Starvation-Stress Response (SSR) of *Salmonella typhimurium*

*Gene Expression and Survival during Nutrient Starvation*

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1. INTRODUCTION

The environments that many pathogenic bacteria encounter as they cycle from their host organism(s) to the external aquatic or terrestrial environments commonly share one general characteristic: they are frequently limiting for bacterial growth (Koch, 1971). A wide variety of environmental factors can play an important role in restricting bacterial growth, e.g., pH, osmolarity, and the availabilities of oxygen as well as essential nutrients (Tempest *et al*., 1983; Roszak and Colwell, 1987). The availability of essential nutrients such as phosphate (P), carbon (C), or nitrogen (N) in these environments is of particular importance in limiting bacterial growth (Harder and Dijkhuizen, 1983). As a consequence, non-spore-forming bacteria, e.g., *Salmonella*, frequently undergo drastic metabolic readjustments in an effort to survive until more favorable conditions are encountered.
Salmonella are common agents of gastrointestinal-based diseases in humans, e.g., gastroenteritis and typhoid fever. As many as 40,000 cases are reported each year resulting in some 500 deaths and huge financial costs; and even so this is likely to represent only a small percentage of actual salmonelloses each year. In humans, the organism is most commonly acquired following ingestion of contaminated food or water, e.g., poultry products. Salmonella typhimurium causes a normally self-limiting “food poisoning” or gastroenteritis in humans, remaining localized within the small intestine. However, in immunosuppressed patients, such as individuals with AIDS, the organism can invade deeper tissue, enter the reticuloendothelial system, and cause a serious systemic disease (Finlay and Falkow, 1988, 1989). The enormous medical and financial burden of salmonelloses has stimulated interest in not only determining how these organisms cause disease, but also how they survive outside their hosts while maintaining virulence potential.

Salmonella, as a consequence of its life-style, endures extended periods of nutrient deprivation in natural aquatic and terrestrial environments while retaining its pathogenic potential. Even within the host, many of the microenvironments this organism encounters may be nutrient limiting, e.g., the human gastrointestinal tract (Koch, 1971). Therefore, the ability of Salmonella, as well as other enteric pathogens, to survive lengthy periods of nutrient deprivation can have a significant influence on virulence, and epidemiology of salmonellosis. In fact, recent evidence from several laboratories implicates a number of environmental factors, including nutrient deprivation, osmolarity, and anaerobiosis, in modulating the expression of Salmonella virulence factors (Miller et al., 1989; Fang et al., 1991; Galán and Curtiss, 1990; Ernst et al., 1990; Lee and Falkow, 1990). This implies an empirical relationship between survival in nature and survival in the host organism.

Relatively little is known about how S. typhimurium, or other enteric pathogens, survives prolonged nutrient starvation. Over the last several years we have addressed this problem by identifying and characterizing genes/proteins required for survival during nutrient starvation in order to define the complex genetic and physiological events involved in this process.

2. ALTERATIONS OF CELLULAR CONSTITUENTS DURING NUTRIENT STARVATION IN SALMONELLA

Druilhet and Sobek (1984) reported that a number of cell components are degraded during starvation of Salmonella enteritidis. Chief among these is the degradation of cellular RNA and proteins. This is in agreement with previous and subsequent studies advocating a role for peptidases and proteases in starvation-survival (reviewed in Miller, 1975, 1987; Reeve et al., 1984; Laz-