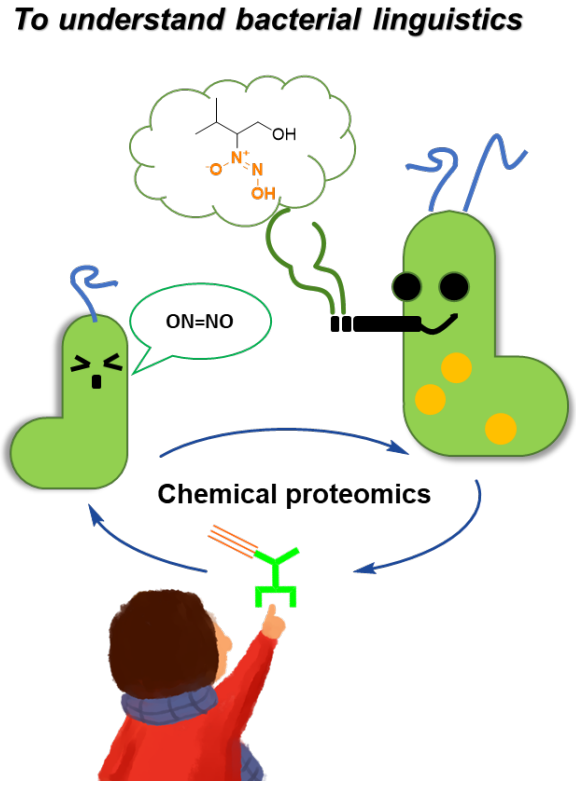
A chemical proteomic approach to unravel the proteome centred around valdiazen

Jiajun Ren,[1] Anugraha Mathew,[2] Leo Eberl,[2] Karl Gademann[1]

[1]Department of Chemistry, University of Zurich, Winterthurerstrasse 190, Zurich, Switzerland
[2]Department of Plant and Microbial Biology, University of Zurich, Zollikerstrasse 107, Zurich, Switzerland

jiajun.ren@chem.uzh.ch

Quorum sensing refers to a special signalling pathway that regulates genes based on the local population density of microbes.[1] Such a cell-density dependent pathway is often involved in complex phenomena in bacteria including biofilm formation, virulence factor regulation, and cross-species communication.[1] The recent discovery of valdiazen marks the first example of a diazeniumdiolate-containing quorum-sensing signal.[2] Such a volatile and heteroatom-packed signal controls the expression of over 100 genes including those involved in the biosynthesis of an antifungal agent, (–)-fragin, in *Burkholderia cenocepacia* H111.[2] In addition, similar signals were shown to be involved in bacterial plant diseases.[3] Building upon the previous genetic and transcriptomic studies on valdiazen, a chemical proteomic strategy was pursued to address the fundamental question—What is the receptor of valdiazen?



This study provides some key challenges and discoveries while working with diazeniumdiolates as a chemical probe in activity-based pulldown experiments.

[1] N. A. Whitehead, A. M. L. Barnard, H. Slater, N. J. L. Simpson and G. P. C. Salmond, *Fems Microbiol Rev*, 2001, **25**, 365–404.
[2] C. Jenul, S. Sieber, C. Daeppen, A. Mathew, M. Lardi, G. Pessi, D. Hoepfner, M. Neuburger, A. Linden, K. Gademann and L. Eberl, *Nat Commun*, 2018, **9**, 1297.
[3] S. Sieber, A. Mathew, C. Jenul, T. Kohler, M. Bär, V. J. Carrión, F. M. Cazorla, U. Stalder, Y.-C. Hsieh, L. Bigler, L. Eberl and K. Gademann, *Sci Adv*, 2021, **7**, 2293.