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Small-molecule inhibitors of bacterial metallo-β-lactamases

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List of publications

Publications from doctoral research period

(1) Tehrani, K. H. M. E., and Martin, N. I. (2018) β-lactam/β-lactamase inhibitor combinations: an update. *MedChemComm* **9**, 1439–1456.

(2) Tehrani, K. H. M. E., Brüchle, N. C., Wade, N., Mashayekhi, V., Pesce, D., van Haren, M., and I. Martin, N. (2020) Small molecule carboxylates inhibit metallo-β-lactamases and resensitize carbapenem-resistant bacteria to meropenem. *ACS Infectious Diseases,* **6**, 1366–1371.

(3) Tehrani, K. H. M. E., Fu, H., Brüchle, N. C., Mashayekhi, V., Prats Luján, A., van Haren, M. J., Poelarends, G. J., and Martin, N. I. (2020) Aminocarboxylic acids related to aspergillomarasmine A (AMA) and ethylenediamine-*N*,*N*'-disuccinic acid (EDDS) are strong zinc-binders and inhibitors of the metallo-beta-lactamase NDM-1. *Chemical Communications* **56**, 3047–3049.

(4) Tehrani, K. H. M. E., and Martin, N. I. (2017) Thiol-Containing Metallo-β-Lactamase Inhibitors Resensitize Resistant Gram-Negative Bacteria to Meropenem. *ACS Infectious Diseases* **3**, 711–717.

(5) Brouwer, M. S. M., Tehrani, K. H. M. E., Rapallini, M., Geurts, Y., Kant, A., Harders, F., Mashayekhi, V., Martin, N. I., Bossers, A., Mevius, D. J., Wit, B., and Veldman, K. T. (2019) Novel carbapenemases FLC-1 and IMI-2 encoded by an *Enterobacter cloacae* complex isolated from food products. *Antimicrobial Agents and Chemotherapy* **63**, e02338-18.

(6) t'Hart, P., Wood, T. M., Tehrani, K. H. M. E., Van Harten, R. M., Śleszyńska, M., Rentero Rebollo, I., Hendrickx, A. P. A., Willems, R. J. L., Breukink, E., and Martin, N. I. (2017) *De novo* identification of lipid II binding lipopeptides with antibacterial activity against vancomycin-resistant bacteria. *Chemical Science* **8**, 7991–7997.

(7) Bergstrom, A., Katko, A., Adkins, Z., Hill, J., Cheng, Z., Burnett, M., Yang, H., Aitha, M., Mehaffey, M. R., Brodbelt, J. S., Tehrani, K. H. M. E., Martin, N. I., Bonomo, R. A., Page, R. C., Tierney, D. L., Fast, W., Wright, G. D., and Crowder, M. W. (2018) Probing the Interaction of Aspergillomarasmine A with Metallo-β-lactamases NDM-1, VIM-2, and

IMP-7. *ACS Infectious Diseases* **4**, 135–145.

(8) Potel, C. M., Tehrani, K. H. M. E., Lemeer, S., Martin, N. I., Heck, A. J. R., and Lin, M.-H. (2018) A New Tool to Reveal Bacterial Signaling Mechanisms in Antibiotic Treatment and Resistance. *Molecular and Cellular Proteomics* **17**, 2496–2507.

(9) Tehrani, K. H. M. E., Wade, N., Mashayekhi, V., Brüchle, N. C., Voskuil, K., Jespers, W., Pesce, D., van Haren, M. J., van Westen, G. J. P., and Martin, N. I. (2020) Novel cephalosporins selectively inhibit the IMP type metallo-β-lactamases. *Manuscript in preparation*

Patents from doctoral research period

(1) 2019 Dutch Patent application filing; Title: "Prodrug metallo-beta-lactamase inhibitors"; Inventors: Martin, N. I., van Haren, M. J., Tehrani, K. H. M. E. Priority date: April 1, 2019.

