Diabetes from beginning to end

"There is a fundamental change that happens to your body when you become insulin resistant that affects you for the rest of your life," says Dr Beatrice Filippi, "I'm trying to understand how insulin resistance happens in diabetes and so how it could be prevented. If we can learn which molecular players are affected by insulin at the earliest stages of resistance, that would be a good start to try to prevent it."

Dr Beatrice Maria Filippi is a biochemist who knows her way around a physiology lab and whose multiple research skills have led her to start her own lab in the neuroscience department at the University of Leeds. She has just arrived back in the UK, from a postdoc in Toronto, to begin her first lab with the support of a University Academic Fellowship.

"I work in metabolism but I look at what role the brain plays, specifically the effect insulin signalling in the brain has on glucose metabolism and feeding behaviour. I've been in physiology for a while so I wanted to be in a place where I could develop my neuroscience skills, Leeds has this expertise," she says.

First steps as a Principal Investigator

The fellowship offers a stipend to start a lab and funding for one PhD student. "So that's how I'm going to start," says Dr Filippi. "I'm excited. I've been focused on insulin signalling in the brain and now I'm going to look more at insulin resistance. I'm still working on my last paper here, it's important because it's the basis of my new research. I've never been able to write anything about the paper in a grant application, so I really want to publish it so that I can use the results to say, 'I have the basis to do this work,' and push ahead with funding applications."

The Brexit vote in May has added pressure. Dr Filippi took up her post in Leeds in August, speaking the Monday following the Brexit vote she said: "I'm planning to apply for EU funding so I just hope that there is no bias in funding awards. If I'm equal with another applicant who is going to work in mainland Europe, I'm already afraid that there will be a bias to give the funding to them because I'm in the UK."

Dr Filippi has spent the past five and half years working as a postdoctoral fellow in Dr Tony Lam's lab at the Toronto General Research Institute, University Health Network. There she honed new skills in physiology experimentation while sharing her own in biochemistry.

"I had a deal with my boss. They were doing biochemistry, but not the way I do it, so when they needed to do a kinase or any other biochemical assay, I would train and supervise them. In return they taught me physiology skills."

It turned out to be a good deal. She says, "if you look at all the papers from my actual lab, I'm there, because whatever they had to do I was helping with the biochemistry."

The move to Toronto in 2010, from her postdoc in Professor Dario Alessi's lab at the Medical Research Council Protein Phosphorylation and Ubiquitylation Unit at the University of Dundee, was a way to capture a new experience and then bring it home. In PPU Dr Filippi's work involved lots of kinase assays to better understand protein phosphorylation.

"At PPU my main paper was about the discovery of how the adaptor protein MO25 activates a series of ST20-related kinases. When I moved to Toronto I wanted to learn new techniques, to move more towards a physiological perspective – what happens to the entire body. So I joined a physiology lab," she says.

Collaboration a bonus to UK research

Of her return to the UK Dr Filippi says: "I like the collaborative way that work is done in the UK that you don't often find in North America. Labs here are much more individualistic, even if you are in a big institute it is hard to collaborate with your neighbours and that just doesn't happen in the UK. I like the way research is done in the UK. I was very happy in Dundee."

A desire to return to Europe also drove the move, the Brexit vote made her family's preparations bittersweet. Dr Filippi is married to fellow PPU alumni Dr Elton Zeqiraj who is also starting a lab at the University of Leeds.

"As a family we really wanted to return. I can work anywhere in Europe and anywhere I go in Europe I can feel at home. The reality is that when you leave, like we have to Toronto, and then return, other European countries feel like home, I was in Germany and I'm Italian and I still felt at home. Europe is my country. I've always felt like there is a common way of thinking. Speaking to British people here in Toronto, we always find things in common. I can't see how Brexit will be good for science or for British people."

Insulin and the brain

Dr Filippi's last paper in Toronto sets the direction for her new research in Leeds.

She is taking a mechanistic approach to the cause of insulin resistance. Starting with the brainstem. Every signal sent from the brain to the body or body to brain traverses the brainstem. It's the body's connectivity hub. It too becomes resistant to insulin when a person develops diabetes.

These early effects will be a future focus for Dr Filippi, she explains: "I'm going to look at what's happening when the brainstem becomes insulin resistant. I'll start there. And then my work is going to focus more on the developmental point of view, so what happens if you develop insulin resistance at an early stage of life. What is the effect on your metabolism at the beginning? And what happens in the future? Whether insulin resistance can lead to neurodegenerative disease."

Dr Filippi's time and work in Toronto has armed her with new skills and set her research in a new direction. "For diabetes research, Toronto is one of the best places in the world," she

says, “the diabetes research centre here is amazing, as is the knowledge and expertise in the labs. For my final paper, I did collaborate with scientists in the lab next door and that turned out to be very fruitful. The way the University Health Network is structured means it’s hard to see the final chain of command, so labs become more individual as they get lost in the system and collaborations can be hard. However, once you make the extra effort to interact with people you can really find amazing expertise. The beauty though, is in the incredible research facilities, you really can find whatever you need.”

