Serum proteomics identifies interferon gamma signaling in idiopathic multicentric Castleman disease

Melanie Mumau, Sheila K. Pierson, Michael Gonzalez, Scott Canna, and David C. Fajgenbaum

1 Center for Cytokine Storm Treatment & Laboratory, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA 19104
2 Children's Hospital of Philadelphia, Philadelphia, PA 19104

**Abstract**

Idiopathic multicentric Castleman disease (iMCD) is a rare and life-threatening hematologic illness involving uncontrolled systemic inflammation due to unknown causes. Hallmark features of iMCD include multiple enlarged lymph nodes with characteristic histopathology, soluble chemokine expression, and the release of proinflammatory cytokines including interleukin (IL)-6 that can lead to multi-organ dysfunction and death. The only FDA-approved drug for iMCD, siltuximab, blocks IL-6 and is effective in treating a portion of patients suggesting other key cytokines may contribute to iMCD pathogenesis.

To uncover other potential pathogenic mediators, we analyzed 1.73 serum samples in the blood of patients with iMCD, 20 lymphoma patients, and 20 healthy controls (HC) and compared it to the blood of patients with rheumatoid arthritis (RA), chronic lymphocytic leukemia (CLL), chronic lymphocytic leukemia (CLL), chronic lymphocytic leukemia (CLL), Chronic Lymphocytic Leukemia (CLL), and 20 lymphoma patients. The analysis revealed 140 significantly upregulated chemokines that were distinct from those seen in RA, CLL, or lymphoma. Furthermore, we observed that IL-6 expression was upregulated in iMCD compared to HC. The expression of IFN-gamma (IFN-γ) and IL-18 were significantly downregulated in iMCD compared to RA, CLL, or lymphoma. Additionally, the expression of IFN-γ was significantly downregulated in iMCD compared to RA and lymphoma.

**Conclusion**

Serum proteomics identifies interferon gamma signaling in idiopathic multicentric Castleman disease. The findings suggest that IFN-γ signaling may be a novel therapeutic target for iMCD.

**References**


**Images**

1. Serum proteomics identifies interferon gamma signaling in idiopathic multicentric Castleman disease. The findings suggest that IFN-γ signaling may be a novel therapeutic target for iMCD.

2. Serum proteomics identifies interferon gamma signaling in idiopathic multicentric Castleman disease. The findings suggest that IFN-γ signaling may be a novel therapeutic target for iMCD.