Curriculum Vitae

Name
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Current Position
Assistant Professor

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Education & Professional Experiences
2012 Ph.D., Molecular Biophysics, New York University, New York, US
2013-2021 Postdoctoral Fellow and Investigator Scientist, MRC Laboratory of Molecular Biology, Cambridge, UK

Research Interests
RNP function in neurodegeneration

Selected Publications

Plaschka C[#*], Lin PC[#*], Clement Charenton and Nagai K*. Cryo-EM structure of a yeast prespliceosome. Nature 2019; 559 (7714): 419-422. # equal contribution [*]corresponding author

Su YL, Chen HC, Tsai RT, Lin PC, Cheng SC. Cwc23 is a component of the NTR complex and functions to stabilize Ntr1 and facilitate disassembly of spliceosome intermediates. Nucleic Acid Res. 2018; 46(7): 3764-3773.

Plaschka C[#], Lin PC[#] and Nagai K. Structure of a pre-catalytic spliceosome. Nature 2017; 546 (7660): 617-621. # Contributed equally.

Lecture Title
Mechanistic Analysis of SMN Polymerization and Its Role in Spinal Muscular Atrophy Pathogenesis

Abstract (500 words maximum)
Spinal muscular atrophy (SMA) is an autosomal recessive neuromuscular disorder characterized by loss of spinal motor neurons. Patients with SMA exhibit progressive proximal muscle weakness and skeletal muscle atrophy. SMA is caused by homozygous deletion or loss-of-function mutation in survival motor neuron 1 (*SMN1*) gene, leading to reduced level of SMN protein. Human also possess a highly similar paralog gene, *SMN2*, which differs from *SMN1* by a critical C-to-T transition in exon 7. This single nucleotide change alters exon 7 splicing, so *SMN2* predominantly produces the C-terminal truncated SMNΔ7 isoform rather than full-length SMN.

Prior co-immunoprecipitation experiments using recombinant SMN showed that SMN can self-associate and assemble into higher-order oligomeric complexes. The

interaction interface was mapped to the C-terminal YG-box domain and downstream residues, which is also the region most altered by exon 7 skipping in SMNΔ7. This oligomeric behavior has been used to explain SMA pathogenesis, as several SMA-associated SMN missense variants exhibit reduced self-association.

Despite previous extensive work on SMN self-oligomerization, it remains unclear how changes in oligomeric state translate into specific defects in SMN function and, ultimately, selective motor neuron vulnerability. In particular, most prior assays focused on SMN self-interaction in isolation and did not directly test how altered oligomerization affects assembly and composition of defined SMN-containing complexes. Using a reconstituted system, we tracked SMN-Gemin assemblies and assessed changes in complex integrity and biochemical activity. This approach provides an experimental framework to connect SMN oligomeric state with SMN-Gemin complex architecture and to probe how SMA-associated SMN variants may perturb RNP biogenesis.