Editorial

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Ribosome Hibernation: Tolerance to Antibiotics

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In bacteria, ribosomes play an important role in protein synthesis mainly at the translational level. Several environmental factors also contribute to determine the translational activity of a bacterial cell. In adverse conditions such as stress or lack of nutrition the ribosomes reduces its translational activity by a process termed as ribosomal hibernation. It includes the formation of functionally inactive 100S ribosome by the dimerization of two 70S ribosomes [1]. The 100S ribosome formation involves the ribosome modulation factor (RMF) and hibernation promoting factors (HPF). A study conducted by Yoshida and co-workers studied in detail the role of RMF and found that it inactivates the ribosomes by covering the peptidyl transferase centre and entrance of peptide exit tunnel [2]. Similarly, HPF also promotes the dimerization of the ribosomes. A study conducted by Ueta et al. evaluated the process of 100S ribosome formation and pointed out that RMF contributes in 90S immature ribosome genesis and binding of HPF convert this 90S ribosome into mature 100S ribosome [3]. In gram negative and gram positive bacteria the mechanism of dimerization varies. In gram negative bacteria both the factors RMF and HPF play a prominent role in dimerization whereas in gram positive bacteria studies have shown the lack of RMF participation in process of hibernation formation. The presence of single long HPF having the C terminus extension is known to promote the ribosomal dimerization in stressful conditions. A study conducted by Basu and coworkers on dimerization of the ribosomes in *Staphylococcus aureus* found that the ribosome hibernation promoted the Staphylococcal survival as well as suggested that the disruption of the 100S ribosome may lead to the increase in the efficacy of the conventional antibiotic treatment [4].

Studies have shown that the hibernation of ribosomes leads to the development of tolerance to antibiotics. A study conducted by Willamson and co-workers on heterogeneity in *Pseudomonas aeruginosa* biofilms identified the presence of ribosome hibernation factors including RMF, PA4463 genes in slow dividing bottom cells. The authors also demonstrated the top active dividing cells are more susceptible to antibiotics such as tobramycin and ciprofloxacin [5]. A study which has demonstrated the dimerization of ribosome promotes the antibiotic tolerance is conducted by McKay et al. and found that the presence of HPF is required for stationary phase cultures of *Listeria monocytogenes* to develop tolerance to aminoglycosides. The authors concluded that hibernation is one of the important factors for the energy conservation, decreases protein production leading to reduction in metabolic activities of the bacterial cell. The overall effect leads to down regulation of protein motive force thereby blocking import of aminoglycosides into the cell and thus preventing its bactericidal affectivity [6].

To conclude several bacteria, mainly those causing chronic infections and those bacteria which have ability to form biofilms, might employ the formation of 100S ribosomes aided by the hibernation promoting factors to avoid killing by antibiotics. We stress the need of the hour for the development of newer strategies that will be having an ability to prevent the dimerization of the ribosomes promoting the efficacy of antibacterial activity of the antibiotics, leading to the reduction of bacterial drug resistance.

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