Immunophenotyping of autoimmune epilepsy by mass cytometry

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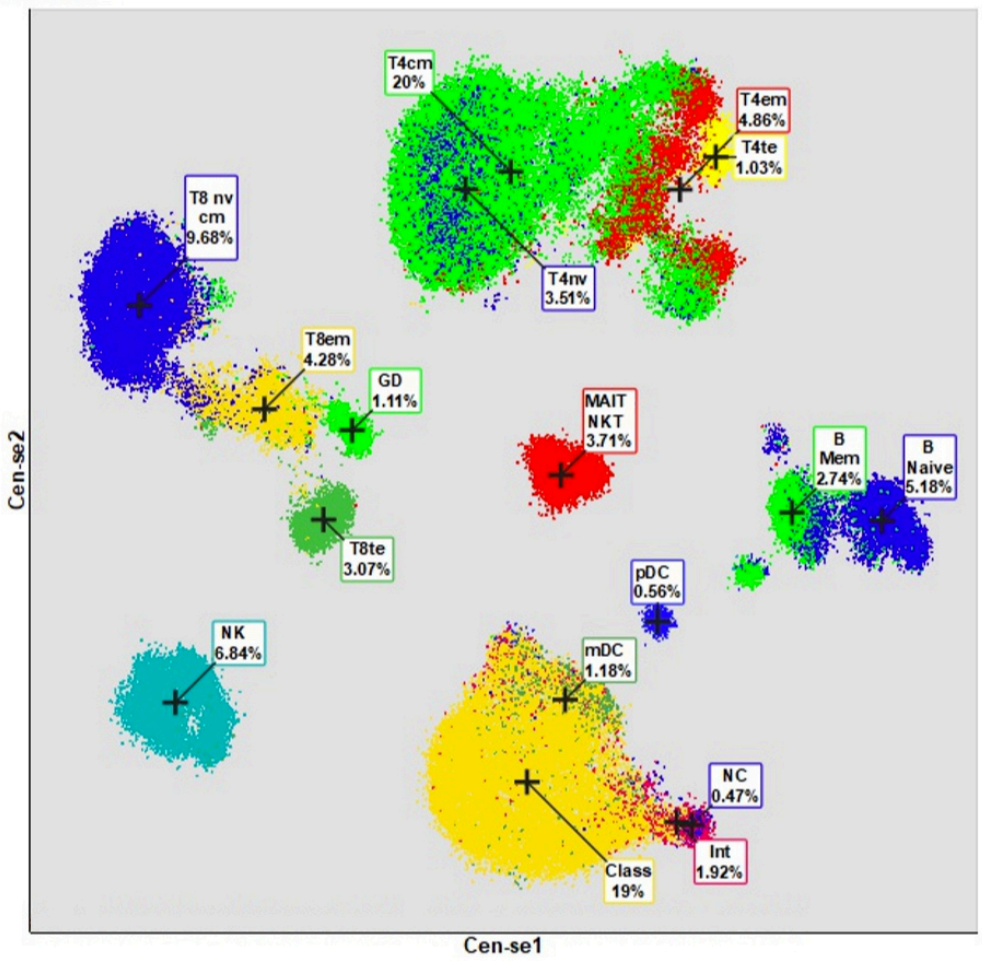
Topic category: Epilepsy

Background: The concept of 'autoimmune epilepsy' is not well-defined. Seizures observed with forms of autoimmune encephalitis are considered a prototypical example of an immune-mediated epilepsy and can respond well to immunotherapy. However, the clinical significance of autoantibodies in more common forms of epilepsy has not been clearly established, and an evidence base to support the use of immunotherapies in such patients is lacking. We hypothesise that a phenotypic signature of peripheral blood leucocytes could distinguish between true autoimmune and non-autoimmune epilepsy – we aim to detect this with mass cytometry, a novel single-cell proteomic method.

Methods: Sera and peripheral blood mononuclear cell (PBMC) samples were obtained from epilepsy patients and controls. Sera were screened for autoantibodies on cell-based assays and primary neuronal cultures. Cryopreserved PBMC samples were stained with a 29-antibody panel targeting all major immune cell populations prior to mass cytometry. Data was analysed using a standardised, supervised method (Gemstone) and with unsupervised clustering-based methods, including DepecheR.

Results: Sera and PBMCs from 50 individuals (epilepsy patients and healthy controls) have been collected. Antibody screening is complete. Mass cytometry experiments will be completed by March 2019. Figure 1 is an example of a 2-dimensional representation of mass cytometry data for one of the healthy control subjects.

Conclusion: The immunocellular phenotype of autoimmune epilepsy is unexplored. Mass cytometry is a method well-suited to identifying distinguishing immunophenotypic characteristics. This work could aid diagnostic clarification and decision-making regarding immunotherapy, potentially improving clinical outcomes.



<u>Figure 1</u>: Cen-se' map (dimensionality reduction plot) of PBMCs from a healthy control subject shows good separation of the major immune cell types, including different developmental stages of B and T cell subsets.

B mem, memory B-cells; *B naïve*, naive B-cells; *Class*, classical monocytes; *Gd*, gamma delta T-cells; *Int*, intermediate (transitional) monocytes; *MAIT NKT*, mucosal associated invariant T-cells & natural killer T-cells; *mDC*, myeloid dendritic cells; *NC*, non-classical monocytes; *NK*, natural killer cells; *PBMC*, peripheral blood mononuclear cells; *pDC*, plasmacytoid dendritic cells; *T4 cm*, central memory CD4 T-cells; *T4 em*, effector memory CD4 T-cells; *T4 nv*, naive CD4 T-cells; *T4 te*, terminal effector CD4 T-cells; *T8 em*, effector memory CD8 T-cells; *T8 nv cm*, naive & central memory CD8 T-cells; *T8 te*, terminal effector CD8 T-cells.