Dissecting innate immunity responses to viral infection at the single-cell level

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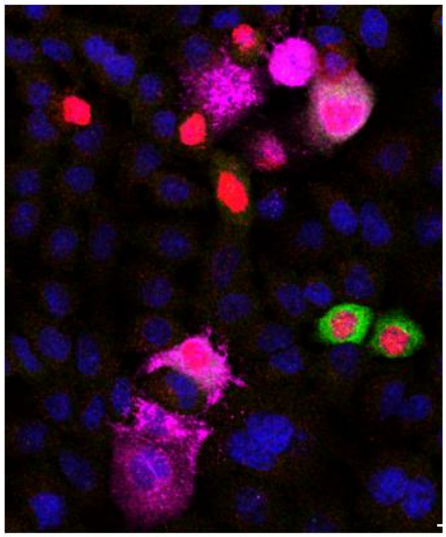
Recognition of viral RNA initiates a signaling cascade culminating in synthesis of interferons (IFNs). Secreted IFNs, by activation of transcription factors of STAT family in surrounding cells, prompt them to prepare for viral infection. Viruses, in turn, convey non-structural proteins to impede the innate immune response. Based on results obtained using single-cell techniques, we proposed an agent (single cell)-based, stochastic, computational model and used it to explain how a infected population of cells can stratify into distinct subpopulations. The winning cells, in response to viral RNA, produce IFNβ (warning yet not infected cells), loosing cells express viral proteins that inhibit innate immune signaling. The proposed model reproduces the experimentally observed complex spatial patterns of respiratory syncytial virus (RSV) spread and dichotomous cell responses.



Immunostained monolayer of A549 cells 24 hours after infection with RSV at multiplicity of infection equal 0.01 (about 1% of cells infected initially).

Winning cells in response to viral RNA activate transcription factor **IRF3 (red)** that triggers synthesis of **IFNβ (green)**.

In loosing cells **viral proteins (magenta)** are expressed and inhibit **IFNβ** synthesis.

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