Dr Filippi believes one of the best parts of scientific culture is the way researchers share opinions that help to develop ideas. Of her time in PPU she recalls: “I remember going to talks with principal investigators and being encouraged to share my opinion. I’ve found that in Toronto, people are respectful of their PI in a way that means they are less likely to speak up and share ideas.”

She says she learnt a lot from Dr Lam’s way of approaching research problems: “I didn’t miss seeking expertise from other labs because Tony has been amazing to work with, he has a vast knowledge of his subject and has taught me a lot.”

Finding balance in a scientific career

Learning how and when to stop or switch tracks is another skill Dr Filippi considers essential in science.

“My first postdoc project at PPU wasn’t going well, but Dario was good at saying ‘this isn’t working’ and suggested another route to try,” she says, “I ended up collaborating with others in the lab to try new ideas. If I had just kept going with the same thing experimentally, I doubt it would have ended so well. It can be hard to stop, especially if you have put a lot of effort into something, but if it’s not working, it’s not working. It’s better to let it go. You need to have a good PI who can recognise that. Dario always did that.”

As Dr Filippi has progressed in her career she has learnt to find balance and the best time to start a new experiment, or not. “I have to say, when I was in Dundee, I was always there at the weekend, but I soon found that an experiment done at the weekend didn’t work. I also knew that if I wanted to rush and start an experiment at 5pm just because I wanted to get it done, most of the time I’d make a mistake, because it was too late in the day. You learn this afterwards. When I moved to Toronto I’d learnt to come in to check things at the weekend, rather than to start new experiments. I would say I found my work balance in my second post doc.”

Her advice for PhD students and first post docs is to learn when to pause: “Sometimes people want to rush to get things finished and I always tell them look you are tired, when you are tired you will make mistakes. The balance is really to know how much you can do and if you are really concentrating on what you are doing. If you make five mistakes because you want to finish an experiment, then taking one extra day to do it well is not going to change anything other than to get a better result. In the end you have to listen to yourself, and if you are tired, go home.”

Following new ideas in academia

When Dr Filippi was looking for a new position in the UK, she focused on academia: “My motivation has always been to develop my own line of research, that’s why I like to be in academia, so I can pursue ideas. When I was younger, I was so idealistic, I thought that science could not be driven by any monetary gain. Now I realise that this isn’t really the case and that academia and industry are becoming more similar but I’ve never seen myself working in a big corporation. Now, I see there are many interesting start-ups and that companies also do excellent research, although I think that the academic path suits me better.”

Part of finding a new role will always involve networking at some level, Dr Filippi’s advice on approach is to follow-up with people you meet in person. “Every time that I have to email someone to ask for something, I always procrastinate,” she says “I’m trying to improve, it’s a matter of personality, I don’t like to ask for things. To interact is different. If you go to a conference and you meet a PI and you like that person and are interested in their work, then it’s easier to get in touch with them. When you are looking for work after your PhD or postdoc, just follow up with an email to say how much you enjoyed interacting with them and ask if they have a position in their lab.”

Final word

“This move for me is all about starting and building my own group. I really hope that I can develop my own line of research, build a lab and transfer some of my knowledge to someone else. Maybe inspire some students to do good research, to like research and do well. That would be good for me. As long as I can do my own research I know I’ll be happy,” Dr Beatrice Maria Filippi.

Career Highlights

2007 Medical Research Council Career Development Fellowship
2003 FIRC (Italian Foundation for Cancer Research) Fellowship

Top Publications

Dr Beatrice Maria Filippi picks her top three papers and tells us why she has chosen each one.

Insulin activates Erk1/2 signaling in the dorsal vagal complex to inhibit glucose production. ***Cell Metabolism****.* 2012 Oct 3; 16(4):500-10.
Filippi B.M., Yang C., Tang C. and Lam T.K.T.

Insulin signals through the dorsal vagal complex to lower food intake.
Diabetes 2014 Mar; 63(3):892-9.
Filippi B.M., Bassiri A., Abraham M.A., Duca F.A., Yue J.T.Y and Lam T.K.T.

“This pair of papers investigates two of the greatest threats facing 21st century healthcare - obesity and type 2 diabetes. The development of more effective preventative and therapeutic strategies is dependent on gaining a greater understanding of the mechanisms that regulate bodyweight and glucose homeostasis. In Toronto I discovered that the dorsal vagal complex in the brainstem, previously unknown to regulate glucose metabolism, senses insulin levels to lower liver glucose production and to decrease food intake.”

MO25 is a master regulator of SPAK/OSR1 and MST3/MST4/YSK1 protein kinases.
EMBO J. 2011 May 4; 30(9):1730-41.
Filippi B.M., de los Heros P, Mehellou Y, Navratilova I, Gourlay R, Deak M, Plater L, Toth R, Zeqiraj E, Alessi D.R.

“In Dundee I acquired a vast knowledge in how to dissect signaling pathways using biochemical and molecular approaches. My main achievement was the discovery of a new mode of activation of SPAK and OSR1 kinases through the scaffold protein MO25. This work was important to understand molecular events that lead to hypertension and could aid the discovery of new hypertension drugs that target SPAK and OSR1.”

University of Leeds profile page

This profile was written by Hazel Lambert of sciencestory.com

ENDS