

# The structural basis of nickel import in *Proteus mirabilis*

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Nickel ( $\text{Ni}^{2+}$ ) is an essential nutrient in various organisms across all kingdoms of life including plants, fungi, eubacteria, and archaeobacteria. As a cofactor,  $\text{Ni}^{2+}$  plays a key role in enzymes like [NiFe]-hydrogenase, nickel superoxide dismutase, CO-dehydrogenase, and urease, which are involved in vital biochemical reactions such as nitrogen fixation, energy production, and detoxification.

*Proteus mirabilis* is a pathogen that primarily affects the urinary system and is a common cause of catheter-associated urinary tract infections. The bacterium relies on  $\text{Ni}^{2+}$  to activate urease, an enzyme that facilitates the hydrolysis of urea to ammonia and bicarbonate. This reaction not only provides a nitrogen source but also plays a key role in the bacterium's pathogenicity.  $\text{Ni}^{2+}$  acquisition in *P. mirabilis* is facilitated by the high-affinity ABC-transporter system YntABCDE. After entering the periplasm, the substrate-binding protein YntA captures nickel and transports it to the transmembrane complex formed by the components YntB, YntC, YntD, and YntE for cellular uptake. Within the cytosol, the chaperone protein UreE, along with other accessory proteins, assists in the incorporation of nickel into urease, ensuring the proper activation of the enzyme.

The ability to acquire and utilise nickel for urease activation is crucial for the pathogenic potential of *P. mirabilis*, contributing to urinary stone formation, biofilm production, and tissue damage in the urinary tract. Understanding this mechanism provides insights into the role of metal ion transport in bacterial virulence and highlights potential therapeutic targets for managing *P. mirabilis*-associated infections. We determined the structures of YntA and YntBCDE using X-ray crystallography and cryogenic electron microscopy, laying the groundwork for unravelling the mechanism of nickel ion transport and its contribution to bacterial virulence, and guiding further investigation into transport function.