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Stress Response in the Model Organism *Escherichia Coli*: Relevance for Antibiotic Resistance and Biofilm Formation

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Abstract—*The stress response enables bacterial populations to survive extreme perturbations in the environment. However, the control of this phenomenon remains poorly understood. Cross-stress protection strongly suggests the presence of central proteins that control the diverse stress responses. In this work, Escherichia coli was used as model to understand the bacterial stress response. A network (SR-PPIN) was generated to represent this condition by integrating the protein-protein interactions of differentially expressed genes in eight stress conditions of pH, temperature, and antibiotics with relevant Gene Ontology terms. The differentially expressed genes were mined from publicly available datasets present in GEO database, protein interactions were obtained from String, network generation was done using Cytoscape3.2.2 and annotation was carried out using DAVID. Networks were also generated for the gene ontology terms antibiotic resistance and biofilm formation in order to study their overlap with stress response. Topological analysis identified 24 proteins central to the SR-PPIN. While the network generated was almost three-fourths of the entire proteome, its central nodes were unique. The well-documented role of 16 central proteins in stress-related phenomena indicated a central control of the response. Cluster analysis of the generated network implicated RNA-binding, flagellar assembly, ABC transporters, and DNA repair as important processes during response to stress. Pathway analysis showed crosstalk of Two Component Systems (TCS) with metabolic processes, oxidative phosphorylation, and ABC transporters. Thus, TCS are likely to orchestrate the stress response. Validation of the results by analysis of cross-stress protection dataset network generated from an independent dataset showed that this network had central nodes identical to the stress response network. The proteins driving the progression of the stress response to antibiotic resistance and biofilm formation were identified and its model was constructed. Discerning central proteins and processes in this model organism has future implications for combating antibiotic tolerance and multidrug resistance.*