ANALYSIS OF THE TUMOUR MICROENVIRONMENT

Ruth Seelige, Senior Scientist, **Pfizer**

Ruth Seelige has a Bachelor and Master of Science in Molecular Biomedicine at the University of Muenster, Germany. She also has a PhD in Molecular Biomedicine at the Max-Planck-Institute for Molecular Biomedicine in Muenster, Germany, focusing on immune cell transmigration into inflamed tissues and cancer. She obtained her Post doc in cancer immunology at the University of California, San Diego, USA in the lab of Jack Bui, focusing on the role of Nrf2 and IL-17D in cancer immunology and viral infections. Ruth is Currently Senior Scientist in In Vivo Pharmacology at Pfizer, focusing on high-parameter analysis of the tumor microenvironment.

Could you explain a bit more about your work in the field?

I started at Pfizer very recently. Before that, I did a postdoc at UCSD in the lab of Jack Bui, which is when I started going into cancer immunology. Before that, I did my PhD in immunology, but it focused more on leukocytes in inflamed tissues, so it was during my postdoc that I was exposed to cancer immunology. I worked on cytokines and the innate immune system there.

Now at Pfizer, our group analyses the tumour microenvironment. We like to call us the "TIL task force" because we do a lot of TIL experiments where we analyse the tumour microenvironment with flow cytometry and single cell RNA sequencing. We also have more innovative studies in which we do mouse model development to find the mouse model that best reflects human cancer.

What are the challenges of targeting and working within the tumour microenvironment for cancer therapies?

For me, while this may be biased, I believe the biggest challenge is to get the cells in. Most of the targets and therapies we have work on cells that are already there. For example, the checkpoint inhibitors don't work if the cells are not present in the tumour microenvironment. You cannot inhibit inhibitory cells that don't exist. Therefore, one of the main challenges is to turn a cold tumour into a hot tumour. I was also working on that during my postdoc.

What do you think are the more important technologies impacting immuno-oncology research currently?

For me, the technology that is most important is flow cytometry because it allows us to easily look at single cells in the tumour microenvironment. Single cell RNA sequencing is also a good technology, but it's much slower and, depending on what kind of expertise you have, data can take much longer to analyse. On the other hand, flow cytometry is a lot faster at giving you data and can allow for quicker decisions. The technology is still evolving with higher parameter machines. I believe the highest one is 35 parameters so far, allowing us to get a good idea of the sum of molecules that are expressed in the cells.

How do you think better preclinical models could improve immuno-oncology drug discovery?

I can only comment on preclinical mouse models as that is what I'm working on, in-vivo. I believe it is very important to have a mouse model that is as close to a human model as possible. For me, that is either a GEM model, that has some defined mutations that are also important for human cancer, or a humanised mouse, that has a human immune system, allowing you to directly look at human PDXs or human cell lines - and really look at the human immune system, even though it is still in a mouse. However, I think the humanised mouse models are not optimised well enough yet. If they ever become more optimised and have less graft versus host disease and more HLA- matched ones are available, then I think that is a good way to look at immuno-oncology.

You recently spoke at our Immuno-Oncology USA Congress. What were the top takeaways of your presentation?

I believe we should focus on the tumour microenvironment as a whole, looking at all of the cells and all of the chemical and physical entities that make up the tumour microenvironment. For developing good tracks, we should find a way to deeply analyse the whole tumour microenvironment. I am unsure whether this may ever be completely possible, but that is what we should aim for.

Secondly, I believe it is very important to develop the right mouse model that best reflects human cancer. For me, the closest would currently be GEM models or humanised mouse models. We should never stop investigating and doing research to make these models better, easier and cheaper.