Abstract:
Cells must control enzyme expression in their metabolic network, because high enzyme levels are costly and low enzyme levels can limit metabolic flux. In my talk, I will show how we created a CRISPR interference library to downregulate the expression of all 1515 proteins in the metabolic network of E. coli. We have studied the complete CRISPRi library with a pooled approach and measured the metabolome and the proteome of 304 CRISPRi strains. I will show how we integrate these multi-omics data to infer feedback mechanisms and to identify substrate-enzyme relationships. In the second part of the talk, I will show how we combine genomics, proteomics, and metabolomics to explore the mechanisms of antibiotic action in E. coli. For example, we measured the antibiotic resistance of 15,120 E. coli mutants, each with a single amino acid change in one of 346 essential proteins. Resistance mutations in essential genes were drug-specific and primarily affected metabolic enzymes. Most mutations that conferred resistance to the beta-lactam antibiotic carbenicillin occurred in genes associated with purine nucleotide biosynthesis, and I will show how we identified the mechanism of purine-mediated resistance.

CV:
Hannes Link received a Diploma in Chemical Engineering from the Technical University Munich in 2005 and a PhD in Biochemical Engineering from the same institution in 2009. He worked as a Postdoctoral Associate at the Institute of Molecular Systems Biology in Zurich (2010-2015) and as an Independent Research Group Leader at the Max Planck Institute for Terrestrial Microbiology in Marburg (2015-2020). Since 2020 he is Professor at the Interfaculty Institute of Microbiology and Infection Medicine of the University of Tübingen.