**Switchable protein interfaces for controlled assembly of biomaterials**

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**Introduction**

The fabrication of nanoscale devices requires architectural templates on which to position functional molecules in complex arrangements. Nature has met this challenge of nanofabrication by exploiting the remarkable ability of proteins to self-assemble into ordered and intricate nanostructures such as the icosahedral lattices of viral capsids. Protein assemblies in nature can also serve as inspiration to build novel templates with defined size and symmetry. Gaining switchable control over assembly and disassembly of these protein nanostructures will enable dynamic protein devices to be created that can sense and respond to specific signals. This presentation will highlight recent engineering of modular protein subunits whose assembly and disassembly can be regulated by specific enzymatic inputs to create novel biomaterials.

**Methods**

Exploiting post-translational modification systems enabled us to regulate the binding kinetics of dimeric coiled coils. The simple interaction motif of coiled coils is well-suited for the testing of protein design and assembly. Synthetic dimeric coiled coils with varying lengths were designed to include a protein kinase A (PKA) or cyclin-dependent kinase 2 (CDK2) recognition motifs in the protein-protein interface, and manufactured as peptides or recombinant proteins. Mass spectrometry was performed to examine *in vitro* phosphorylation of the coiled coils, and surface plasmon resonance was used to measure the modulation of electrostatic interactions present at the interface.

**Results and Discussion**

Coiled coils containing specific kinase recognition motif were efficiently phosphorylated by PKA or CDK2. The presence of a phosphoserine residue in the coiled coil interface significantly changed the binding kinetics of particular coiled coils. Notably, some peptide and protein pairs form significantly more stable coiled coils upon phosphorylation, with a dimer lifespan increased approximately ten-fold longer. The reversibility of the binding kinetics was also demonstrated by the addition of a phosphatase enzyme to remove phosphate groups from the interfaces. The switchable interfaces are now being applied to control the assembly and disassembly of protein and DNA nanostructures – including electrically conductive protein nanowires.

**Conclusion**

The ability to control protein interactions with post-translational modifications will enable the design of dynamic protein devices capable of sensing enzymatic activity in physiological environments. The switchable interfaces should also function *in vivo* for novel applications such as disassembly of nanocages for drug delivery and release upon modification and new types of biosensors.

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