Poster Presentation

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The unique regulation of Fe-S cluster biogenesis in a Gram-positive bacterium

J. Santos[1, 2], S. Macedo-Ribeiro[1], P. Pereira[1]

[1]Instituto de Biologia Molecular e Celular, Universidade do Porto, Porto, Portugal, [2]Instituto de Ciências Biomédicas de Abel Salazar, Universidade do Porto, Porto, Portugal

The ubiquitous iron-sulfur (Fe-S) cluster-containing proteins are involved in countless biological routes and play crucial roles for the functioning of both prokaryotic and eukaryotic cells. The transcription factor IscR, of the helix–turn–helix family, was first implicated in repressing expression of the ISC (Iron Sulfur Cluster biogenesis) pathway and was shown to contain a [2Fe–2S] cluster. Promoters controlled by IscR belong to two distinct sequence groups [1] and the [2Fe-2S] cluster of IscR was shown to be essential for regulation of type-1 promoters (isc, yadR, yhgI), while apo-IscR is responsible for the regulation of type-2 promoters [2]. The proposed model for IscR action consists on a mechanism for Fe-S biogenesis fine-tuned by the cellular Fe-S cluster status. Despite recent advances in understanding the regulation of isc and suf operons by environmental signals, the features of IscR target-site recognition and the structural changes that alter the DNA binding specificity of IscR upon ligation of the [2Fe-2S] cluster are unknown. To understand how IscR recognizes two different DNA motifs, we solved the three-dimensional structures of free apo-IscR and of its complex with a type-2 target sequence, the hya promoter from the hydrogenase-1 operon [3]. These experimental models revealed some of the molecular details of the unusual environmentally modulated recognition of two distinct promoter consensus sequences by IscR, using a single predicted helix–turn–helix DNA binding motif. To our knowledge, IscR is the only transcription factor that is active in both the apo and holo-forms and which displays cofactor-mediated modulation of its DNA binding specificity. This work was funded by Fundação para a Ciência e a Tecnologia (Portugal) through grant PTDC/BBB-BEP/2127/2012 (EU-FEDER funding through COMPETE FCOMP-01-0124-FEDER-028116) and PhD fellowship SFRH/BD/66461/2009 to JAS.

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