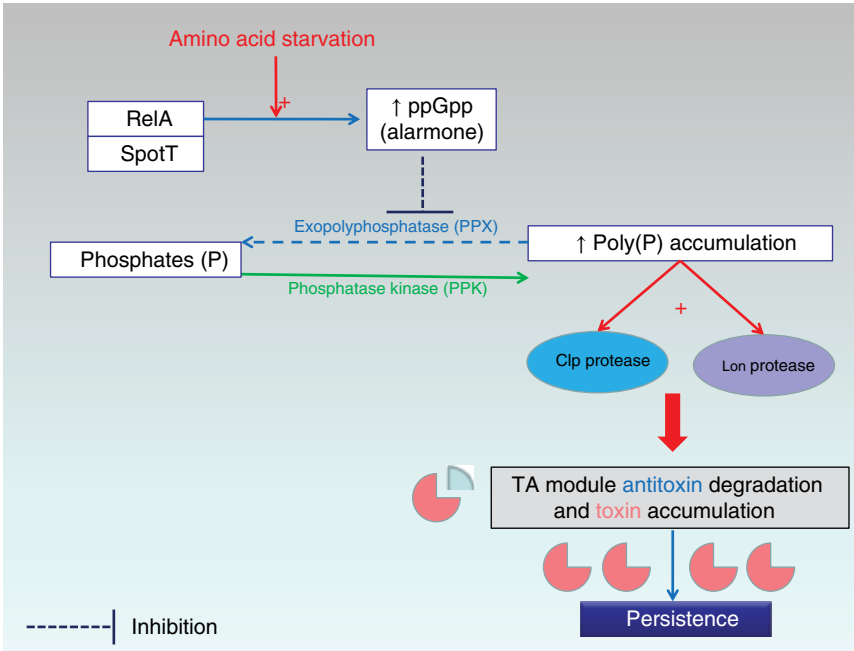


**Figure 9.1** Interrelation between activation of the toxin–antitoxin (TA) system by nutrient starvation, persister formation, and antibiotic resistance (or tolerance). Examples of toxins in TA modules: couple cell division (CcdB), ParE, pneumococcal epsilon-zeta (pezT), *Escherichia* zeta toxin (ezeTA), death on cure (Doc), HokB, MqsR (motility quorum-sensing regulator), MosT (TA module, within the integrative and conjugative element SXT), MazF, RelE, VapC, HipA.

### 9.2.5 Small Colony Variants (SCVs), Persistence (Persisters), and Toxin–Antitoxin (TA) Systems

#### 9.2.5.1 Small Colony Variants (SCVs)

SCVs are characterized by impaired growth, with downregulation of genes involved in metabolism and virulence, whereas genes important for persistence and biofilm formation are upregulated (Mirani et al. 2015). Rugose SCVs of *S. aureus* have increased expression of the *pel* and *psl* polysaccharide gene clusters, decreased expression of motility functions, and a defect in growth with some amino acid and tricarboxylic acid cycle intermediates as sole carbon sources (Starkey et al. 2009). An extensive inflammatory response was also stimulated in *S. aureus*, causing significant damage to the surrounding host tissue, promoting phagocytic evasion, and stimulating neutrophil reactive oxygen species (ROS) production (Pestrak et al. 2018). Rugose SCVs also elicited a reduced chemokine response from polarized airway epithelium cells compared with wild-type strains (Starkey et al. 2009). Bacterial aggregation and