THE AUTHOR FILE

Sarah Teichmann

Team sports and team efforts lead to a new tool that helps with immune profiling.

T cells are an immune cell family of dazzling diversity. Each T cell—there are roughly 10^8 T cells in

a mouse's blood-stream, whereas people have around 10^{13} T cells—has a unique cell surface receptor (TCR) that can detect a specific invader and trigger an immune response. This diversity comes courtesy of V(D)J recombination: three gene segments mix and match to form unique

α - and β -chains for each TCR type.

Studying TCR diversity on a single-cell level with high-throughput sequencing is challenging. Short reads do not readily map to this region. “Essentially there is no reference,” says Sarah Teichmann, senior group leader at the European Bioinformatics Institute (EBI), which is where she does her *in silico* work. Her wet lab is next door at the Wellcome Trust Sanger Institute, where she has just become head of the cellular genetics program. She also cofounded the EBI-Sanger Single Cell Genomics Centre.

To better understand how T cell genetics shapes T cell function, Teichmann and her group have developed a computational tool called TraCeR that reconstructs TCR sequences from single-cell transcription data sets. “It’s telling you about the recombination that’s happened at the DNA level by analyzing the RNA level,” she says.

To study which VDJ segments are recombined and how, the lab needed to perform *de novo* assembly. To aid in this task, the researchers built electronic recombinomes, imaginary stretches of DNA covering as many combinatorial options as possible. TraCeR uses the recombinomes to find and line up reads from TCR transcripts such that assembly becomes possible. The software lets researchers study the TCR in the context of the transcriptome, and it gives them a view of T cells busily at work.

As it turns out, T cell clones can be genetically identical, but their transcriptional identities and their work roles are diverse, says Teichmann. “Even though they’re identical twins, they’re doing very different things,” she says. Such knowledge opens the door for much exploration, she says, for studies of autoimmune disease, tumor immunology and the evolution of the immune system.

A random blood sample cannot provide data that shows what the software can do, nor can an *in vitro* experiment. “The power of this method doesn’t really become clear until you profile an immune response,” she says. Generating that response took time and teamwork with researchers who had experience with a *Salmonella* mouse model.

This project brings genomics together with Teichmann’s other passion, understanding protein complexes, and, she says, “I want to keep on working in that direction.” For example, she wants to focus on immune synapses, which includes cell-cell interaction between T cells and other cells such as helper T cells.

In Teichmann’s lab people come from many countries, and she fosters a welcoming, international atmosphere. She was born in Germany, her father is German, her mother is American and she has been in the UK since deciding to study there as an undergraduate. Teichmann obtained her PhD degree in computational biology at the Medical Research Council (MRC) Laboratory of Molecular Biology, which is affiliated with the University of Cambridge, and she was a postdoctoral fellow at University College London with Janet Thornton. Teichmann landed her first faculty position at MRC and has been at the EBI since 2013.

“Sarah is outstanding in many ways,” says Thornton, who is the director emeritus of EMBL-EBI and who has a research group at the EBI. Teichmann asks clear questions, discusses and takes advice to assure the quality of her work. She knows how to bring disparate scientists together to address a problem of mutual interest. “In this way she pushes back the boundaries,” says Thornton. She mentors young scientists, including her female colleagues, “encouraging them to be focused, ambitious and go-getting.” Teichmann is generous, always willing to help and engage with others to work on world-class science, says Thornton.

Researchers are trained to focus on their own projects, but science cannot really be done alone. “At the end of the day most things are a team effort,” says Teichmann. There may be a team captain, but every player counts. Teichmann first embraced the team spirit playing handball, basketball and tennis. “Sports have been really important throughout my life,” she says. Becoming a professional athlete did more than cross her mind. “I think as a teenager I would have loved to,” she says. Right now her time is taken up with work and family, but she hopes to soon spend more time on the courts.

Vivien Marx

Stubbington, M.J.T. *et al.* T cell fate and clonality inference from single-cell transcriptomes. *Nat. Methods* **13**, 329–332 (2016).

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