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Colloque IVB : Signalisation et régulation cellulaire

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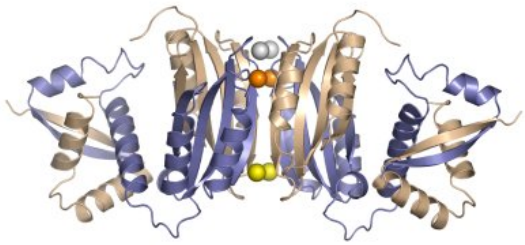
Structural basis of the nickel response in *Helicobacter pylori*

Helicobacter pylori is an Gram-negative bacterium that colonizes the human stomach and causes severe gastric diseases. Its survival in the human stomach depends on its adaptive response to acidity that is essential for its survival to low pH. Nickel is an essential element in *H. pylori* metabolism as it is a cofactor for the abundant urease enzyme, the predominant pH neutralizing effector Nickel-response regulation is known to occur via HpNikR, a DNA binding protein homologue of NikR of Escherichia coli. HpNikR controls the expression of both nickel activated and repressed genes.

We have determined the crystal structure of the full length HpNikR in the apo state at 2.05Å [1]. As expected, this structure displays the same fold as its homologues from *Escherichia coli* and *Pyroccocus horokoshii* albeit with subtle different surface properties and quaternary arrangement. We also present the crystal structures of HpNikR that were obtained by incubating the crystals in the presence of several Nickel concentrations as well as HpNikR mutants.

These structures show how nickel ions are incorporated within the tetrameric arrangement in three different Nickel binding sites. Together with the in vivo study of structure-based NikR mutants, nickel- [2] and DNA-binding studies, our results shed light on a fine sensing mechanism that allow the bacteria to sense nickel and trigger the transcription of several essential genes



[1] Dian, C., Schauer, K., Kapp, U., McSweeney, S.M., Labigne, A. and Terradot, L. (2006) Journal of Molecular Biology 361(4), 715-30.

[2] Fauquant, C., Diederix, R.E.M., Rodrigue, A., Dian, C., Kapp, U., Terradot, L., Mandrand-Berthelot, M.A. and Michaud-Soret, I. (2006) Biochimie 88(11), 1693-705.