Interview Transcript — Dr Fred Menko

We're at the University of Cincinnati where the Fourth BHD Symposium has just concluded. I'm Jill Woodward and I'm here with Dr Fred Menko. Dr Menko, can you summarise the research that you presented here at the Symposium?

There's two main subjects. One was renal imaging in BHD: what would be the best recommendation. So what you need is data to base the recommendation upon, so we presented some data from our centre: the advantages and disadvantages of CT scan, MRI scan, renal ultrasound for imaging were presented and that was as a contribution to a panel discussion. And the other presentation was on a family with a *FNIP1* germline mutation, which is a new finding in this gene which leads to a disorder which resembles Birt-Hogg-Dubé syndrome and it's called familial multiple discoid fibromas. It has been published as a separate clinical entity and now I presented the genetic background of this disease.

Can you talk about how seeing patients affects your research approach?

It affects it greatly, because I'm not in basic research and I'm very glad that other people are doing this basic research. I work in a clinical genetics centre. About 40% of all patients that we see is for cancer genetics. What I do is evaluation of clinical care, so it's directly related to patient care or to the families that I see. So the questions that people have or the problems that they face directly affect research. And for example when a patient comes to the clinic with metastatic renal cancer—when he told me that after a reunion of the family he found out that, in a bunch of the family that we had seen before, that Birt-Hogg-Dubé syndrome was diagnosed. He was a distant relative, was diagnosed with metastatic renal cancer after he developed haematuria. Now we usually say to the patient "this is a letter for your family; please inform them". And usually that's about it. But it doesn't work—that's also known. About 50% of those at risk will come forward and be tested. And that is a problem in genetics in general. There are efforts, there are guidelines on how to do this, but now this is an important signal from a patient. Do all efforts in BHD patients. When you diagnose it, some mutation carrier, don't stop until all the relatives and the distant relatives, if at all possible, have been informed.

What difficulties have you faced in your projects?

The challenges for research in my—in my work is to get the time and energy needed for research apart from the clinical work seeing patients and doing all the things that are necessary for the daily work.

You're an author of a frequently cited paper on the diagnosis and treatment of BHD in the Lancet Oncology. In the paper it stated that there are no established guidelines for the clinical management of renal cancer in BHD. How far away are we from establishing those guidelines?

It's always difficult to get guidelines in one centre, then you have to get guidelines for different centres, there are different hospitals... but I think one of the most important outcomes of this meeting was that we now will have consensus about important aspects. Since I'm also editor of a journal *Familial Cancer* which has published abstracts of previous conferences. We now also agreed that the main outcomes of this meeting, which will include recommendations—it has to be, it has to get, the format hasn't been decided upon—but to have the abstracts of this meetings, some reviews of this meeting, a contribution from the patient group, and some form of the outcome of the panel discussion—the recommendations will be in there. So I think this conference in an important next step. The translation of recommendations to clinical practice: that's another story, that's another difficulty but I think this is important.

As you mentioned, you're one of the editors of the journal Familial Cancer. During those years that you've been editor, what would you consider the most significant changes in research?

Well, what I think is most exciting, important, is the translation into therapy. That you get the development of cancer genetics from diagnosis where you can diagnose a disorder, such as Birt-Hogg-Dubé syndrome, and know what the phenotype is and know how to diagnose the lesions that may develop at an early stage like renal tumours; that is one field. And now it moves to insight into molecular pathogenesis, insight into signalling pathways—how does it come about that a deficiency of Folliculin leads to Birt-Hogg-Dubé syndrome? So the clinical genetics moves from only diagnosis to important for therapy. So that was presented also here, the rapamycin trial for skin lesions. Rapamycin, to stick to that example, is a treatment for

patients who unfortunately might develop metastatic renal cancer. Then you use the molecular insight in Birt-Hogg-Dubé syndrome for therapy. So that's a development, that's a new field.

What could the future look like for research into familial cancers?

Again, I think insight into molecular pathways so to be more able to offer patients therapies based on diagnosis instead of only... Well, to have a diagnosis is important because then you know in the family who is susceptible, who is not susceptible after DNA testing. And if you have good insight into the disorder, you can protect patients from disease by early diagnosis of curable stages of tumours so it's important to have a diagnosis. But then the development of therapies based on the insight into the molecular pathology—it is what I said about general—how general development of clinical genetics also applies for different consequences for patients.

How has the Symposium been for you this year?

Great. It was great to—in several ways. First of all by meeting the people again, the colleagues. Because you can—there is no substitute for meeting colleagues. And then especially in this small field where there are relatively few people working on it, to meet the colleagues and to speak to them about patient care and research, there is no substitute for that. That's one. And I think the other thing is the panel discussion with the clinical recommendations where consensus was reached; I'll take that home and be happy that this has been reached. So that's important. And the other good thing about this conference was the large group of patients who were here. I met with them. It was important to hear their stories because I also with [Dr Jorge] Toro was chairing this Thursday morning session and trying to get the most out of the panel discussion. So it has been important to speak to patients and family members before the panel discussion to hear what's going on, what questions they have. I should know, I know patients, I've seen many patients. But it's different to speak to patients at a conference like this and again learn what questions they have. So that was the other important thing. Colleagues, the consensus on guidelines, and the contribution of the patient groups.

Dr Fred Menko, thank you very much for talking with us today.

Very happy to do so.