M2D4: Evaluate protein structures

- Quiz
- Prelab discussion

- Examine structure of pfFKBP35 and FKBP12
- Examine structures of small molecules

Homework

Data Figure and Results

Create a data figure for the SDS-PAGE gel and write the accompanying results section

Data for each group is linked on Class Data page

Figure

- Format / label the gel image
- Write a figure title and caption

Results text

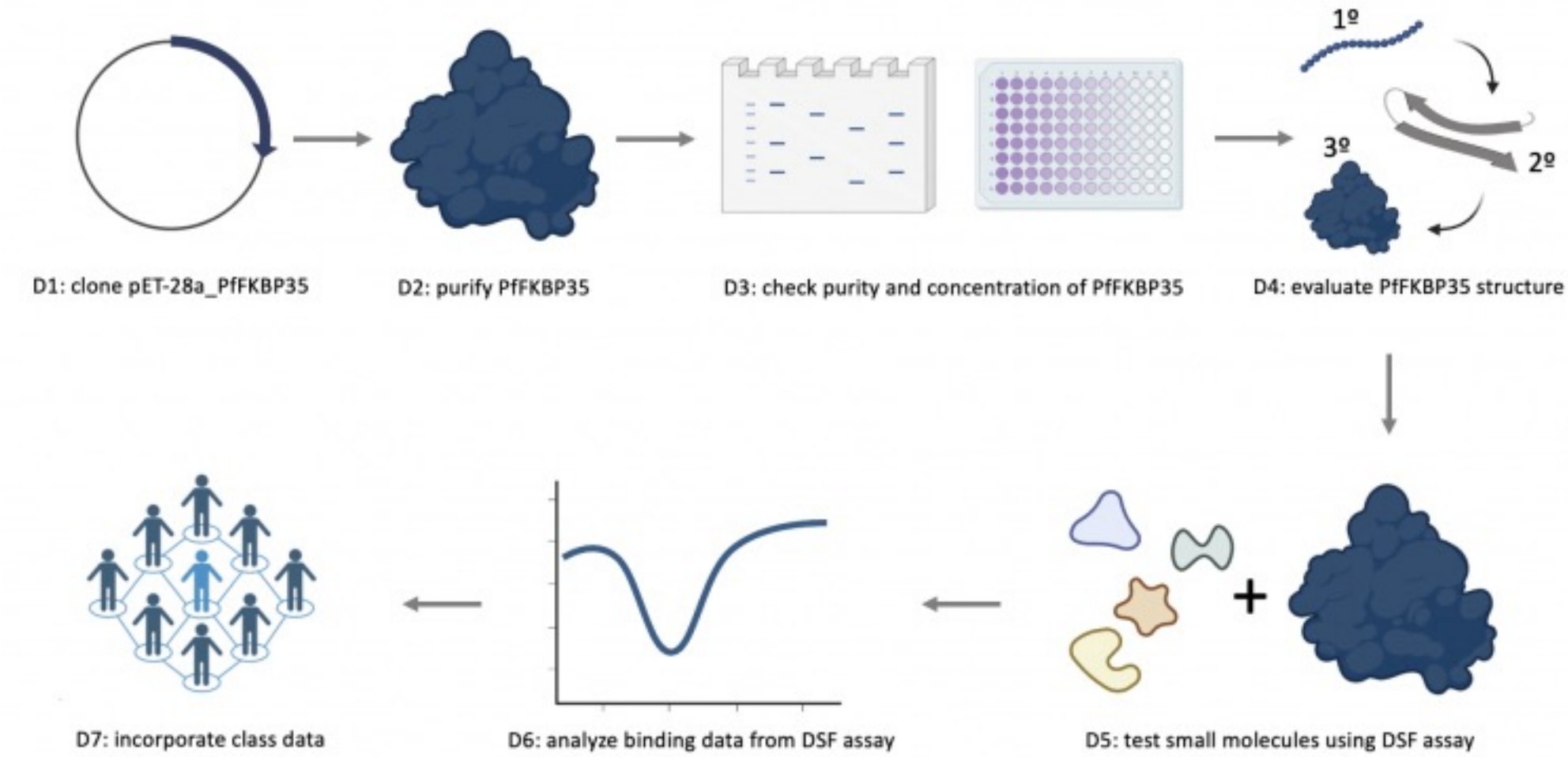
- Write a results section corresponding to the data (in paragraphs!)
  - Explain all data shown
  - DO NOT include interpretation of data (this will be done in the discussion section)

Lab work

Assess structure of protein targets and small molecules

Mod2 overview

Research goal: Test small molecules for binding to the *Plasmodium falciparum* FKBP35 protein using a functional assay.



Review of Mod2 concepts

- What is the overall problem we are concerned with in Mod2?
- What is the protein target we purified for examination?
- What is the human homolog of this protein target, and why is its presence problematic for our long-term goal?
- What type of potential drugs are we testing in our assay?

What are small molecules and why are we using them?

