Studies on protein dynamics with an expanded amino acid repertoire

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With few minor variations, the genetic code is universal to all forms of life on earth. Synthetic biology, however, endeavours to undo this frozen accident of evolution and create organisms with an expanded genetic code by the heterologous expression of evolved aminoacyl-tRNA synthetase/$tRNA_{CUA}$ pairs. These mediate the incorporation of unnatural amino acids in response to blank codons, grafting exciting new properties on proteins; for use as spectroscopic probes, UV-inducible crosslinkers, functional groups for bioorthogonal conjugations or posttranslational modifications *(1)*. Orthogonal ribosomes, on the other hand, provide a parallel translational machinery in *E. coli* that has lost its evolutionary constraints. Evolved variants of these ribosomes translate amber or quadruplet codons with enhanced efficiency *(2)*.

My lab is using these amazing tools to study biological processes, especially the dynamic properties of eukaryotic chromatin. Using genetically encoded UV-crosslinkers, we have identified a cascade of events that drives the condensation of chromosomes in mitosis *(3)*. Our results indicate that during early mitosis, phosphorylation of H3 S10 by Aurora B kinase controls the recruitment of the lysine deacetylase Hst2p to nucleosomes and thus the deacetylation of K16 on H4. As a consequence, the tail of H4 starts interacting with neighbouring nucleosomes, promoting chromatin condensation. This cascade of events provides a condensin-independent driving force of chromatin hypercondensation during mitosis.

We are also using bioorthogonal chemistries to label proteins with fluorophores. I will present recent developments towards an efficient strategy for the production of proteins labelled with FRET pairs *(4)* and how we use it to investigate protein conformational dynamics *(5)*.

References

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