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Anne Monette, PhD

Research Associate,
HIV-1 RNA Trafficking Lab, Lady Davis Institute



Meijuan Niu

Research Technician,
HIV-1 RNA Trafficking Lab, Lady Davis Institute



Andrew Mouland, PhD

Senior Investigator, HIV-1 RNA Trafficking Lab,
Lady Davis Institute

Professor, Departments of Microbiology & Immunology
and Medicine, McGill University

Cell Reports

Pan-retroviral Nucleocapsid-Mediated Phase Separation Regulates Genomic RNA Positioning and Trafficking

Anne Monette, Meijuan Niu, Lois Chen, Shringar Rao, Robert James Gorelick, and Andrew John Mouland

This paper explores how liquid-liquid phase separation (LLPS) of cellular components is important for many cellular processes from transcription to mRNA trafficking to mRNA translation. LLPS involves the promotion of the assembly of condensates in the form of membraneless organelles (MLOs) that promote protein-protein and protein-DNA/RNA interactions to establish order inside cells. Proteins, RNAs and other cellular components self-organize into liquid-like droplets known as condensates providing spatial organization in the cell. One such MLO is the stress granule that the HIV-1 RNA Trafficking Laboratory has shown to be anti-viral in nature (Nat. Comm., 2014; Paper of the Month, June 2014). Viruses, specifically HIV-1 and other retroviruses, are obliged to assemble in specific regions of the cell. This paper demonstrates for the first time that these viruses promote LLPS to favour replication and genomic RNA localization. They achieve this via the activity of the small Zinc-coordinating nucleocapsid proteins of HIV-1 and other retroviruses. The disruption of nucleocapsid function, by abrogating Zinc coordination, repositions the HIV-1 genomic RNA, potentially blocking virus expression. The role for MLO/SG assembly in HIV-1 replication favours the notion that LLPS plays an important role in the timing and positioning of key viral components during the retroviral replication cycle. HIV-1 nucleocapsid is a highly conserved domain in retroviruses, but harbours several drugable domains that remain viable targets for therapeutic intervention. As per this report, the nucleocapsid's role in LLPS may represent a lead to identifying a promising new target for treatment.

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