QCB Evenings

Wednesday, April 6 • 4:00pm • Chemistry C122

Half-PEGylated Particles Evade Macrophage Uptake as Effectively as Fully Coated Ones

Lucy Sanchez, Yu Lab

A major challenge associated with therapeutic nanoparticles is their rapid clearance by immune cells, such as macrophages, before reaching their targeted destination in the body. Nanoparticles are detected by immune cells due to the adsorption of blood serum proteins on the particle surfaces. Attaching a protective layer of polymers onto particle surfaces has been shown to prevent serum protein adsorption. The problem with this method is that the bulky polymer chains have been shown to block the cell targeting ligands from binding cell-surface receptors. We report a method to spatially decouple the bulky polymer chains and cell-specific ligands by designing bifunctional two-faced Janus nanoparticles. We investigated the macrophage internalization efficiency of Janus nanoparticles and determined the mechanisms of uptake. We show that the half-PEGylated Janus nanoparticles have similar internalization efficiencies as commonly used nanoparticles that are fully coated with PEG. This result will provide new insights into designing more effective therapeutic nanoparticles.

The Effect of Stochastic Gene Expression on Protein Multimerization

Kyle Hagner, Setayeshgar Lab and Lynch Lab

Many proteins assemble into multimeric structures, with a large fraction being homomers with an even number of subunits that can vary substantially among phylogenetic lineages. As protein-protein interactions (PPI) require productive encounters among subunits, such variation might partially be explained by variation in cellular protein abundance. The protein abundance in turn depends on the intrinsic rates of production and decay of mRNA and protein molecules, as well as rates of cell growth and division. We present a stochastic model for prediction of the multimeric state of a protein as a function of these processes and the free energy associated with binding interfaces. We demonstrate favorable agreement between the model prediction and a wide class of proteins using E. coli proteome data. As such, this platform, which links rates of transcription, translation, mRNA and protein decay, and protein association/dissociation with protein abundance and quaternary structure in growing and dividing cells can be extended to evolutionary models for the emergence and diversification of the multimeric nature of proteins.

By modeling proteins as sequences of hydrophobic (H) and polar (P) residues on a cubic lattice, PPI can be viewed as the effect of pairwise interactions between H residues across an interface, with each pair contributing a fixed free energy gain to the interaction. The partition function for protein aggregates can be solved for a given total protein concentration, yielding a distribution of assemblies. These distributions can be used to investigate the dependence of an appropriately defined fitness function on protein sequence.

All QCB Trainer Lab Personnel are invited to attend.
Food and beer will be provided.