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Specificity, cross-talk and adaptation in Interferon signaling

ANTON ZILMAN, University of Toronto

Innate immune system is the first line of defense of higher organisms against pathogens. It coordinates the behavior of millions of cells of multiple types, achieved through numerous signaling molecules. This talk focuses on the signaling specificity of a major class of signaling molecules - Type I Interferons - which are also used therapeutically in the treatment of a number of diseases, such as Hepatitis C, multiple sclerosis and some cancers. Puzzlingly, different Interferons act through the same cell surface receptor but have different effects on the target cells. They also exhibit a strange pattern of temporal cross-talk resulting in a serious clinical problem - loss of response to Interferon therapy. We combined mathematical modeling with quantitative experiments to develop a quantitative model of specificity and adaptation in the Interferon signaling pathway. The model resolves several outstanding experimental puzzles and directly affects the clinical use of Type I Interferons in treatment of viral hepatitis and other diseases.