Docket #: S23-263

Preventing and Treating Respiratory Viral infections Using Sialylated Fc Ligands

Stanford researchers have found that sialylated Fc ligands can be used to modulate immune responses to respiratory viral infections.

Severe respiratory viral infections can trigger an aberrant inflammatory response that damages lung tissue and compromises gas exchange in the alveolar space, potentially leading to lethal complications such as respiratory failure. Immunoglobulins, comprised of Fc and Fab regions, regulate this inflammatory response, affecting the severity of viral diseases and effectiveness of vaccines. The Fc region is relatively constant among different antibodies in the same class, while the Fab region, also known as the antigen-binding fragment, is highly variable. Current immunoglobulin treatments for respiratory viral infections involve antibodies with Fab regions specific to the target viral protein, which limits their usage against different types of viral infections.

Researchers at Stanford have shown that intravenous administration of immunoglobulin G with sialylated Fc domain, or even sialylated Fc ligand alone, helps preserve lung function after respiratory viral infection (Figure 1). The addition of sialic acid induces conformational changes that promote interactions with anti-inflammatory SIGN receptors. This approach can be applied against any viral strain, eliminating the need for adjustments when novel viral strains and mutations emerge.

Figure

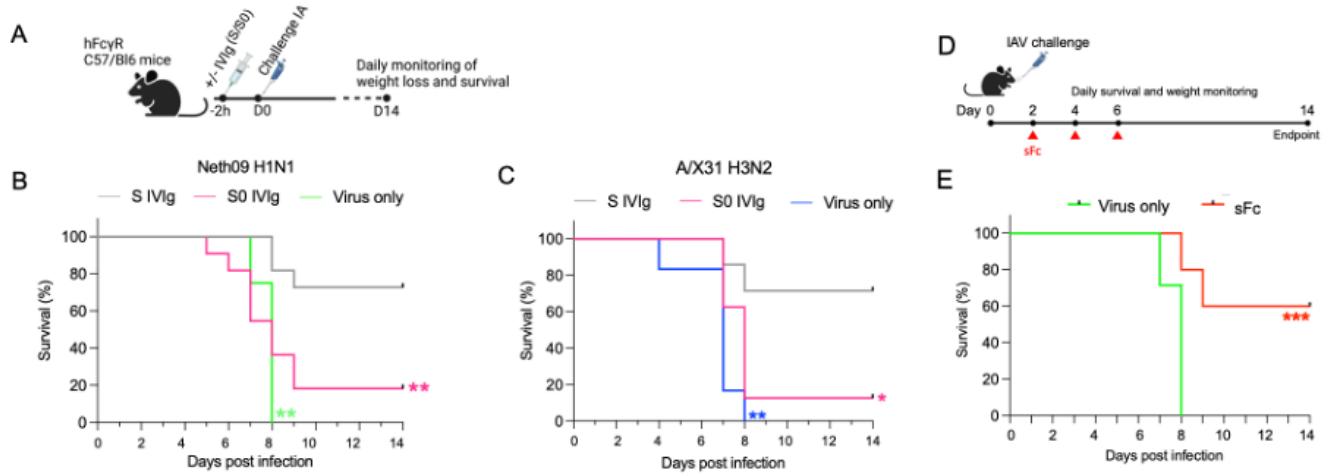

Figure Description: **A-C)**Intravenous injection of immunoglobin G with sialylated Fc domain (S IVIg) after viral infection with A/Netherlands/09 H1N1 and A/X31 H3N2. **D-E)** Intravenous injection of sialylated Fc (sFc) after viral infection with A/Netherlands/09 H1N1. Both approaches improve survival. (Image credit: the inventors)

Stage of Development
Pre-clinical

Applications

- Lung infections (influenza, SARS-CoV-2, etc.)

Advantages

- Generic treatment method for all viral strains. No adjustment needed in case of emergence of novel viral strains and viral mutations.

Publications

- Wang T. T. (2019). IgG Fc Glycosylation in Human Immunity. *Current topics in microbiology and immunology, 423*, 63–75.
- Saborni Chakraborty, Bowie Yik-Ling Cheng, Desmond L. Edwards, Joseph C. Gonzalez, David Kung-Chun Chiu, Hong Zheng, Courtney Scallan, Xinrong Guo, Gene S. Tan, Greg P. Coffey, Pamela B. Conley, Patrick S. Hume, William J. Janssen, Derek E. Byers, Philip A. Mudd, Jeffery Taubenberger, Matthew Memoli, Mark M. Davis, Katrin F. Chua, Michael S. Diamond, Evangelos Andreakos, Purvesh Khatri, Taia T. Wang. Sialylated IgG induces the transcription factor REST in alveolar macrophages to protect against lung inflammation and severe influenza disease. *Immunity*, 2024 (online 13 November 2024), ISSN 1074-7613.

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