Small molecules, big problem

Image credit: Joe Belcovson, Salk Institute

"When you move from academia to industry you have to leave your ego behind. Noone puts a drug into the clinic by themselves," says Dr. Anna Zagorska.

"In my search for new small molecules to treat fibrosis, I collaborate closely with clinical researchers, biomarker experts and scientists who specialise in pharmacokinetics and pharmacodynamics. I get to see the whole process of how a drug is developed from a basic research idea all the way to a prescription for a patient in a clinic. It's exciting. I haven't been here long but I'm already starting to understand what is needed at all stages of drug development."

Dr. Anna Zagorska is a research scientist at <u>Gilead Sciences</u> in California. She works in pre-clinical research looking for new drug targets to develop therapies to treat liver and lung fibrosis.

Much of her work is focused on non-alcoholic steatohepatitis or NASH, a silent disease with few early symptoms that has the same destructive effect on the liver as alcohol abuse or viral hepatitis. In NASH, fat, inflammation and scarring stop the liver working well. It affects people even if they only drink a little alcohol or none at all. Up to five in every 100 people living in the US population may have NASH.

"There is really no treatment for NASH so there's a huge need among patients. Gilead is investing a lot in exciting research programmes around NASH. The small molecule work ties back to the kind of work I did on protein kinase inhibitors during my PhD in Dundee. It will be so rewarding if I can contribute to a new treatment that helps people," says Dr. Zagorska.

Focus on results

In her hunt Dr. Zagorska wastes little time: "You really have to take huge responsibility and apply real rigour to experimental design because if we want to move something into the clinic there has to be absolutely zero doubt that it will benefit patients. I design experiments in a way that will quickly reveal whether our hypothesis is correct. Time and people are valuable assets so go, or no go, decisions are made fast in research here."

The need to be flexible and move between research projects is one of the things that attracted Dr. Zagorska to a career in industry. As a postdoc in <u>Dr. Greg Lemke's</u> lab at the <u>Salk Institute</u> in California, Dr. Zagorska already knew she would make the move to industry, she says: "I have two strong motivations - being closer to patients in the clinic and working on projects that progress fast. Of course you can do translatable research in academia but it is easier to do it in a setting that is designed for it. As a scientist I am interested in many different things and always want to learn about new areas and new biology. Being in a dynamic industry environment where

the key thing that describes a person is being flexible suits me, I find the chance to change between projects and priorities exciting."

Strong science in a small city

The Division of Signal Transduction Therapy (DSTT) collaboration at the Medical Research Council Protein Phosphorylation and Ubiquitylation Unit at the University of Dundee (PPU) where Dr. Zagorska completed her PhD in Professor Dario Alessi's lab was useful in helping her to secure a role in industry. She says, "Dario's lab has this really careful detailed understanding of basic biology and through the collaboration with companies I learnt how to work with small molecule inhibitors. The fact that I did my PhD in PPU actually helped me to get my job. It made my CV stand out because in the cell signalling field PPU is recognisable even here in the US. I didn't need to go and explain where Dundee was. People already knew how rigorous my training would have been."

A global network

Of her PhD she says: "Dundee is special because you have great science in a small city. People come from all over the world and because we all lived nearby we grew close. It's not like London where everyone disappears at the end of the day. I built strong relationships with people who were there at the same time. I loved the social aspect and keep those friendships now. The other thing I liked about being in Scotland was Munro bagging. Weekends in the mountains were, for me, an important part of living there."

Dr. Zagorska's career has taken her around the world. She grew up in Poland where she originally wanted to study marine biology. Her family persuaded her that biotechnology would be more practical in Poland. At Salk, she says, she worked next door to the <u>Scripps Institute of Oceanography</u> and it makes her smile.

When Dr. Zagorska was living in Dundee she set her heart on a postdoc in the US. She interviewed in several places and found what, for her, was an ideal lab at the Salk Institute. She spent five years there researching tyrosine kinase receptors and their role in both inflammation and liver disease. When the time came to look for a job in industry she said the network she had built so far was crucial.

"It's worth building your network early, rather than waiting until you are looking for a job. It is always easier to get invited for an interview if you have an internal referral. I think the best network that you can have is one built of your peers. You will benefit from it much later in the future. You don't need to know a director or a head of department, these people will not remember you but there are peers you can easily meet at the posters at a conference and you can use LinkedIn to build lasting contacts, it works," she says.

Early lab work

As an undergraduate Dr. Zagorska spent a lot of time working in the lab. "When I was studying biotechnology I worked in a lab from my first year. In Poland, a lot of the research work is done by student volunteers. I was so confident and I made many mistakes but that's how you learn. By the time I started my PhD I had years of practice and thought I was relatively experienced in the lab. But those four years in PPU made a difference and taught me how to carefully design, control, execute and analyse my experiments. Now I don't work in the lab much anymore, but every day I use skills I learned during my PhD and postdoctoral training."

Team work is essential

"Team work is crucial in industry," says Dr. Zagorska. "Everyone has a different role in helping to get a drug target validated. In an academic lab you have collaborators but usually they are people with similar expertise to your own so they can help you a bit, but your project is your project. In industry you are a part of a project that involves so many more people - from chemists to lawyers. I'm learning so much I feel like my neurones are being rewired!"

Last word

Dr. Zagorska says: "In Gilead I have responsibility for my research in the sense that I'm really accountable for everything I do. I like the environment this creates and I think it drives excellence. I'm still early in my career, I always think that in science hard work is essential but you need a little luck too."

Career Highlights

2014 Nomis Foundation Award

2011 – 2014 Human Frontier Science Fellowship

2010 Tim Hunt Prize for Cell Biology

2005 – 2009 Wellcome Trust PhD Fellowship

2005 Polish Ministry of Education Award

2004 Estreicher Fund Award

Top Publications

Dr. Anna Zagorska describes the importance of each paper to her research career.

Diversification of TAM receptor tyrosine kinase function.

Nat Immunol. 15(10):920-8. Zagorska A, Través PG, Lew ED, Dransfield I, Lemke G. (2014)

"This paper is a summary of my postdoctoral work, it covers the details of truly

fascinating TAM receptor biology."

New roles for the LKB1-NUAK pathway in controlling myosin phosphatase complexes and cell adhesion.

Science Signal. 3:ra25. Zagorska A, Deak M, Campbell DG, Banerjee S, Hirano M, Aizawa S, Prescott AR, Alessi DR.(2010)

"The key publication from my time as a PhD student in Professor Dario Alessi's lab. I am still proud of how precise and rigorous this study was."

Monoclonal 1- and 3-Phosphohistidine Antibodies: New Tools to Study Histidine Phosphorylation.

Cell 162(1):198-210 Fuhs SR, Meisenhelder J, Aslanian A, Ma L, Zagorska A, Stankova M, Binnie A, Al-Obeidi F, Mauger J, Lemke G, Yates JR 3rd, Hunter T. (2015)

"This paper is a great example of how cross-disciplinary collaboration can help problem solving. Advance chemistry, antibody biology, biochemistry and cell biology join to shed light on one of outstanding questions in biology - histidine phosphorylation"

LinkedIn Profile

Dr Anna Zagorska

This PPU alumni profile was written by Hazel Lambert of sciencestory.com