

## SBS Seminar Announcement

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### Structural insights into the cyanobacterial heterocyst differentiation

#### Abstract

Initiation and pattern formation of heterocyst differentiation of cyanobacteria is tightly controlled by two master regulators: NtcA and HetR. Accumulation of 2-oxoglutarate (2-OG) in cyanobacteria constitutes the signal of nitrogen starvation. We solved three crystal structures of NtcA from the cyanobacterium *Anabaena*: the apo form, and two ligand bound forms in complex with either 2-OG or its analogue 2,2-difluoropentanedioic acid. All structures assemble as homodimers, with each subunit composed of an N-terminal effector-binding domain and a C-terminal DNA-binding domain connected by a long helix (C-helix). The 2-OG binds to the effector-binding domain at a pocket similar to that used by cAMP in catabolite activator protein, but with a different pattern. Comparative structural analysis reveals a putative signal transmission route upon 2-OG binding. A tighter coiled-coil conformation of the two C-helices induced by 2-OG is crucial to maintain the proper distance between the two DNA-binding helices for recognition. Activation of NtcA will trigger the expression of HetR, which is crucial for the development of heterocysts.

On the other hand, HetR is inactivated by a PatS-derived penta- or hexapeptide (RGSGR/PatS-5 or ERGSGR/PatS-6) in the vegetative cells, maintaining a regular pattern of heterocysts. Here we reported the 2.80 Å crystal structure of HetR complexed with a 21-bp palindromic DNA, 5'-gcgaggggtctaaccctcat. Each monomer of HetR consists of three domains: an N-terminal DNA-binding domain, a middle flap domain and a C-terminal hood domain. Two monomers cross each other to form an extensively entangled dimer, with the two helix-turn-helix motifs gripping the palindromic DNA. Structural analyses and DNA-binding assays indicated that the central 5'-gggn<sub>5</sub>ccc motif at the major grooves is indispensable for recognition by HetR. Moreover, we determined the crystal structure of the hood domains of HetR in complex with the inhibitory peptide PatS-6. Structural comparisons enable us to propose a putative mechanism of HetR inactivation by PatS-6.

**Wednesday, 04 February 2015 3.00pm to 4.00pm SBS Classroom 2 (SBS-01n-22)**

**Host: Asst/Prof Lu Lei**