science and wanted to be a "scientist". I credit my father for fostering my interest in science by showing me as a young child how magnets work, pointing out the constellations in the night sky, and helping me find interesting creatures and plants along the trails we hiked together.

10. Where do you see yourself in 10 years?

I will probably continue the study of families with inherited kidney cancer syndromes at the NCI, but I also hope to do some traveling and look forward to playing with my grandchildren!

11. What's the best advice you've been given?

We are only here for a short time so try to make a positive contribution to the world every day, strive to keep your work life and your home life in a healthy balance, and don't forget to stop and "smell the roses"!

12. Do you have a scientific hero, dead or alive?

Dr. Berton Zbar, lab chief of the Laboratory of Immunobiology at the NCI, was my mentor and scientific adviser for nearly 15 years until his retirement in 2004. My approach to scientific research has been greatly influenced by his advice and counsel. He has been my role model throughout my scientific career and I am indebted to him for the many valuable lessons learned under his scientific guidance.

Back to 'Getting to know you'

Click for Mark's Story

BHD personal story: Mark, New Zealand

Mark is a registered user of www.BHDSyndrome.org and has previously contributed to the forum.

1. When did you first get diagnosed?

A surgeon first suggested I might have BHD in late-2006. It took about 3 months to get an appointment with the genetics clinic, have some blood drawn, and then get the results back.

2. What symptoms prompted the BHD diagnosis?

I'd just been in for surgery to sort out a recurring pneumothorax. My surgeon was puzzled by the family history of pneumothoraxes. A few months later he had some down time and spent the day digging around looking for conditions that could explain that family history. He suggested my family might have BHD.

3. What impact did the diagnosis have on you?

It was actually quite nice to have an explanation for my family's long-standing problems with collapsed lungs. We didn't know too much about the other BHD symptoms at that stage.

4. Have you explained BHD to family members?

Yes.

5. What implications do you think it has it had on your family?

Nearly all of that side of my family have now had the genetic testing and we've discovered several family members who have BHD but who haven't (to date) had any manifestation of it.

6. Where did you go for more information on BHD Syndrome?

All the usual sources … eMedicine, Wikipedia etc … and then more recently I discovered the bhdsyndrome site.

7. Do you have advice for people who are looking for a diagnosis?

No special advice really … just that it's better to know what your medical situation is rather than to be in the dark.

8. ***Has it affected you as a parent? E.g. telling your children, starting a family, genetic counselling.***

Not yet, because my children are 1 and 3 years old. But it does make me watch them a little more closely to see if they get any skin bumps etc etc.

9. Do you have tips and advice for caregivers?

No.

10. What are your current symptoms?

None. I've had operations on both my lungs now and I don't imagine they can collapse again. I have a CAT scan or an ultrasound on my kidney in alternate years, but I don't seem to have any problems there so far.

11. What treatment are you having, and have you had?

No current treatment

12. Do you have advice for people living with the BHD?

Stay fit. Both times I've had pneumothoraxes I've been very fit, and I believe it does make a big difference to how badly it affects you and how quickly you bounce back.

13. What has been your experience of the healthcare system and healthcare professionals?

Very good

14. Has BHD had any health insurance implications for you?

Not really. I live in New Zealand and we have a public funded health system here. I do have private health insurance too, but that's really focused on just non-essential elective surgery.

15. What are your thoughts for the future?

Just to keep having regular annual checkups on my kidneys.

16. What advice would you give to someone who has just been diagnosed with BHD?

It seems that with good medical care then BHD isn't anywhere near as serious as many other medical conditions. Sure, it's not great, but there are a lot of things that are worse.

If you would like to participate in our 'Getting to know you!' feature, please contact us at contact@BHDSyndrome.org

If you would like to submit information or a topic for the next newsletter, please contact the editor at info@bhdsyndrome.org

Myrovlytis Trust *Birt-Hogg-Dubé Family Alliance*

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