Adventures with iron-sulfur cluster-containing regulators: elucidation of sensing mechanisms

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The ability to sense and respond to various key environmental cues is critical for the survival and adaptability of bacteria, including pathogens. The particular sensitivity of iron-sulfur (Fe-S) clusters has been exploited in nature through the evolution of multiple sensor-regulator proteins that utlilise an iron-sulfur (Fe-S) cluster as their sensory module. Upon detection of their particular analyte (via some kind of chemistry involving the cluster), they coordinate a global transcriptional response. The fragility and sensitivity of these Fe-S clusters makes studying such proteins difficult, and gaining insight of what they sense, and how the sense it and then transduce the signal to affect transcription, is a major challenge. Trying to understand how bacteria sense O_2 and iron levels[1,2], and the advent of oxidative or nitrosative stress[3-5], has been a major focus of my research group for nearly 20 years. Here, I will discuss some of the highly elegant sensing mechanisms employed by Fe-S cluster-containing regulators, along with some of the novel biophysical approaches[6] we have used to gain structural and functional insight. These highlight a remarkable variety in the way that nature has evolved to utilize these ubiquitous protein cofactors.

References:

[1]Crack et al (2017) *Proc. Natl. Acad. Sci. U.S.A*. **114**, E3215-E3223

[2]Pellicer Martinez et al., (2019) *eLife*. **8**, e47804

[3]Crack et al., (2020) *J. Am. Chem. Soc*. **142**, 5104 – 5116

[4]Kudhair et al., (2017) *Nat. Commun.* **8**, 2280

[5]Volbeda et al., (2017) *Nat. Commum*. **8**, 15052

[6]Crack and Le Brun (2021) *Coord. Chem. Rev.* **448**, 214171