Report from the International Myeloma Society Annual Meeting 2025

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Firstly, I would like to thank the UK Myeloma Society and Menarini Stemline for their travel bursary, which supported my attendance at the IMS Annual Meeting this year in Toronto, Canada. Being relatively new to myeloma research, this conference provided me with an invaluable opportunity to learn more about the field and to network with many outstanding researchers who are driving progress in this disease. Overall, it was a highly enriching event that greatly contributed to my career development and reinforced my motivation to continue research in this area.

During the conference, I was fortunate to have my abstract titled *"Investigating the Role of the BAFF-APRIL System in Promoting Progression of Smouldering Myeloma (SMM)"* selected for a poster presentation. In this project that was very much a team effort, we explored how the BAFF-APRIL system may regulate progression from SMM to MM, using bioinformatics and immunophenotyping methods on data generated from patient samples collected through the COSMOS and RADAR clinical trials, in combination with integrated publicly available datasets. Our findings suggest that alterations in this signalling axis may indeed be significant across myeloma progression, co-opting key interactions between myeloid cells and plasma cells within the bone marrow microenvironment. During the poster session, I had the opportunity to engage in insightful discussions with other researchers interested in this topic in myeloma, which provided valuable feedback and advice on potential next steps for our work.

The conference offered an excellent mix of clinical and translational research, exposing me to many patient-centric topics that I had not previously encountered in depth during my training. This broader perspective will certainly inform how I approach my own research going forward. The plenary session on the first day featured an amazing keynote lecture by Prof. Tak Mak from the Princess Margaret Cancer Centre, who discussed the identification of tumour-reactive gamma-delta T cells and their role in responses to antibody-drug conjugates (ADCs). A key takeaway was that the expansion of these tumour-reactive gamma-delta T cells serves as a significant predictive biomarker for good response in patients. Prof. Mak also introduced a novel prediction algorithm, *PreGame*, which can identify tumour-reactive γδTCRs from scRNA-seq data. I found this keynote particularly relevant, as gamma-delta T cells have more recently gained increasing attention. Unlike conventional alpha-beta T cells, they can recognize and kill target cells in an MHC-unrestricted manner. This property makes them especially promising candidates for developing 'off-the-shelf' immunotherapies for MM, bypassing the limitations of TCR-based therapies that require HLA matching, being an exciting area to watch!

Many of the oral abstract sessions were equally engaging and covered a wide range of topics. A particular highlight for me was a presentation by Manoj Bhasin's group, which explored single-cell immune atlas data from the MMRF CoMMpass cohort, which was produced from a large, multi-centre study. They identified dynamic features and changes within both the tumour and the immune microenvironment that differentiated patients with good versus poor therapeutic responses. Their work highlighted the importance of B-cell reconstitution post-ASCT treatment for sustained response and revealed the overexpression of cancer-testis antigens in poor responders. Another great talk by Bruno Paiva focused on tracking cell-of-origin clones in

myeloma, a topic that aligns closely with my interest in tumour evolution. Interestingly, their findings indicated that only a small fraction of precursor B cells shared the BCR clonotype of tumour plasma cells, with minimal mutational similarities that could drive malignancy. This suggests that these precursors are more likely passenger cells rather than true tumour reservoirs. Finally, another excellent single-cell dataset from the MIDAS study enabled detailed analysis of the immune microenvironment in the context of Isa-KRD treatment. The study revealed immune profile differences between MRD+ and MRD– patients following therapy, showing coordinated changes across multiple immune cell types, which is a clear sign of total immune remodelling.

Overall, the conference covered an impressive range of topics, including precursor disease, CAR-T biology, the immune microenvironment, therapeutic advancements, and patient disease management, among many others. Lots of the research highlighted in this conference is greatly relevant to the research being done in our own lab and have provided great ideas and findings to share with the group. Beyond just the science, the conference also offered an incredible opportunity to experience the beautiful city of Toronto. One of the highlights was the gala dinner held at Casa Loma, a stunning historic mansion that provided a perfect venue for an evening of excellent food, entertainment, and conversation. It was a wonderful setting to connect with others in a more relaxed atmosphere, though of course, scientific discussions were never far away!

Altogether, I had an amazing experience at IMS and am deeply grateful for the opportunity to attend. It was inspiring to travel and exchange ideas with other researchers from UCL and UCLH, to learn about the breadth of ongoing myeloma research, and to build new connections within the community. Once again, I would like to extend my sincere thanks to the UK Myeloma Society and Menarini Stemline for their generous travel bursary, which made my attendance possible.