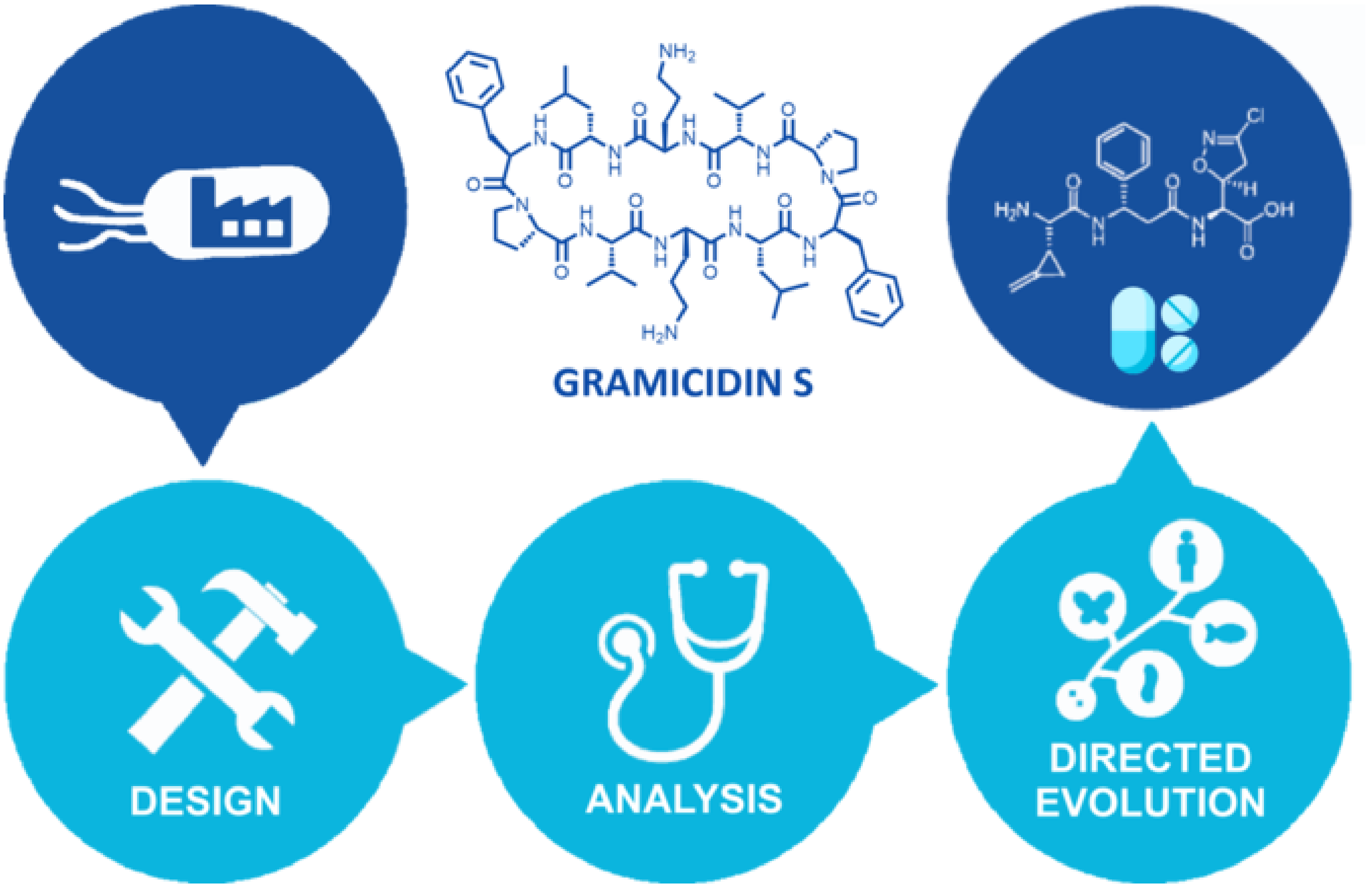

Biosynthetic pathways for natural products have explored a vast chemical ‘space’ during evolution but synthetic biologists seek to expand this space even further. Modular architectures of biosynthetic pathways seem to favor evolutionary diversification – they also invite synthetic biologists to reshuffle and engineer their parts into non-natural arrangements. Structurally tailored natural products resulting from such efforts could potentially benefit medicinal chemistry since natural products often show biological activities. While the pioneering works of natural product engineers have afforded many promising examples of ‘unnatural natural products’, they have also highlighted a need for more straightforward and reliable engineering tools.

Our group investigates the modular pathways biosynthesizing nonribosomal peptides, such as the antibiotics gramicidin S and penicillin or the immunosuppressant cyclosporin. We aim to develop more robust methods for repurposing nonribosomal peptide synthetases (NRPSs). Our efforts build on mechanistic studies of engineered synthetases, novel high throughput screening methods and their application in laboratory evolution experiments. Directed evolution recapitulates the evolutionary process described by Charles Darwin in a targeted and accelerated fashion and may allow creation of artificial peptide synthetases rivaling the catalytic prowess of natural enzymes.

Listen to Hajo's interview with Wirkstoffradio (German)

or the presentation "Wege aus der Antibiotikakrise mit synthetischer Biologie" (German)