

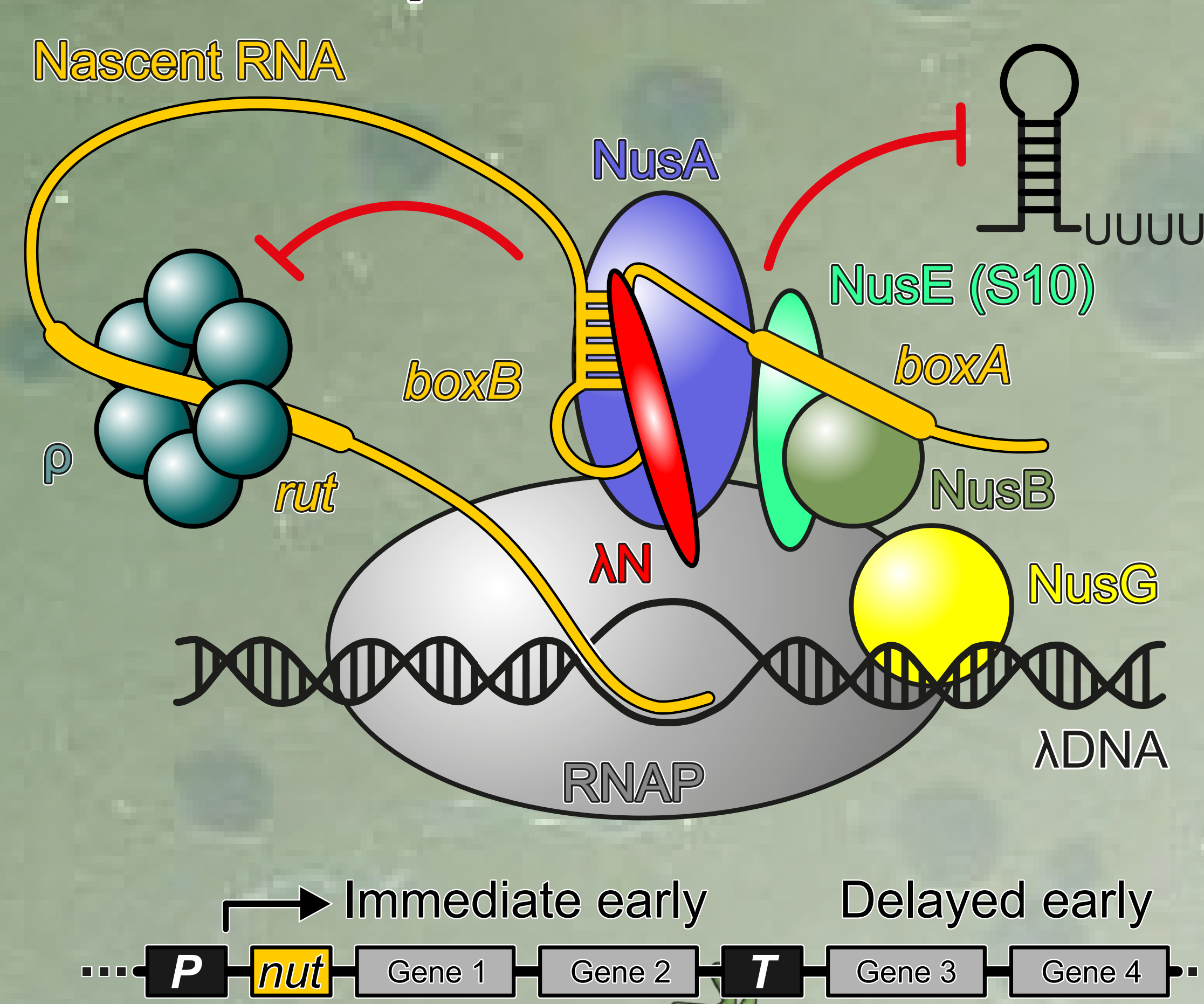
Structural Biology

Hijacking a cell's transcription machinery

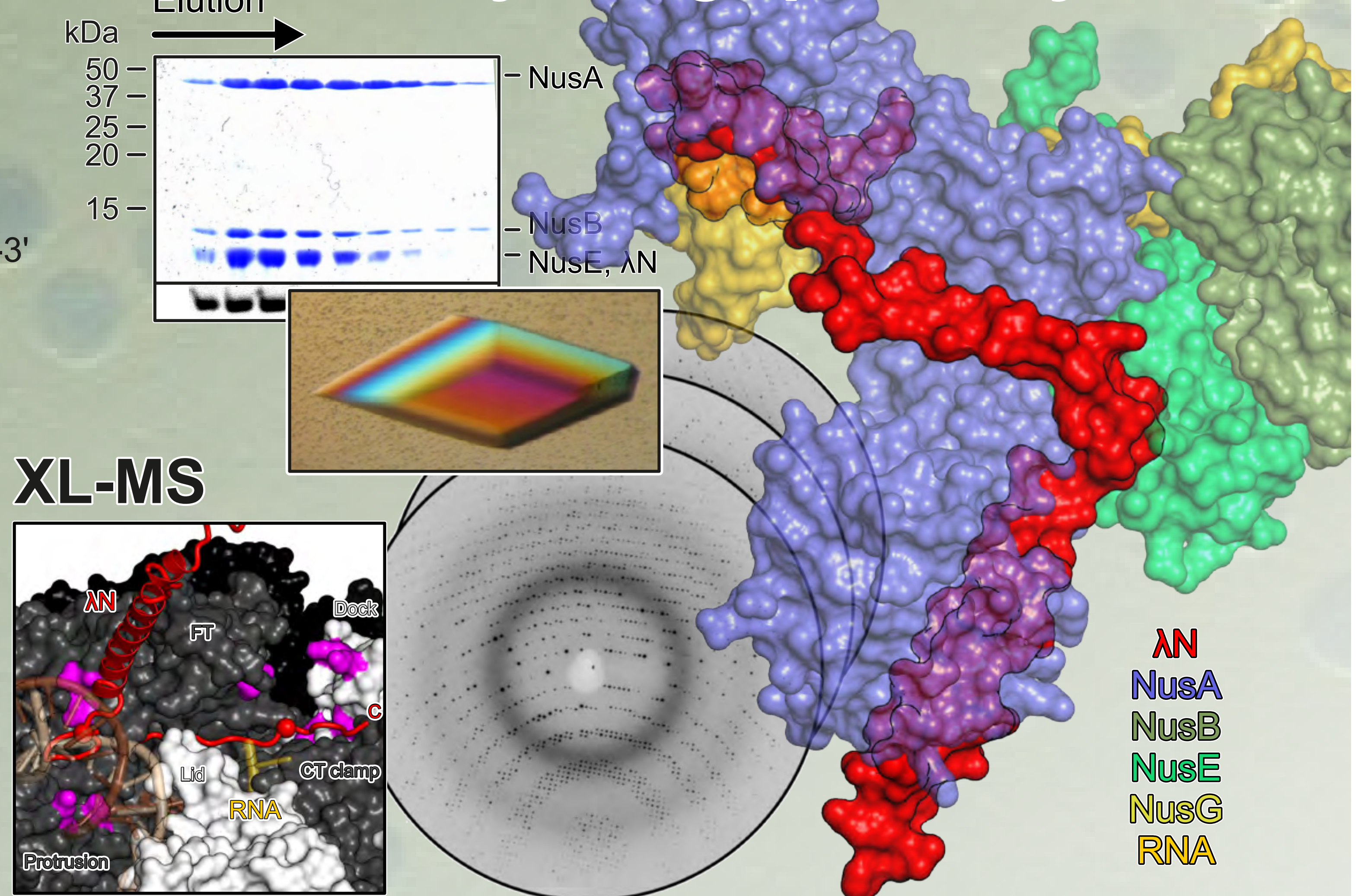
Summary

Bacteriophage λ N protein, a model anti-termination factor, binds nascent RNA and host Nus factors, rendering RNA polymerase resistant to all pause and termination signals. A 3.7 Å-resolution cryo-electron microscopy structure and structure-informed functional analyses reveal a multi-pronged strategy, by which the intrinsically