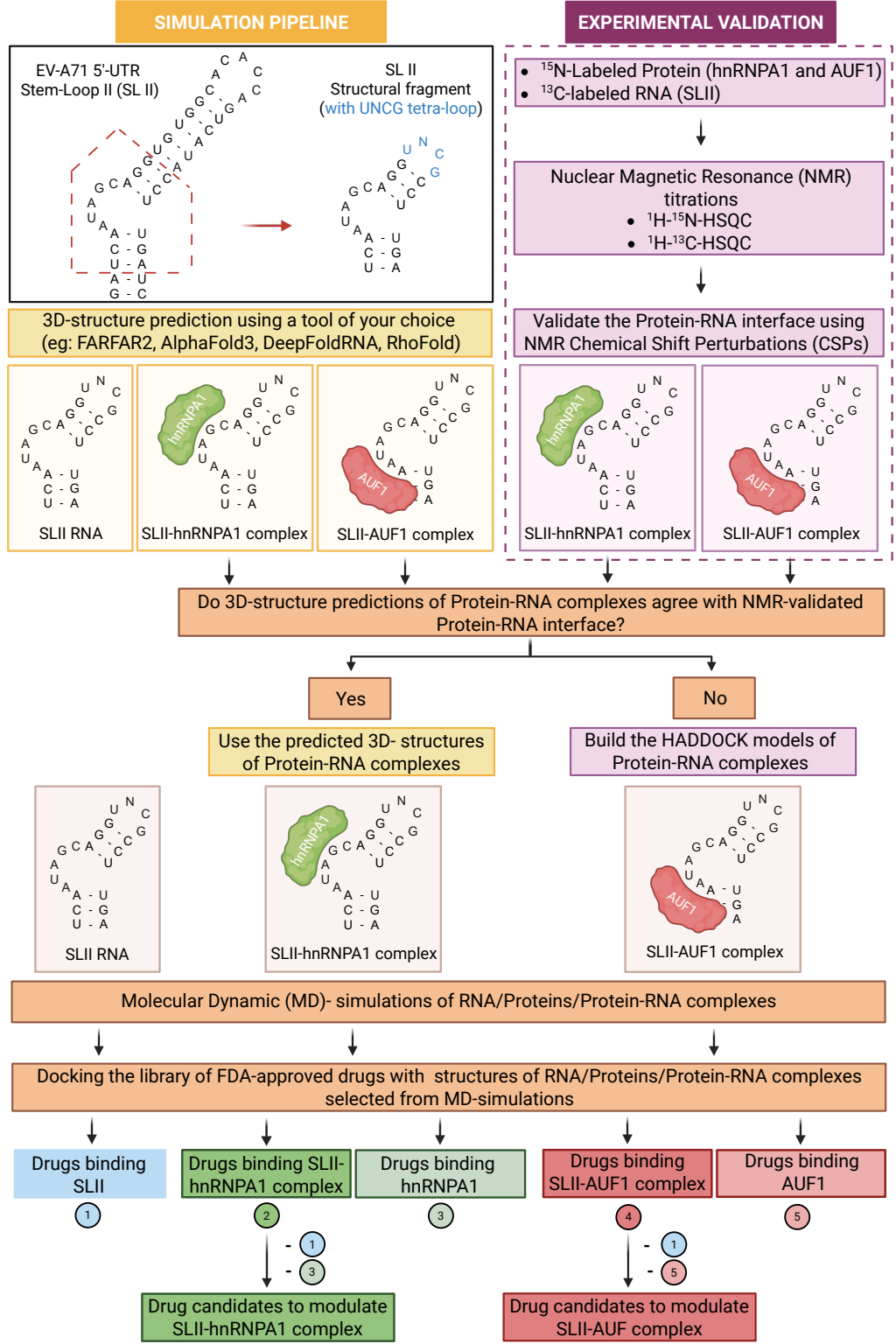
SIMULATION PIPELINE
EXPERIMENTAL VALIDATION
EV-A71 5'-UTR
Stem-Loop II (SL II)
SL II
Structural fragment
(with UNCG tetra-loop)
• 15N-Labeled Protein (hnRNPA1 and AUF1)
• 13C-labeled RNA (SLII)
Nuclear Magnetic Resonance (NMR) titrations
• 1H-15N-HSQC
• 1H-13C-HSQC
Validate the Protein-RNA interface using NMR Chemical Shift Perturbations (CSPs)
3D-structure prediction using a tool of your choice
(eg: FARFAR2, AlphaFold3, DeepFoldRNA, RhoFold)
SLII RNA
SLII-hnRNPA1 complex
SLII-AUF1 complex
SLII-hnRNPA1 complex
SLII-AUF1 complex
hnRNPA1
AUF1
Do 3D-structure predictions of Protein-RNA complexes agree with NMR-validated Protein-RNA interface?
Yes
No
Use the predicted 3D- structures of Protein-RNA complexes
Build the HADDOCK models of Protein-RNA complexes
SLII RNA
SLII-hnRNPA1 complex
SLII-AUF1 complex
Molecular Dynamic (MD)- simulations of RNA/Proteins/Protein-RNA complexes
Docking the library of FDA-approved drugs with structures of RNA/Proteins/Protein-RNA complexes selected from MD-simulations
Drugs binding SLII
Drugs binding SLII-hnRNPA1 complex
Drugs binding hnRNPA1
Drugs binding SLII-AUF1 complex
Drugs binding AUF1
1
2
3
4
5
- 1
- 3
- 1
- 5
Drug candidates to modulate SLII-hnRNPA1 complex
Drug candidates to modulate SLII-AUF complex