Nutrient-responsive bistable switch governs the flagellar regulon in *Salmonella typhimurium*

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***Short Abstract* —YdiV is responsible for the repression of flagellar synthesis in *Salmonella enterica* serovar Typhimurium which acts as an anti-$FlhD_4C_2$ factor. Moreover, FliZ-dependent activation of P_{class2} promoters is more pronounced in low nutrient condition and is achieved by repression of the ydiV gene by FliZ. YdiV expression is enhanced in poor media and greatly reduced in rich media. Thus, FliZ and YdiV, in poor media, form an overall positive feedback loop which results in a bistable motility phenotype. This study aims to characterize the extent of bistability within the flagellar network in *Salmonella enterica* serovar Typhimurium.**

I. Background

Availability of nutrients in the cellular environment plays a key role in switching between motile or sessile phenotypes. However, the response to nutritional cues could be very different even in closely related species. For example, E. coli upregulates flagellar synthesis under low-nutrient conditions whereas *Salmonella enterica* serovar Typhimurium downregulates flagellar synthesis under low-nutrient condition [1,2,3]. YdiV, an anti-$FlhD_4C_2$ factor, is responsible for nutritional control of flagellar gene in *Salmonella*. YdiV expression is enhanced in poor media and greatly reduced in rich media. Also, activation of class 2 genes by FliZ is achieved by repression of YdiV by FliZ [4]. Thus, FliZ and YdiV, in poor media, form an overall positive feedback loop which results in a bistable motility phenotype.

II. Results

To investigate the effects of nutrients on motility phenotype, cells were grown in Minimal media supplemented with 0.2% glucose and various concentration of yeast extract (YE). The percentages of motile and sessile cells were determined using microscopy. It was observed that wild type cells are completely sessile when grown with no YE and completely motile when grown with 2% YE. Also, the percentage of motile and sessile cells can be tuned with the amount of YE in the media.

Quantification of gene products at single cell resolution using flow cytometry revealed heterogeneity of the underlying genetic circuitry and validated the existence of two stable, ON and OFF, states. Simultaneous measurement of a representative class 2 gene and ydiV expression revealed that ydiV expression decreases with increasing nutirient concentration and is higher in OFF state compared to ON state. Moreover, flagellar gene circuit displays non-linear kinetics and hysteresis with YdiV providing the threshold to prevent the feedback loop from activating all the cells.

III. Conclusion

These results reflect that microbial strategy is to conserve resources and energy during challenging condition by committing only a portion of population to motility. These observations reinforce the view that bacteria vary the phenotypes as a form of bet-hedging strategy [5]. The architecture of underlying genetic circuit enables them to achieve this goal.

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