unstructured λ N directly modifies RNA polymerase interactions with the nucleic acids and subverts essential functions of NusA, NusE and NusG to reprogram the transcriptional apparatus. λ N repositions NusA and remodels the β -subunit flap tip, which likely precludes folding of pause/termination RNA hairpins in the exit tunnel and disrupts termination-supporting interactions of the α -subunit C-terminal domains. λ N invades and traverses the RNA polymerase hybrid cavity, likely stabilizing the hybrid and impeding pause/termination-related conformational changes of polymerase. λ N also lines upstream DNA, seemingly reinforcing anti-backtracking/anti-swiveling by NusG. Moreover, λ N-repositioned NusA and NusE sequester the NusG C-terminal domain, counteracting p-dependent termination. Other anti-terminators likely utilize similar mechanisms to enable processive transcription.

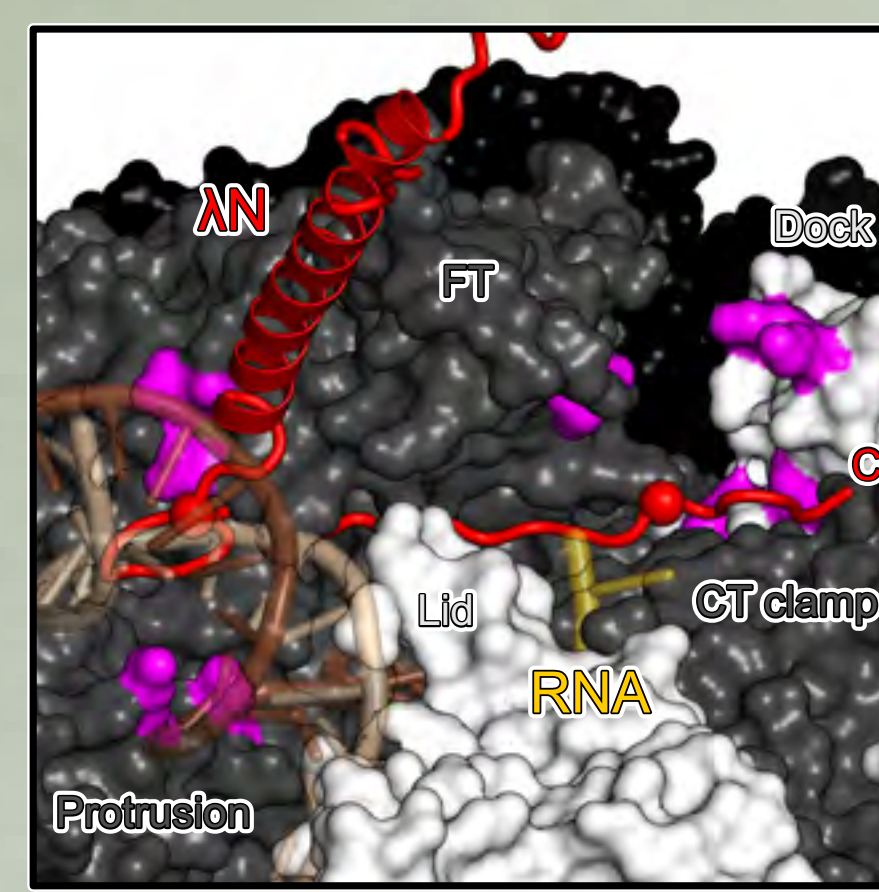
Phage λ protein N-mediated transcription anti-termination



