Interview Transcript – Dr. Derek Lim

I'm Jill Woodward. I'm at the Third BHD Symposium; joining me is Dr Derek Lim. Dr Lim, can you tell me a little bit more about the research that you've presented?

I presented basically the work that I've been carrying out on the clinical aspects of research into Birt-Hogg-Dubé Syndrome. So what I have been doing is visiting all Birt-Hogg-Dubé patients who agreed to take part in our study in the UK. The main aim is to really get as much clinical information from them, to learn from them. So, for example, at what ages the various manifestations of Birt-Hogg-Dubé has affected them and also try and find out if there are any rare manifestations that we as clinicians or researchers need to be aware about. Because although there has been a few studies that have been done, we still feel that there's lots more to learn from our patients with Birt-Hogg-Dubé syndrome. One of the other aims is to try and work out what the age-related risks are for the other manifestations in order to define a surveillance programme for our patients as well.

You're leading a resource initiative for the Folliculin mutation database. What are the goals of this database and how are you hoping it will be used?

So when we first set up this database for the *Folliculin* gene, so one of the main aims is for this to be the main resource for variants in the *Folliculin* gene itself. So it would be of benefit for clinicians, people who work on *Folliculin* in diagnostic labs across the world, as well as research laboratories as well. So one of the troubles when one is looking at the *Folliculin* gene is trying to find, to know about, all known *Folliculin* variants, and sometimes it's very hard to go through the medical literature to try and pick out those papers that have recorded those changes in the gene. So in a sense what we've done is we've put it all in one place on the database that's available on the internet, so people can access this information from that website. So it will contain information on all the sequence variants that have been published in the medical literature, but also new or unpublished or novel variants that can be uploaded by diagnostic labs throughout the world as well. So in a sense it provides information for people who are doing gene testing for *Folliculin* and also researchers. And it sort of helps foster collaborations within laboratories and researchers working on Birt-Hogg-Dubé, as well as clinicians who are seeing patients who have the sequence change in *Folliculin*.

You're also involved with the BHD Registry in the UK. What is it and how has that been helpful so far?

So in the UK, it was in 2007 when the gene testing for Birt-Hogg-Dubé was made available as a diagnostic service. And since then a registry of patients who have tested positive for this gene change was available. And what we've done is to approach the clinicians who've referred the patients for testing to see if they, the patients themselves, would consent to be involved in a cohort of Birt-Hogg-Dubé patients we could then follow-up as part of our research. And that's in a sense how we started with our clinical research project into Birt-Hogg-Dubé syndrome.

As a clinical research fellow, do you also see patients?

So I'm a clinician, so I'm trained in clinical genetics. So I do see patients, not only with Birt-Hogg-Dubé syndrome, but also with other inherited genetic conditions for example. But my main work in the research has been concentrating on Birt-Hogg-Dubé syndrome as I mentioned earlier: visiting patients and examining them and learning more about the history of how they've been affected with Birt-Hogg-Dubé syndrome. So as a clinical research fellow that's often very useful to have that experience because we often reflect what we find in the laboratories in the research, and how it may relate to what we see in patients. And so I think it's a very useful skill to have.

How has your research added to our understanding of BHD syndrome?

One of the things that we've looked at is for example how patients have presented with Birt-Hogg-Dubé syndrome. So a number of our patients were mainly diagnosed because of their skin manifestations. And therefore because they can be quite variable, in some patients it can be quite mild, whereas in other patients it can be more severely affected, so some of the mild cases may not necessarily be presented to the doctors. So we're probably under-diagnosing or under-recognising the condition especially if they're very mild. So in a sense it's more to raise awareness to other clinicians that we should be looking at things more closely.

Can you talk about what you were working on before you got into the BHD research field?

I was working in a Clinical Genetics department in Birmingham in the United Kingdom, as part of my training to be a clinical geneticist I also undertook a research project into Beckwith-Wiedemann syndrome, which is another genetic condition, although a bit different from Birt-

Hogg-Dubé syndrome, where patients can present with tumours especially during childhood, and especially affecting the kidneys. With that aspect, the research I was mainly doing more work in the laboratory, trying to look more into the genetics of Beckwith-Wiedemann syndrome.

How did you get into the field of clinical genetics?

I trained as a paediatrician. So during my clinical work I came across lots of patients and families with severe genetic conditions and from that time I developed a keen interest in clinical genetics as a speciality: how they've been involved with these families and why they were diagnosed for example. So that's when I got into clinical genetics training about half-way through my paediatrics trainings.

Do you collaborate with other institutions in BHD and if so how is this helping your work?

In terms of the clinical aspects and the molecular aspect of Birt-Hogg-Dubé syndrome, I work very closely with the BHD working group in Birmingham University, so colleagues who are post-docs and PhD students, as well as my supervisor Professor Eamonn Maher, relating what we find clinically and what has been discovered in the lab as well. In addition, because I am sort of curating the European BHD Consortium and the *Folliculin* mutation database, so I work very closely with other diagnostic labs across Europe and keep them updated on what we're finding in terms of sequence changes or even detected deletions or duplications in the gene, so there's lots of collaboration in there.

How have you found the Symposium this year?

I think it's been really exciting. A lot of new information has been shared among all the different research groups working on BHD, not only from the clinical aspects of BHD but also what's been discovered in terms of how the *Folliculin* gene functions and giving us more insight into different pathways that have not been described before in relation to the *Folliculin* gene. So I think it's exciting that we get to hear this first hand and to get a whole range of experts on BHD in one meeting.

At the symposium we've heard lots of calls for more research needed; what specific areas do you think would help move the research forward?

At the moment, I think we have got interest from people with backgrounds in, with an interest in kidney cancers and dermatologists. I think it would be useful to have more researchers who are working on the lung aspects in genetics or in cell biology because that's one of the manifestations which is probably not as much represented in the BHD field currently, I think. So it would be useful to get more pulmonologists involved in the research.

What do you think the BHD research field is going to look like in about 5-10 years and what are you hoping for?

We hope that as we understand a lot more about the *Folliculin* gene and the protein and which pathways it works in, we'll be able to identify the new agents or drugs that we could use to help treat patients and I think that's been the main goal of the research that's being done in Birt-Hogg-Dubé syndrome. So I think it's an exciting time from what we can expect in the next 5-10 years.

You mentioned that BHD is under-diagnosed; how can we improve on that?

What we've been doing is trying to take what we find in our clinical research to various clinicians that may be involved with patients with Birt-Hogg-Dubé syndrome for example trying to present our work to the dermatologists, to the patients [*sic*] who work in the respiratory field, so in thoracic surgery and the pulmonologists, for example, as well as other clinical geneticists, so in order to try and raise awareness of Birt-Hogg-Dubé syndrome as a condition. We've worked with the Myrovlytis Trust to develop some patient information leaflets and also information leaflets that patients can give to their own general practitioner or any doctors that they come across explaining about Birt-Hogg-Dubé syndrome and what it is and how it will affect patients. So we're sort of trying to get the message out there so that more doctors can easily recognise the condition.

Dr Derek Lim, thank you very much for speaking with us today.