

Abstract submitted for – ACA Hot Structures

This session will be comprised of talks describing exciting new results in structural biology. The majority of talks will be selected from submitted abstracts.

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Defining Allostery and Interactions Regulating Apoptosis-Inducing Factor

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DNA damage signaling and repair pathways can intersect with and impact cellular activity at sites far from damaged DNA, linking a cell's metabolic state to recovery of genomic integrity. Hyperactivation of the single strand break repair (SSBR) signaling enzyme poly(ADP-ribose) polymerase-1 (PARP-1) induces consumption of the metabolite NAD⁺ and induction of cell death by parthanatos. Release and nuclear accumulation of mitochondrial Apoptosis-Inducing Factor (AIF) is a key event in linking PARP-1 signaling to parthanatos. We are examining allosteric switching of AIF architecture as the molecular mechanism that regulates this transition. Using small-angle x-ray scattering (SAXS), X-ray crystallography, and molecular dynamics simulations, we have defined molecular pathways linking AIF's NADH active site to sites of allostery. We are furthermore extending these insights to understand how mitochondrial sorting factor CHCHD4 regulates higher-order oligomerization in AIF.