Probing cellular heterogeneity with RNA Fluorescence in situ Hybridization

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ABSTRACT

Phenotypic heterogeneity refers to variation exhibited by isogenic population of cells in homogeneous environments. This phenomenon is exemplified in bacteria as the formation of persisters and existence of subpopulations especially on exposure to stressful conditions. The implications of this phenomenon are relevant to Biotechnology as is the case with inducible expression systems for large scale protein production. Population studies fail to identify and probe this phenomenon which demands sensitive single cell studies to detect variability.In this study we attempt to investigate transcriptional heterogeneity in the well studied Arabinose Operon and its correlation to previously established protein expression level variability via RNA Fluorescence *in situ* hybridization. The study showed surprising results with population at the lowest induction exhibiting higher mRNA content than the population at the highest induction. These results suggest that if proven correct RNA level heterogeneity among cells may not represent the observed heterogeneity in protein expression levels. This study paves a way towards developing the technique of FISH further to quantify transcripts of interest per cell with the help of super resolution imaging.

Keywords: Phenotypic heterogeneity; bacterial heterogeneity; Arabinose operon