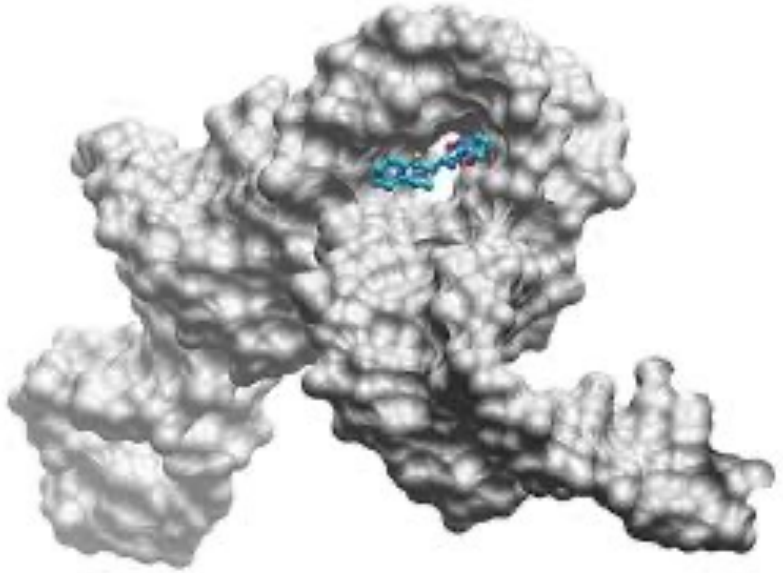
- Small molecules
  - Mw < 500 Da
  - Natural or synthetic
  - Frequently comprised of Carbon/Nitrogen/Oxygen

<u>Why Small molecules?</u>

- Can design molecules to fit with target protein surface features
- Membrane permeable
- Orally bioavailable

Our small molecule library is based on FK506

- known binder



Structural assessment of target and ligand interactions

- Structural assessment of protein targets and putative binders are key to development of novel therapeutics

Allows us to:

- Create 3D rendering of macromolecules like proteins
- Compare sequences, motifs, and folding of protein targets
- Can dock putative ligands and assess molecular interactions

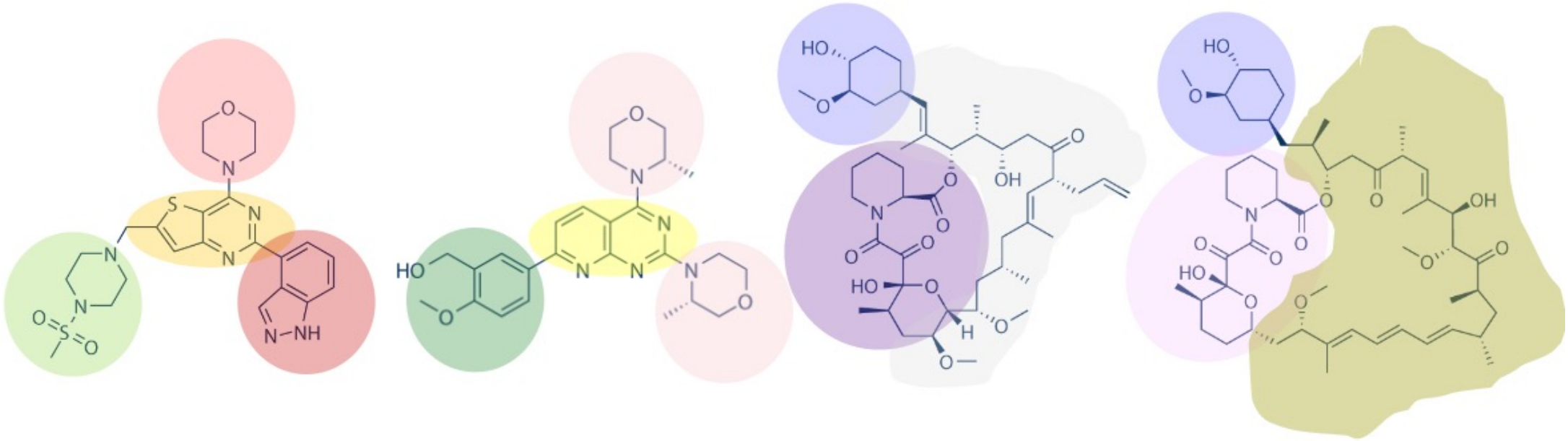
Resources for computational assessment of proteins

- Online databases
  - Uniprot: collects known information about protein sequence, function, homology with other proteins
  - Protein Data Bank: collection of structural information about proteins

- Pymol
  - Python-based program that uses molecular information embedded in PDB files to combine sequence and 3D rendering information for proteins
  - Allows multiple forms of visualization
  - Compare proteins and dock putative ligands

Assessment of small molecule structure

- Chemdraw
  - Allows conversion from chemical sequence into structural rendering to easily compare shapes and functional groups across multiple small molecules



For today…

- Align and compare FKBP35 and FKBP12 to identify key places of overlap
- Examine chemical structures and identify key shared and unique features between small molecules to be tested
- Use this information to build a picture about predicted binders to FKBP12 vs FKBP35