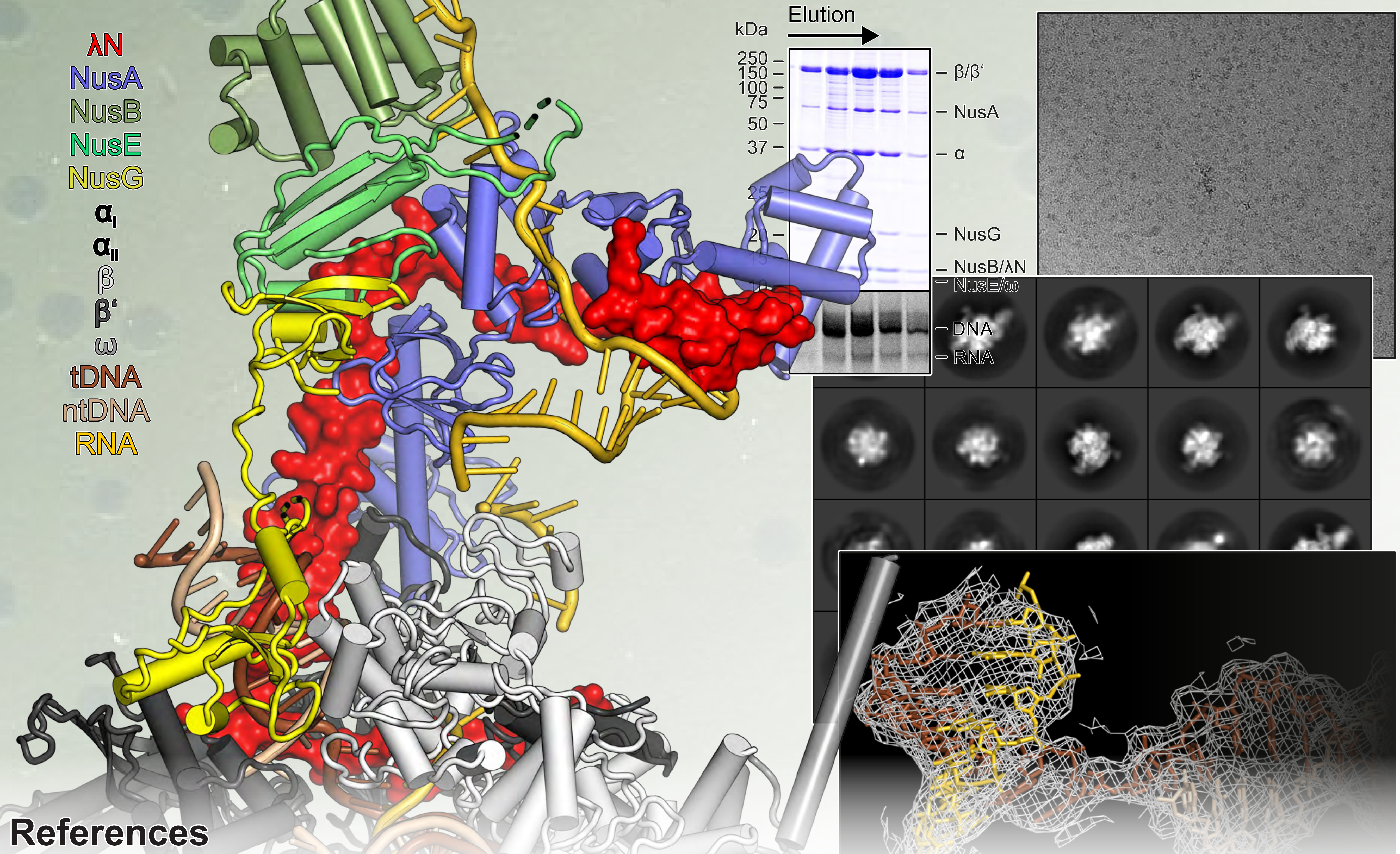
Crystallographic analysis



XL-MS



Single-particle cryo-EM analysis



References

- Krupp F, Said N, Huang YH, Loll B, Bürger J, Mielke T, Spahn CMT, Wahl MC (2019) Structural basis for the action of an all-purpose transcription anti-termination factor. *Mol Cell*, in press.
- Said N, Krupp F, Anedchenko E, Santos KF, Dybkov O, Huang YH, Lee TC, Loll B, Behrmann E, Bürger J, Mielke T, Loerke J, Urlaub H, Spahn CMT, Weber G, Wahl MC (2017) Structural basis for λ N-dependent processive transcription antitermination, *Nat Microbiol* 2, 17062.