Engineering viral vectors for non-invasive and specific gene delivery to the brain and body

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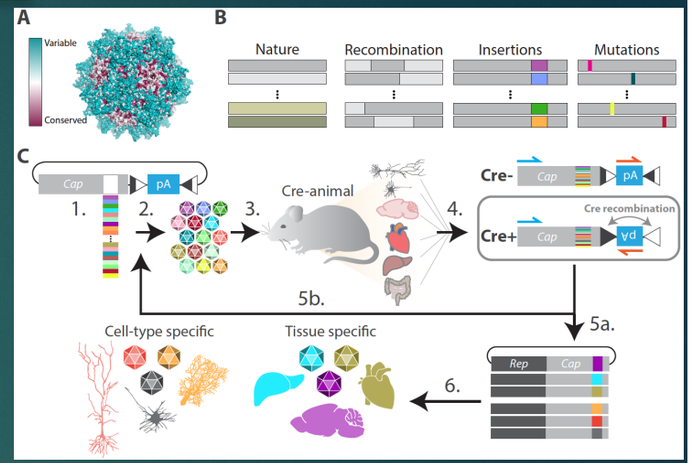
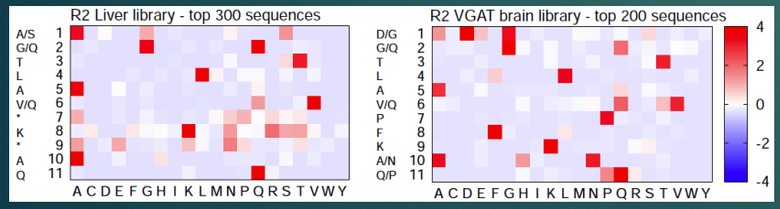
- Current practice for gene delivery vectors:
  - Systemic BUT non-specific to reach liver, heart, muscle, lung
  - Stereotaxic brain surgery—invasive and can cause hemorrhages and non-uniform expression over a limited volume.
- To address this limitation, we have developed viral-vector selection methods based on directed evolution methods (for which Caltech's Frances Arnold won Nobel Prize in Chemistry this year) to identify engineered capsids capable of reaching target cell-populations across the body and brain after noninvasive systemic delivery



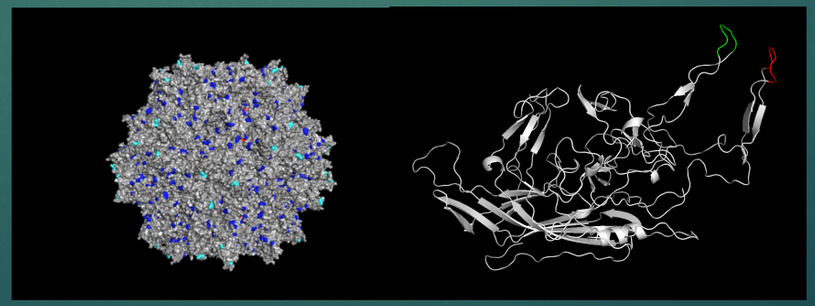
Challenge 1: ML for library mining and prediction

Theoretical space (~1 billion variants) undersampled by necessity. R2 has tens of thousands of variants, use enrichment.

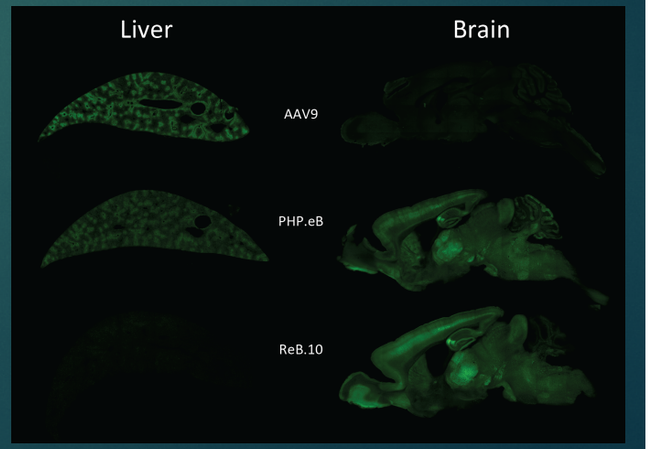


Challenge 2: Structural Modeling

Design/Speed up Rosetta algorithms as now 10,000 CPU hours per structure for each variant



We can generate viral diversity and apply selective pressure for desired properties e.g. delivery that is strong in the brain AND weak in the liver



This technology could improve human health by permitting the developing of novel therapeutics addressing unmet medical need