

# Johns Hopkins University

## Department of Biology Seminar Series

Thursdays, 4:00pm

For more information go to: <https://bio.jhu.edu/events>

Zoom link: <https://zoom.us/j/97925356454?pwd=bjNuTlY1dlU9BcXcvRFdleis2TVNadz09>

March 9th, 2023 - Mudd 100



**Marian Kalocsay**

Department of Experimental  
Radiation Oncology

MD Anderson Cancer Center

Host: Christian Kaiser

## “Signaling receptor dynamics resolved by proximity proteomics”

Notch signaling relies on ligand-induced proteolysis to liberate a nuclear effector that drives cell fate decisions. The location and timing of individual steps required for proteolysis and movement of Notch from membrane to nucleus, however, remain unclear. We used proximity labeling with quantitative multiplexed mass spectrometry to monitor the microenvironment of endogenous Notch2 after ligand stimulation in the presence of a gamma secretase inhibitor and then as a function of time after inhibitor removal. Our studies show that gamma secretase cleavage of Notch2 occurs in an intracellular compartment and that formation of nuclear complexes and recruitment of chromatin-modifying enzymes occurs within 45 minutes of inhibitor washout. This work provides a spatiotemporal map of unprecedented detail tracking the itinerary of Notch from membrane to nucleus after activation and identifies molecular events in signal transmission that are potential targets for modulating Notch signaling activity.