7.18C: The Stringent Response

The stringent response is a stress response that occurs in bacteria in reaction to amino-acid starvation or other stress conditions.

LEARNING OBJECTIVES

Explain the function of the alarmone (p)ppGpp in the stringent response

KEY TAKEAWAYS

Key Points

- The stringent response is signaled by the alarmone (p)ppGpp.
- In *Escherichia coli*, (p)ppGpp production is mediated by the ribosomal protein L11 and the ribosome-associated protein RelA.
- In other bacteria, stringent response is mediated by a variety of RelA/SpoT Homologue (RSH) proteins. Some only have synthetic, hydrolytic, or both (Rel) activities.

Key Terms

- **stringent response**: The stringent response, also called stringent control, is a stress response that occurs in bacteria and plant chloroplasts in reaction to amino-acid starvation, fatty acid limitation, iron limitation, heat shock, and other stress conditions.
• **alarmone**: Alarmone is an intracellular signal molecule that is produced due to harsh environmental factors.

• **amino-acid starvation**: The amino acid response pathway is triggered by a shortage of any essential amino acid.

The stringent response, also called stringent control, is a stress response that occurs in bacteria and plant chloroplasts in reaction to amino-acid starvation, fatty acid limitation, iron limitation, heat shock, and other stress conditions. The stringent response is signaled by the alarmone (p)ppGpp and modulating transcription of up to 1/3 of all genes in the cell. This in turn causes the cell to divert resources away from growth and division and toward amino acid synthesis in order to promote survival until nutrient conditions improve.

In *Escherichia coli*, (p)ppGpp production is mediated by the ribosomal protein L11. The ribosome-associated protein RelA with the A-site bound deacylated tRNA is the ultimate inducer. RelA converts GTP and ATP into pppGpp by adding the pyrophosphate from ATP onto the 3' carbon of the ribose in GTP releasing AMP. pppGpp is converted to ppGpp by the gpp gene product, releasing Pi. ppGpp is converted to GDP by the spoT gene product, releasing pyrophosphate (PPi). GDP is converted to GTP by the ndk gene product. Nucleoside triphosphate (NTP) provides the Pi. It is converted to nucleoside diphosphate (NDP).

In other bacteria, stringent response is mediated by a variety of RelA/SpoT Homologue (RSH) proteins, with some having only synthetic, hydrolytic, or both (Rel) activities. The disable of stringent response by distruption of relA and spoT in *Pseudomonas aeruginosa*, produces infectious cells and biofilms that have nutrient limitations. They are more susceptible to antibiotics.

During the stringent response, (p)ppGpp accumulation affects the resource-consuming cell processes replication, transcription, and translation. (p)ppGpp is thought to bind RNA polymerase and alter the transcriptional profile, decreasing the synthesis of translational machinery (such as rRNA and tRNA), and increasing the transcription of biosynthetic genes. Additionally, the initiation of new rounds of replication is inhibited and the cell cycle arrests until nutrient conditions improve. Translational GTP involved in protein biosynthesis are also affected by ppGpp, with Initiation Factor 2 (IF2) being the main target.

Chemical reaction catalyzed by RelA: \[\text{ATP} + \text{GTP} \rightarrow \text{AMP} + \text{pppGpp} \]

Chemical reaction catalyzed by SpoT: \[\text{ppGpp} \rightarrow \text{GDP} + \text{PPi}\]