Peptide synthesis away from the central dogma

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Ribosomes synthesize all proteins, but they are not the only important cellular peptide-bond making megaenzymes. Nonribosomal peptide synthetases (NRPSs) are also true macromolecular machines, having modular assembly-line logic, a complex catalytic cycle, moving parts and many active sites. NRPS products include classics therapeutics (penicillin, cyclosporin, and modern billion-dollar antibiotics (daptomycin) and anti-cancer agents (dactinomycin). We have performed structural and functional analyses of components of the NRPS systems responsible for the syntheses of the antibiotic gramicidin, the siderophore bacillibactin and the anti-algae bacillamide. I will discuss results from these studies and the insight they provide into the superdomain and supermodular architecture, conformational changes and mechanisms of tailoring NRPSs use to synthesize their important bio-active products.