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Structure-based design of NAD+ analogues targeting bacterial NAD kinases, promising targets for new antibiotics

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Multi-drug resistance is a major public health problem that requires the urgent development of new antibiotics and therefore the identification of novel bacterial targets. The activity of nicotinamide adenine dinucleotide kinase, NADK, is essential in all bacteria tested so far, including many human pathogens that display antibiotic resistance leading to failure of current treatments. Inhibiting NADK is therefore a promising and innovative antibacterial strategy since there is currently no drug on the market targeting this enzyme. Through a drug design approach based on substrate-derived fragments, we have recently developed NAD^+-competitive inhibitors of NADKs, which displayed *in vivo* activity against *Staphylococcus aureus* or *Pseudomonas aeruginosa* in animal models of infection [1-3].

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