Streptococcus mutans is a human pathogen highly adapted to the oral cavity and a key component of dental plaque. It has an important role in polymicrobial biofilm diseases like caries, periodontitis and endocarditis, all of which are correlated with systemic non-communicable diseases (arthritis, cardiovascular disease). *S. mutans* forms strong biofilms, is tolerant to low pH, and has a sophisticated quorum sensing system for interspecies and intraspecies communication. An exceptionally high rate of horizontal gene transfer is reflected in its genome architecture and the open pan genome of this species [1,2].

Since classical antibiotics act mainly against cells growing in planktonic culture, a new antibacterial screen was established using membrane damage of *S. mutans* biofilms as a sensitive read-out. Carolacton, a secondary metabolite from the Myxobacterium *Sorangium cellulosum*, was discovered to damage biofilm viability of *S. mutans* [3]. It can be incorporated into dental filling material to prevent secondary caries [4]. The mode of action of Carolacton was investigated using a systems biology approach, including culture density resolved transcriptome and proteome analysis, knockout of genes, reverse engineering of regulatory networks, and mathematical modeling. A one-component membrane bound serine-threonine protein kinase, PknB, confers susceptibility to carolacton, resulting in changes in the quorum sensing network, mutacin synthesis, autolysis, acid tolerance and cell division [5]. The underlying transcriptional regulatory network was reconstructed, and the effect of carolacton on the interactome was modeled and experimentally confirmed [6]. Population heterogeneity is an intrinsic trait of the *S. mutans* quorum sensing system [7]. It will be exploited for the development of pathoblockers using fluorescent reporters for autolysin genes.