BiophysTO Lunchtime Seminar Series

Date

Monday, July 8, 2019
[12:10 (noon)]

Location

McLennan, MP606
60 St George Street

Pizza & refreshments provided

Dr. Gnana S. Gnanakaran

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Transport of signals and drugs across membranes

I will discuss two examples where we have used a variety of theoretical approaches along with experimental data to address the complexity of membranes that presents a formidable challenge to conventional biophysical approaches. For the transport of signals across cellular membrane, we suggested a previously unknown molecular mechanism for T-cell activation based on the preferential binding and localization of the intrinsically disordered cytoplasmic signaling tails, which are easily modified by the presence of different lipid species and by the physical state of the membrane. Moreover, in a biological membrane with liquid-ordered and liquid-disordered domains, we show that specific lipids may play a significant role in immunoreceptor signaling and similar mechanisms may be possible in a broader context in RAS-RAF, a critical signaling pathway in cancer. For the transport of drugs across membranes, Gram-negative bacteria in particular represent unique challenges due to the combined effects of their low permeability outer membranes and their non-specific efflux pumps. Specifically, we have shown that the low permeability of the two-membrane cell envelope in P. aeruginosa and the insufficient chemical diversity of potential antibiotic compounds present a challenge to antibiotic discovery. We employ a novel machine learning approach to identify the key descriptors and molecular fragments within a drug compound governing membrane permeability. This approach allows high-throughput screening of functionally relevant fragments and offers an alternative way to search the chemical space for novel antibiotic candidates.

Host: Dr. Sarah Rauscher

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