



# Joan Wood Lecture Series

*Celebrating Women in Science. Showcasing Careers in Biology.*

Wed., Nov. 1, 2023 • 4 p.m. • Myers Hall 130

## Non-standard viral genomes are intrinsic elements of the virus community

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The López laboratory investigates the mechanisms involved in the recognition and control of viruses that infect the respiratory tract, including respiratory syncytial virus and parainfluenza viruses, such as the murine virus Sendai. The laboratory focuses on understanding how different components of a virus population affect the interaction of the virus with the host and on the genesis and function of non-standard severely truncated replication defective forms of viral genomes that accumulate naturally during infection with RNA viruses. These types of viral genomes, formerly known as defective interfering (DI) viral genomes or defective viral genomes (DVGs), were first described over sixty years ago, but their biological role was overlooked until recently. Using a battery of molecular biology, imaging, and bioinformatics tools that allow the identification and differentiation of nonstandard and standard-viral genomes, the laboratory discovered that non-standard genomes of the copy-back type (cbVGs) are fundamental components of single strand negative sense RNA viruses and play a critical role in determining the infection outcome. Among the most important discoveries, the work revealed that cbVGs impart a functional heterogeneity among infected cells. Cells that accumulate large numbers of cbVGs are engaged in an antiviral and pro-survival program, while cells with little or no cbVGs turn into virus-producing machines. Most importantly, the laboratory identified cbVGs as the primary stimulators of the host immune response against multiple RNA viruses and gathered fundamental insight into the viral structures necessary to elicit strong antiviral responses. This work led to the development of synthetic cbVGs-derived oligonucleotides that maintain the natural ability to stimulate immunity and can be used as adjuvants during vaccination. The most significant contribution of the López lab to date is the demonstration that cbVGs accumulate in humans naturally infected respiratory syncytial virus and that detection of cbVGs in respiratory secretions can be used to predict the clinical outcome of infection. To achieve these goals, the laboratory developed a battery of tools for the study of non-standard viral genomes, including a robust bioinformatics pipeline (VODKA2) for their identification after NGS sequencing.



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