Natural products are a major source of bioactive molecules that find applications in agriculture, nutrition and medicine. Animals, plants and microorganisms are known to produce a large variety of molecules through precisely programmed biosynthetic pathways. Polyketide compounds represent a large family of natural products which exhibit diverse biological functions such as antitumor, anti-inflammatory, antimicrobial, antiviral and anti-cholesterol activities. Polyketides are synthesized by a group of enzymes called polyketide synthases (PKSs). PKSs are classified into types I, II and III according to different structures and mechanisms of these enzymes. Type I PKSs are giant modular enzymes that consist of a series of catalytic domains [1], while type II PKSs are discrete small enzymes that form multi-enzyme complexes to synthesize aromatic polyketides [2]. Type III PKSs are single enzymes that form homodimers, which contain a single active site in each monomer to catalyze the priming, extension, and cyclization reactions iteratively [3]. Understanding and engineering of PKSs and associated enzymes will allow us to create pharmaceutically important molecules. Three parts of my dissertation research will be included in my dissertation. First, we identified a silent chromomycins gene cluster in Streptomyces reesei scleroticus, and turned the chromomycins non-producer strain to a high producer by engineering the two regulatory genes. Second, we identified the spirolaxine producing gene in Sporotrichum laxum, and synthesized the alkylresorcinols, the precursor of spirolaxine, in E. coli. Third, we identified a type I non-reducing PKS and engineered a synthetic pathway to produce pharmaceutically valuable compounds emodin and endocrocin.