PRESS RELEASE

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Scientists at The Wistar Institute Clone Several New Anti-Interferon Antibodies - Developing Future Therapeutic Candidates with Broad Application Potential

Honored as the Top Read in the September 15 Issue of the *Journal of Immunology*

PHILADELPHIA — (September 16, 2024) — New research from The Wistar Institute's Montaner lab — led by Wistar Executive Vice President, director of the HIV Cure and Viral Disease Center, and Herbert Kean, M.D., Family Professor, Luis Montaner, D.V.M., D.Phil. — has successfully isolated and cloned fully human antibodies that can block specific Type-I interferon molecules *in vitro*; their discovery has an array of potential clinical & research applications, enabling scientists with a new way to investigate the role of specific Type-I interferons in a variety of diseases. The work, published in the paper "Cloning and functional characterization of novel human neutralizing anti-interferon-alpha and anti-interferon-beta antibodies," has been honored as the Top Read in the September 15 issue of the *Journal of Immunology*.

As an immunomodulating subtype of cytokine — an inflammatory molecule class that our bodies release in response to stress — Type I interferons, or IFNs, help the immune system combat disease, cancer, and viral diseases in particular. Type I IFNs include several specific IFNs that can aid in the modulation of how our immune systems respond to infection, but when they become dysregulated or over-expressed, they can also contribute to shutting down the immune system. In HIV infections, Type I IFNs have been observed to produce paradoxical effects, working for and against the virus simultaneously.

Due to the complexity and ambiguity of how best to therapeutically target IFNs' broad effects on immune control, scientists in the Montaner lab sought to develop several antibodies to target and

selectively block two major but distinct Type I IFNs: interferon alpha (IFN-α) and interferon beta (IFN-β). First author Emmanouil Papasavvas, Ph.D., and his collaborators sought to take advantage of the body's natural immune response in persons receiving IFN-α or IFN-β treatment, as these persons can generate their own anti-IFN antibodies.

Using cryopreserved blood plasma samples from these same persons receiving IFN-α or IFN-β treatment, respectively, the team successfully isolated and cloned four selective anti-IFN antibodies, two against IFN-α and two against IFN-β. The success of the novel approach taken — which leveraged the pooling of complementary DNA from original samples to optimize cloned antibodies — circumvents more complex techniques to derive monoclonal antibodies. Having demonstrated their antibodies' ability to selectively block IFN-α or IFN-β *in vitro*, the team predicts that future studies *in vivo* will yield similar promising results.

"These novel, effective human antibodies against specific Type I interferons have the potential to be an indispensable tool for understanding and ultimately serving as immunotherapy against cancer, autoimmune or infectious disease conditions," said Dr. Montaner.

"We are very pleased with our methodological proof-of-concept report, and I believe it will lead to exciting future work," agreed Dr. Papasavvas. "With the ability to selectively target and inhibit specific interferons, scientists will have a valuable tool for developing future therapies."

Co-authors: Emmanouil Papasavvas, Lily Lu, Matthew Fair, Isabela Oliva, Joel Cassel, Sonali Majumdar, Kar Muthumani, and Luis J. Montaner of The Wistar Institute; Karam Mounzer of the Jonathan Lax Immune Disorders Treatment Center; Jay R. Kostman of the Jonathan Lax Immune Disorders Treatment Center and the John Bell Health Center; and Pablo Tebas and Amit Bar-Or of the Perelman Center for Advanced Medicine.

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