AtoSC two-component signal transductiom system in *Escherichia coli* constitutes sensor kinase AtoS and response regulator AtoC. AtoSC signaling is induced by acetoacetate, spermidine as well as human secretions and extracellular calcium towards AtoS autophosphorylation and subsequently to AtoC phosphorylation towards the regulation of its downstream targets. AtoSC is a key regulator of central bacterial mechanisms including short-chain fatty acid catabolism through the regulation of *atoDAEB* operon, chemotaxis, motility, adaptation, poly-(R)-3-hydroxybutyrate (cPHB) biosynthesis, as well as mechanisms affecting antibiotics resistance, establishing its homeostatic role in bacterial physiology. During the present Ph.D. Thesis, the AtoSC signaling mechanism was further elucidated, through studies of additional interactions between its constituents and the regulatory roles of AtoC N-terminal domain in combination with its inducers, towards the regulation of its downstream targets *atoDAEB* operon and cPHB biosynthesis. Furthermore, new AtoSC inducers were identified that are sensed during the signal transduction. Considering the key role of AtoSC in pathogenic and symbiotic processes and AtoSC expression in pathogenic *E. coli*, three inhibitors of AtoSC signaling (Closantel, RWJ-49815 and TNP-ATP) were indentified. They inhibit AtoS autophosphorylation and AtoS to AtoC phopshotransfer. The consequences of this inhibition on physiological processes that are regulated by AtoSC, establish AtoSC as a target for antibacterial agents. AtoSC regulates cPHB biosynthesis and intracellular distribution, through *atoDAEB* operon upon its established inducers. Furthermore, it is capable to regulate cPHB through additional mechanisms, attributed to its constituents separately in the absence or presence of inducers, with AtoC being the most effective. Interplay between β-oxidation and fatty acid biosynthesis including AtoSC participation regulates cPHB biosynthesis in *E. coli*. AtoSC up-regulates the biosynthesis and accumulation of storage polyhydroxyalkanoates, PHB and P(3HB-co-3HV), in recombinant *phaCAB*$^{+}$ *E. coli*, expressing the PhaCAB enzymes from *Alcaligens eutrophus.* The acetoacetate-induced AtoSC optimizes the biopolymers production quantitatively, the cellular biopolymer content and qualitatively, as well as enhances the HV incorporation in the copolymer P(3HB-co-3HV). AtoSC regulates PHB and P(3HB-co-3HV) biosynthesis through *atoDAEB* operon as well as additional processes, attributed to its constituents separately in the absence or presence of inducers, with AtoC being the most effective. Interplay between β-oxidation and fatty acid biosynthesis including AtoSC participation regulates polyhydroxyalkanoate biosynthesis in recombinant *phaCAB*$^{+}$ *E. coli*.