Novel Biological and Clinical Insights into POEMS Syndrome: Pathophysiology and Real-World Treatment Outcomes from Japan

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POEMS syndrome is a rare multisystem disorder characterized by polyneuropathy, monoclonal plasma cell dyscrasia, and markedly elevated levels of vascular endothelial growth factor (VEGF). Although VEGF is a key mediator of disease manifestations, the biological mechanisms underlying its overproduction have long remained unclear.

Recent genomic, transcriptomic, and single-cell analyses have demonstrated that clonal plasma cells in POEMS syndrome are biologically distinct from those in multiple myeloma and monoclonal gammopathy of undetermined significance (MGUS). These cells lack canonical myeloma driver mutations and exhibit highly restricted usage of the IGLV1-40 and IGLV1-44 light chain germlines across diverse ethnic groups. Single-cell RNA sequencing has further revealed unique transcriptional signatures, including downregulation of major histocompatibility complex class II–related genes and enrichment of plasma cell populations that are negative for both CD19 and HLA-DR.

Alongside these biological insights, we present real-world clinical outcomes from a nationwide survey of POEMS syndrome in Japan, utilizing the Transplant Registry Unified Management Program (TRUMP) database of the Japanese Society for Hematopoietic Cell Transplantation. Analysis of patients who underwent autologous stem cell transplantation demonstrated favorable long-term survival, delineated relapse patterns, and confirmed post-transplant normalization of VEGF as a significant prognostic factor.

By integrating molecular mechanisms with large-scale, registry-based clinical data, this study redefines POEMS syndrome as a distinct plasma cell disorder and establishes a robust framework for biomarker-guided disease monitoring and optimization of transplant-based therapeutic strategies.