Designing Peptides *For* or *Against* Cell Permeability

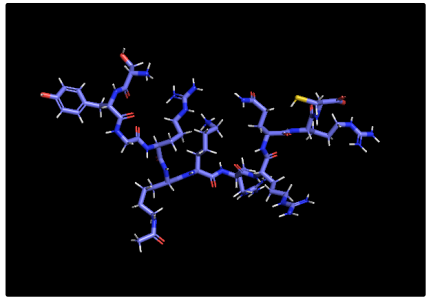
- Mechanisms of Permeability
  - *Creating Pores*
  - *Endocytosed/Pinocytosed*
  - *Passively Crossing Membrane*

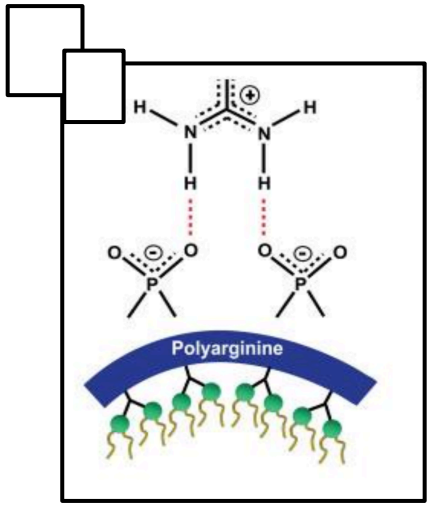
- Design Peptides *For* or *Against*
  - *Cationic (Arg rich) & Hydrophobics*
    - Drives permeability
    - Interacts with membrane
    - Induces Actin reorganization
  - *Anionic*
    - Selects against clearance by kidneys

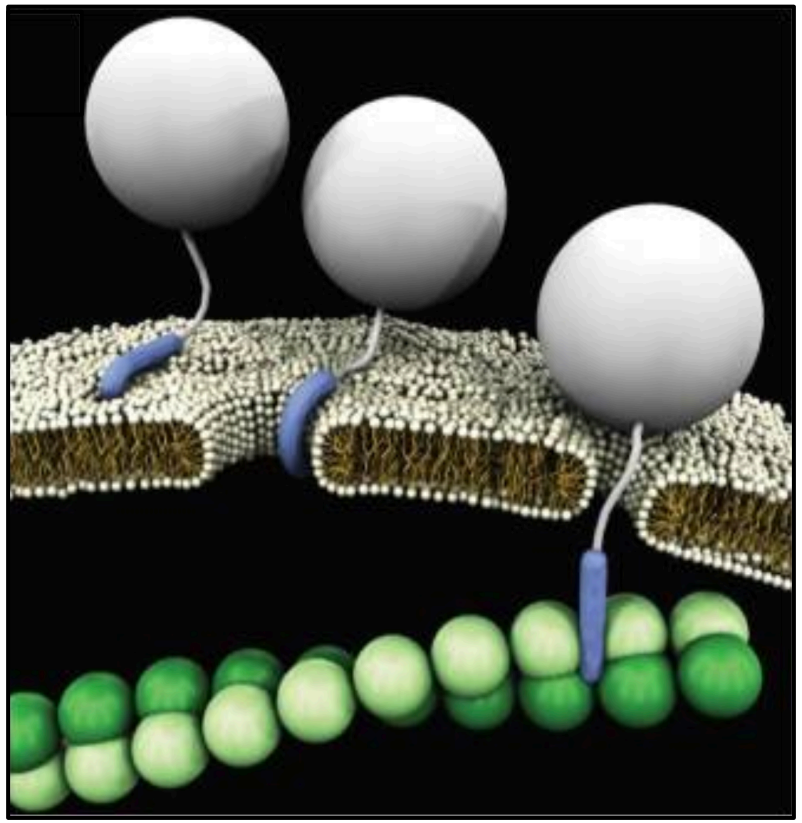
Iterative Design between computation and wet lab

- Peptides modeled *with* & *without* hydrophilic environment
- Designs are selected to be most favorable to desired environment

Example: Tat Peptide from HIV is Arg rich







Translocation of HIV TAT peptide and analogues induced by multiplexed membrane and cytoskeletal interactions.
Mishra A, Lai GH, Schmidt NW, Sun VZ, Rodriguez AR, Tong R, Tang L, Cheng J, Deming TJ, Kamei DT, Wong GC. Proc Natl Acad Sci U S A. 2011 Oct 11;108(41):16883-8.