(2) 2019 Dutch Patent application filing; Title: "A novel class of lipidated glycopeptide antibiotics with potent antibacterial activity"; Inventors: Martin, N. I., van Groesen, E., Tehrani, K. H. M. E., Wade, N. Priority date: September 24, 2019.

Publications from previous research works

(1) Tehrani, K. H. M. E., Mashayekhi, V., Azerang, P., Sardari, S., Kobarfard, F., and Rostamizadeh, K. (2014) Synthesis and antimycobacterial activity of novel thiadiazolylhydrazones of 1-substituted indole-3-carboxaldehydes. *Chemical Biology and Drug Design* **83**, 224–236.

(2) Tehrani, K. H. M. E., Azerang, P., Esfahani Zadeh, M., Mashayekhi, V., Kobarfard, F., and Sardari, S. (2013) One Pot Synthesis and Biological Activity Evaluation of Novel Schiff Bases Derived from 2-Hydrazinyl-1,3,4-thiadiazole. *Chemical and Pharmaceutical Bulletin* **61**, 160–166.

(3) Mashayekhi, V., Tehrani, K. H. M. E., Amidi, S., and Kobarfard, F. (2013) Synthesis of Novel Indole Hydrazone Derivatives and Evaluation of Their Antiplatelet Aggregation Activity. *Chemical and Pharmaceutical Bulletin* **61**, 144–150.

Curriculum Vitae

Kamaleddin H.M.E. Tehrani was born in 30 July 1987 in Tehran, Iran. He studied pharmacy in Shahid Beheshti university of medical sciences and graduated with Pharm.D. degree in 2011. The subject of his thesis was synthesis of novel hydrazone derivatives with antimycobacterial activity. He continued his research activities in collaboration with Professor Farzad Kobarfard and Dr. Shohreh Mohebbi until he joined Professor Nathaniel Martin's group in September 2014 as a PhD student. The primary focus of his research since then has been development of novel inhibitors of bacterial metallo-β-lactamases. As a PhD researcher he acquired a range of practical skills including organic synthesis, spectral characterization of organic compounds using NMR and LCMS, HPLC analysis (analytical and preparative), thermodynamic profiling of binding interactions using isothermal titration calorimetry, biochemical enzyme kinetics and inhibition assays, and antimicrobial activity assays. During this time, he supervised 4 bachelor and master projects leading to a number of publications and manuscripts under preparation. His research efforts to date have resulted in 2 patents, 21 papers (8 from PhD, 13 from previous research positions), and 6 manuscripts currently submitted or under preparation.

Afterword

No clouds, no full moon, not much light pollution. Sky is full of stars. It is the summer of 2006 and I am about to sleep on the rooftop of my childhood house in Shiraz. My father comes upstairs unexpectedly and sits down in front of me. “You wanted to talk to me earlier today. Here I am. What is it about?” I tell him how I picture my future, and what my goals and ambitions are. I tell him that I like to study abroad to become more scientifically capable and competent to serve my country the best I can. Then he starts. Like life in Shiraz, his talking is slow, with long pauses between his words. “Whatever your plan is, you should look at your life with a global perspective. Even better with a cosmic perspective. And wherever you go to live and study, be a curious student of their culture. Try their food, learn their social norms, their history and their way of life”. Now I’m in Utrecht lying in bed in my apartment, watching the old George Carlin on Youtube. He reminds me of my father, not only because he is unapologetically honest and doesn’t try to protect anyone’s feelings, but also because of what he says about national and ethnic pride: “... pride should be reserved for what you achieve or attain on your own, not because of something that happened by the accident of birth”. For someone who chose to make his world as big as the world allows him to, someone who feels he belongs to everywhere and nowhere, someone who lives between two fears of the unknown, someone who leaves a lot behind to travel light, moments of hesitation and self-doubt are frequent. In such moments I think about Carlin’s words and that slow conversation with my father under a sky full of stars.