

# Nitrogen Signaling: New Structure-Centered Discoveries

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The nitrogen flow affects all species in the biosphere and is a key, highly regulated process. Bacteria, cyanobacteria and plants play particularly important roles in the assimilation branch of this process. They have a dedicated system for nitrogen regulation, centered around the very widespread regulatory protein PII, which is under allosteric regulation by 2-oxoglutarate and nucleotides and by posttranslational modification of its flexible T-loop. My laboratory was central in clarifying how PII controls arginine accumulation in cyanobacteria (and plants) and how it carries out in cyanobacteria its gene regulatory roles via an adaptor protein, PipX, and a transcriptional regulator, NtcA. More recently, we have contributed to advance our understanding of this regulatory system. We will review here these advances, including: 1) DNA targeting of this regulatory system and ways of deactivation of the cyanobacterial transcriptional regulator NtcA; 2) additional regulatory functions of PipX when in complex with PII; 3) the structure of PipX in solution and the role of its C-terminal helix in PipX extra signaling; 4) extension of PII signaling to extreme salt environments, highlighting adaptation of signaling to high salinity; 5) structure of the transcriptional regulator AmtR of the industrial microorganism *Corynebacterium glutamicum*, as first step towards understanding PII regulation in this organism; 6) structure of posttranslationally modified PII from *E. coli* and the posttranslational modification cascade; and 7) expanding the PII regulatory universe via PipY, a pyridoxal-dependent protein. Our efforts have included collaborations with other laboratories (Drs. Bonete, Contreras, Neira and Pineda, in Alicante, Elche and Valencia) and have brought novel understanding of nitrogen regulation centered on protein PII across different phyla. Supported by grants from the Spanish Government (BFU2014-58229-P) and Valencian Government (PrometeoII/2014/029).