Single cell immune profiling of lymphocytes from autoimmune encephalitis-associated teratomas reveals novel clonally expanded cell populations

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Background and aims

Approximately one third of patients with NMDA receptor antibody encephalitis also have an ovarian teratoma. Lymphoid follicular structures have been identified within encephalitis-associated teratomas, but the precise immune phenotypes within these structures remain poorly understood. We used massively high-throughput immunophenotyping to uncover the identity of these cells and their potential functional relevance to autoimmune encephalitis.

Methods

Ovarian teratoma-associated lymphocytes and matched peripheral blood were obtained from two patients with NMDA receptor antibody encephalitis. B cells (CD19+ CD20+) and antigen-experienced T cells (CD3+ CD4+ CD45RA-) were sorted and processed using the 10X Chromium combined VDJ and 3' RNA-seq kit. Histopathological analysis of identified lymphoid follicles within teratoma was undertaken with immunohistochemistry.

Results

Successful libraries were generated on 23,996 single cells. Dimensionality reduction identified a clear division between B cells and T cells within the teratoma-associated lymphocytes (Figure 1). Unexpectedly, the B cells showed only a small number of minimally expanded clones. However, there was a large clonal population of expanded NKT cell-like lymphocytes (Figure 2). A selected analysis of ligand-receptor interactions predicted significant cell-cell interactions between B cells and NKT cells (can you state more – e.g. predicted molecules?) – or would you prefer to keep quiet?! .

Conclusion

We have found that the B cell compartment within teratomas showed extreme polyclonality, suggesting an unconventional immunisation process. High-throughput single cell immunoprofiling identified a hitherto unreported population of NKT cells resident within teratomas, which our analysis predicted to have a role in modulating B cell responses. This has the potential to form the basis for novel therapeutic pathways targeting NKT cell-regulated pathways.

Disclosure

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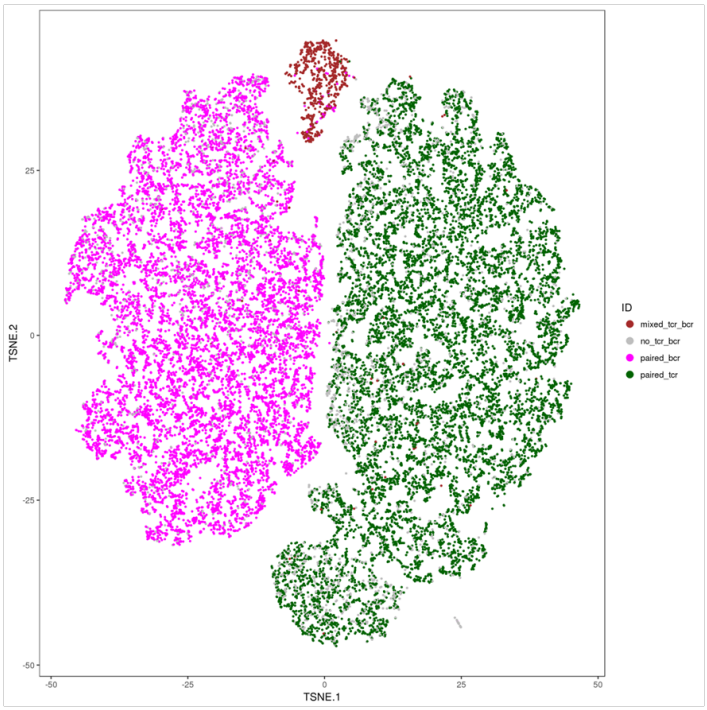

Figure 1 Clustering of lymphocytes is predominantly by B or T cell lineage. Cells are coloured by the presence of a detectable B cell receptor (magenta), T cell receptor (green), or both B and T cell receptors (brown). Dimensionality reduction was undertaken using tSNE.

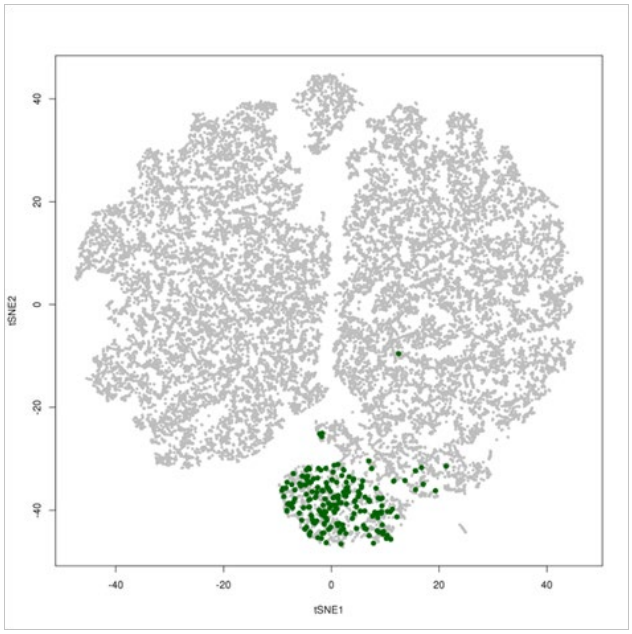

Figure 2 A clonally expanded NKT cell population is enriched within the teratoma-associated T lymphocyte compartment. Cells expressing a particular, clonal T cell receptor and gene pathways characteristic of NKT cells are shaded in green.