Erwinia amylovora is the causal agent of the devastating disease fire blight of apple and pear, and pathogenesis includes primary infection of flowers and shoots followed by further systemic spread through host trees. We have shown that cyclic di-GMP (c-di-GMP) plays a critical role in regulating transitions between type III secretion and biofilm formation during E. amylovora pathogenesis. Intracellular levels of c-di-GMP are modulated by diguanylate cyclase (DGC) enzymes that synthesize c-di-GMP and phosphodiesterase (PDE) enzymes that degrade c-di-GMP. The E. amylovora genome encodes five diguanylate cyclase (DGC) enzymes that synthesize c-di-GMP and three phosphodiesterase (PDE) enzymes that degrade c-di-GMP. We have demonstrated that pdeA and pdeC are the two most active phosphodiesterases in virulence regulation in E. amylovora Ea1189, and that either pdeA or pdeC exert a strong regulatory effect on amylovoran expopolysaccharide synthesis and biofilm formation. In contrast, the deletion of two or more pde genes was required to affect motility. When all three pde genes were deleted, an autoaggregation phenotype and filamentous growth habit was observed. Results of a suppressor screen demonstrated that eagA, encoding a peptidoglycan hydrolase, suppressed the autoaggregation phenotype. EagA was also shown to regulate the Znu zinc uptake system in response to c-di-GMP, and we are currently studying the role of zinc in E. amylovora virulence. Hfq-dependent small RNAs including ArcZ and RprA also regulate specific virulence determinants in E. amylovora, and we have recently shown that ArcZ is a direct post-transcriptional regulator of the flhDC operon. Two other small RNAs, OmrAB and RmaA, also regulate flagellar motility by acting primarily on the master regulator, FlhD, but also through additional factors.