EMJ Interview

Pavel Tolar

Division of Infection and Immunity, Institute of Immunity and Transplantation, University College London, UK

Pavel Tolar spoke with EMJ about his path to immunology, role in education, and fantastic achievements in his career.

Q1 What led you to embark upon a career in immunology and specifically in researching B cells?

When I studied medicine in Prague, I became interested in how cells make decisions to regulate various functions of the body. I thought immune cells were particularly interesting because they respond to unpredictable threats. I wanted to study lymphocytes but got a place in the lab of Peter Draber who was researching mast cells. This was my first exposure to the field of allergy, and I carried out my PhD there. Then, I joined a B cell lab headed by Susan Pierce at the National Institutes of Health (NIH) in the USA. The work on B cells was even more captivating, and we soon started making fascinating observations using imaging of live B cells, which was new at that time.

Q2 What would you say has been your most important discovery to date during your research on B cells?

When I founded my own lab back in Europe, at the National Institute for Medical Research and later at the Francis Crick Institute in London, UK, we discovered that B cells are very good at ripping foreign antigens from immune cells that collected and displayed these antigens on their surfaces for B cells to see. The mechanical vigour of the B cells intrigued us, and we described that the mechanical forces with which B cells pull on things actually help them to determine the quality of the binding of their B cell receptors to the foreign matter. This is similar to testing how sticky a surface is by touching it with a finger. Similarly to a very sticky surface, a strong B cell receptor binding promotes a stronger mechanical response and allows the B cells to extract more of the antigen. This helps B cells with better B cell receptors to dominate the immune response, and the system produces the highest quality antibodies.

More recently, we found that B cell activation works differently in B cells that express IgE. Their B cell receptors limit rather than promote their responses. For example, their B cell receptors curtail their lifetime once they become antibody-secreting cells, making IgE production transient. This natural regulation of IgE B cells may be broken in allergy. It seems that I circled back to studies of allergy after all.

Q3 In your research, you use myriad approaches, including immunology, genetics, biophysics, imaging, and nanotechnology. How

does this collaborative approach work on a logistical level and which is your favourite approach to use?

I have always been interested in using new and alternative approaches in biology. Biophysics, imaging, and computation are my favourites. However, it is challenging to pursue all of these approaches in one lab because it is not possible to recruit the best experts for each of these areas. Maybe the better route is for several labs to collaborate. Still, we do need to have an open mind because not all labs from different disciplines understand each other. A successful interdisciplinary collaboration is a great achievement.

Q4 Which new advances in immunology are you most excited about?

I think that high-throughput approaches brought power of scale to immunology. In B cell immunology, they transformed how we think about antibody specificity as well as the decisions that individual B cell clones make to produce antibodies binding to different targets. It is an interesting challenge to deconvolve the large sets of data into a mechanistic understanding of how things work.

Q5 In 2013, you were awarded the European Molecular Biology Organization (EMBO) Young Investigator Award. Could you tell us a little about this honour and how it has impacted your career?

Winning the EMBO Young Investigator Award was my dream as a student. The award opens fantastic access to EMBO resources and to the EMBO research community. EMBO support their researchers with almost no bureaucratic burden, which just makes research so much more enjoyable.

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Q6 In 2021, you began to work at University College London (UCL), UK, as Professor of B Cell Immunology. How are you finding your role and how does it differ from heading your own lab?

I am now part of a relatively new immunology department at UCL called the Institute for Immunology and Transplantation, which is becoming the largest cluster of immunologists in London. As a bonus, it is also a group of very nice people. The research remains the same; however, I now also teach, and we have more student projects in the lab.

Q7 As an educator, where do you think your focus will lie in the coming years?

We have been incorporating more B cell immunology into the UCL immunology lectures. I am also helping to run an interactive module that helps students to read and interpret research papers. I think this is a very important skill as it involves the very essence of scientific and logical thinking. Everybody should be trained in this.

Q8 You have published widely on B cells, writing and collaborating on many papers. Do you believe that there is a current gap in the literature, and which specific topics should be given more attention?

I think we still do not understand the principles that drive major decisions by which B cells regulate antibody production (e.g., to proliferate, die, or differentiate into antibody-secreting cells). Without this knowledge, it is difficult to understand how different types of B cells and B cells with different specificities for antigen respond to vaccines and infections. It is also hard to predict how B cells become a vehicle of diseases, such as in autoimmunity, lymphoma, or allergy. Many of the genes underlying human B cell deficiencies and diseases remain unidentified. There is a huge amount of work to be done here.

Q9 How has COVID-19 impacted your working model and the way that you approach your research?

With the worst of the pandemic hopefully behind us, I think we are left looking back and learning some lessons from how we worked over the past couple of years compared with normal times. I like the idea of being more flexible in where you work and how you meet. It is good to be back to discussing ideas in person; however, working online opens new possibilities as well as reduces travel, and we all became much better at this.