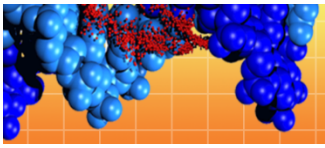

CENTER FOR BIOINFORMATICS & COMPUTATIONAL BIOLOGY

BIOINFORMATICS 2016 SPRING SEMINAR SERIES

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MONDAY, May 2, 2016
3:30pm
DBI Room 102

Digital biological signaling: pulsatile dynamics in the DNA damage response

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ABSTRACT: Living cells use complex signaling pathways to detect environmental stimuli and generate appropriate responses. As methods for quantifying intracellular signaling have improved, several signaling pathways have been found to transmit information using signals that pulse in time. The transcription factor p53 is a key tumor suppressor and stress-response regulator that exhibits pulsatile dynamics. In response to DNA double-strand breaks, the concentration of p53 in the cell nucleus increases in pulses with a fixed amplitude, duration, and period; the mean number of pulses increases with DNA damage. p53 regulates the expression of over 100 target genes involved in a range of cellular stress responses including apoptosis, cell cycle arrest, and changes in metabolism. p53 pulsing directly impacts p53 function: altering p53 dynamics by pharmacologically inhibiting p53 degradation changes patterns of target gene expression and cell fate. In this talk, we will describe our efforts to use a variety of approaches including live-cell imaging, computational modeling, and single-cell transcriptional profiling to identify the regulatory mechanisms generating p53 dynamics and the functional consequences of the dynamics in terms of the regulation and coordination of target gene expression. Our findings help delineate how p53 orchestrates the complex DNA damage response and give insight into how a broad range of biological signaling pathways make use of dynamics to encode biological information.