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► To cite this version:

Rahila Rahimova, Pauline Nogaret, Valérie Huteau, Clarisse Leseigneur, Muriel Gelin, et al.. Structure-based design of NAD⁺ analogues targeting bacterial NAD kinases, promising targets for new antibiotics. The Biochemistry Global Summit, 25th IUBMB Congress, 46th FEBS Congress, 15th PABMB Congress, Portuguese Biochemical Society (SPB); IUBMB; FEBS; PABMB, Jul 2022, Lisbon, Portugal. pp.24, 10.1002/2211-5463.13442 . hal-03854164

HAL Id: hal-03854164

<https://hal.science/hal-03854164v1>

Submitted on 24 Nov 2022

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

R. Rahimova^I, P. Nogaret^{II}, V. Huteau^{III}, C. Leseigneur^{IV}, M. Gelin^I, D. Clément^{III}, O. Dussurget^{IV}, G. Labesse^I, S. Pochet^{III}, A. Blanc-Potard^{II}, C. Lionne^I

^ICentre de Biologie Structurale (CBS), CNRS UMR 5048, INSERM U 1054, University of Montpellier, Montpellier, France, ^{II}Laboratory of Pathogen Host Interactions (LPHI), CNRS UMR 5235, University of Montpellier, Montpellier, France, ^{III}Institut Pasteur, Université de Paris, CNRS UMR3523, Unité de Chimie Biologique Epigénétique, Paris, France, ^{IV}Institut Pasteur, Université de Paris, Sorbonne Paris Cité, Unité de Recherche Yersinia, Paris, France

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].

Funding and supports: Agence Nationale de la Recherche (ANR-17-CE18-0011-02), Institut Pasteur, Centre National de la Recherche Scientifique (CNRS), Institut National de la Santé et de la Recherche Médicale (INSERM), University of Montpellier.

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