Interview Transcript – Dr Seung-Beom Hong

We're at the Third BHD Symposium. My name is Jill Woodward and I'm speaking with Dr Seung-Beom Hong today. Dr Hong, can you describe the work that you presented at the Symposium?

Basically I worked on the regulation of TFE3 transcription factor, which is regulated by Folliculin and also by AMPK and FNIP1 and FNIP2.

And how has this research added to our understanding of BHD?

So far we didn't have the clear downstream target molecule which is regulated by the Folliculin tumour suppressor gene. So I tried to identify the downstream molecules that is regulated by BHD and the *Folliculin* tumour suppressor gene. Indeed, the TFE3 is the downstream molecule involved in the regulation of AMPK, and FNIP is also involved.

Now why is that important?

So TFE3 is a kind of very interesting transcription factor, which is regulating tumour progression and also metabolic disorders.

Can you elaborate on the significance of TFE3?

So BHD syndrome, we didn't know what it's doing, but now through my study we found the downstream molecule, the TFE3 which is regulating the metabolic pathways, and also in connection with AMPK and FNIP1. So that adds up the develop processes which is regulated by Folliculin. Then we can kind of in the future target what kind of processes we can block or activate to treat some kind of tumour progression or something like that.

What do you mean by downstream?

Downstream is — so we think Folliculin has some function. So in the patients the *Folliculin* gene is inactivated. So downstream is: if you have no Folliculin, then as a result of the inactivation of *Folliculin* BHD gene, then there is a subsequent event happening in the cell. So

that's what we call the downstream event of the first inactivation event. So we traced down the downstream event, and then using that as a marker, or tracer, we go back to the first event: what is the function of Folliculin. By knowing the downstream event, we can also trace back to the original function of the BHD.

So talk about the techniques that you use in your lab?

I use a lot of techniques such as gene expression microarray and also cell biological techniques. I mean, localising where the protein is located in the cell: whether it's located in the cytoplasm or in the nucleus. And also treat a lot of drugs to see whether the localisation of protein is altered by some kind of drugs or chemicals.

Did your project present any special challenges or difficulties?

So at the beginning, because everybody knows that the Folliculin has no similar proteins known, so we struggled a lot to find what is the mechanism, the processes regulated by Folliculin. So I tried many methods, and finally I found some clue using gene expression microarray and found clear downstream target molecule which is regulated by Folliculin and of course AMPK.

What do you consider to be the wider implications of your research?

So far people are focussed on the mTOR signalling: the relationship between BHD and mTOR signalling. But now I'm thinking, my research suggests that Folliculin and AMPK on the progression of tumours. So this is kind of a new concept: the AMPK involvement in tumourgenesis. So this can be also because AMPK is so much implicated in energy metabolism and tumour cells they need a lot of energy, so AMPK signalling should be contributing [to] other types of tumours also. So by characterising this pathway, we can also apply this system to checking out [if] other tumours also can be developed by the AMPK or Folliculin.

What are your future plans for research?

I'm working on the regulation of TFE3 by Folliculin and AMPK. So I want to see more of the details and details of mechanism. How Folliculin and AMPK is going to regulate the TFE3 and

also the downstream processes, the cellular processes which is regulated by Folliculin and TFE3 and also by AMPK.

Can you give us an idea of what you were working on before you got into BHD research?

So I used to work on mouse modelling of VHL syndrome. VHL syndrome is another inherited cancer syndrome which cause the renal cancer development. After studying some time on VHL, BHD gene was newly discovered and I had much more interest on BHD so I moved to the field on BHD.

So it seems a lot of researchers came into the BHD field from VHL. Can you talk about how the two diseases relate to one another?

So VHL syndrome is another type of renal cancer syndrome. The thing from the VHL study, people found the HIF transcription factor is a downstream molecule of VHL and that HIF transcription factor is very important in energy metabolism. So through the BHD study we found another transcription factor which is also very important in energy metabolism. The TFE3 transcription factor is very important in energy metabolism. Even though two different transcription factors, the outcome is the defect in energy metabolism. In that sense maybe they share some homology. Even though the mediator can be different, but the overall outcome of the defect should show some similarities.

Can you talk about what you think the BHD field will look like in the next 5-10 years?

Through this Symposium I've learned a lot and I attended last year meeting and this is my second participation to this Symposium, and I found pretty much progress is going on. So after 5 or 10 years with this speed, we can go further and probably can target some kind of molecule which is maybe applicable to the patients for treat the disease.

Dr Hong, thank you very much for taking the time to speak with us.

Ok, thank you very much.