

Henriette Dodte¹, Anke Fuchs^{2,3,4}, Tjalf Ziemssen¹, Katja Akgün¹

- 1- *Center of Clinical Neuroscience, Department of Neurology, University Hospital Carl Gustav Carus, Technical University of Dresden, 01307 Dresden, Germany.*
- 2- *GMP Facility, DFG-Center for Regenerative Therapies Dresden, Center for Molecular and Cellular Bioengineering, Technische Universität Dresden, Dresden, Germany.*
- 3- *Department of Hematology, Medical Clinic I, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany.*
- 4- *DFG-Center for Regenerative Therapies Dresden, Center for Molecular and Cellular Bioengineering, Technische Universität Dresden, Dresden, Germany.*

Mass Cytometry (CyTOF) Exploration of Cellular Immunity in Natalizumab-Associated PML: Implications for Patient Prognosis and Treatment Strategies

Progressive multifocal leukoencephalopathy (PML) is a fatal neurodegenerative disease resulting from John Cunningham Virus (JCV) infection in immunosuppressed patients. PML presents with rapid progression of focal neurological deficits. Currently, no cure for PML has been proven effective, and overall survival depends on the effective reconstitution of cellular immunity. Moreover, PML occurs in multiple sclerosis (MS) patients as a complication of immunomodulatory antibody therapy with Natalizumab (NAT). Despite the severity of PML and the lack of effective therapies, little is known about the cellular immune response. This research aims to elucidate the underlying mechanisms of failed cellular immunity in PML, focusing on patients undergoing immunomodulatory NAT therapy. Our study employs Mass cytometry (CyTOF) and enzyme-linked immunosorbent spot (ELISpot) assay to analyze biobanked peripheral blood mononuclear cells (PBMC) samples from NAT-treated patients with and without JCV seroconversion to understand the underlying mechanisms of failed cellular immunity. By assessing viral status through ELISpot and investigating leukocyte subsets using a broad-range CyTOF antibody panel, our findings aim to uncover novel risk markers in the context of PML. This research holds the potential to improve patient prognosis, enhance clinical outcomes, and contribute to the development of treatment regimens.