XVI Congreso Nacional de Biotecnología y Bioingeniería
21 al 26 de Junio de 2015 Guadalajara, Jalisco, México.
Guadalajara

Functionality of microbial phenotypic heterogeneity in bioprocesses: analytical single cell approaches and control strategies

Frank Delvigne
University of Liège, Gembloux Agro-Bio Tech, Passage des Déportés, 2 5030 Gembloux, Belgium
E-mail address F.Delvigne@ulg.ac.be
Key words: biosensors, flow cytometry, microfluidics

Microbial phenotypic heterogeneity is known to be naturally present in isogenic population and can be attributed to the stochastic nature of the biochemical reactions. An important question at this level was to determine whether such stochastic behavior exhibits some functionality, i.e. how single cell heterogeneity leads to population level strategies [1]. One of this strategies, called bet-hedging, is known to give a competitive advantage to the population, by leading for example to a persistent phenotype able to survive to antibiotics exposure. Persistence has been recently recognized to occur during diauxic shift of several microorganisms [2][3], a mechanism often encountered during industrial bioprocesses. Additional experiments have pointed out a significant impact of microbial phenotypic heterogeneity at the level of the metabolic fluxes [4][5]. Taken altogether, these results point out the fact that microbial phenotypic heterogeneity plays significant role on bioprocesses performances and robustness [6]. In order to highlights the occurrence of microbial phenotypic heterogeneity during bioprocesses, two single cell technologies will be evaluated. The first device involves the use of on-line flow cytometry for the physiological profiling of population heterogeneity in bioreactors [7]. The second device is based on a single cell microfluidics allowing the cultivation of individual bacteria in constant environment [8]. These devices will be used in order to track the expression of destabilized GFP based on the activation of the ribosomal promoter *rrnB*. The results show a strong modulation of phenotypic plasticity in both devices and the appearance of rare phenotypes. On the basis of these results, future strategies aiming at controlling phenotypic heterogeneity in bioprocesses are proposed.

1. Martins BMC, Locke JCW Microbial individuality: how single-cell heterogeneity enables population level strategies. Curr Opin Microbiol 24:104–112.

2. Solopova A, van Gestel J, Weissing FJ, et al. (2014) Bet-hedging during bacterial diauxic shift. Proc Natl Acad Sci U S A 111:7427–7432. doi: 10.1073/pnas.1320063111

3. Kotte O, Volkmer B, Radzikowski JL, Heinemann M (2014) Phenotypic bistability in Escherichia coli's central carbon metabolism. Mol. Syst. Biol. 10:

4. Van Heerden JH (2014) Lost in Transition: Startup of Glycolysis Yields Subpopulations of Nongrowing Cells. Science 343:1–9.

5. Delvigne F, Zune Q, Lara AR, et al. (2014) Metabolic variability in bioprocessing: implications of microbial phenotypic heterogeneity. Trends Biotechnol 32:608–616.

6. Delvigne F, Goffin P (2014) Microbial heterogeneity affects bioprocess robustness: Dynamic single cell analysis contribute to understanding microbial populations. Biotechnol J 9:61–72.

7. Brognaux A, Han S, Sorensen SJ, et al. (2013) A low-cost, multiplexable, automated flow cytometry procedure for the characterization of microbial stress dynamics in bioreactors. Microb Cell Factories. doi: 10.1186/1475-2859-12-100

8. Grunberger A, Wiechert W, Kohlheyer D (2014) Single-cell microfluidics: opportunity for bioprocess development. Curr Opin Biotechnol. doi: 10.1016/j.copbio.2014.02.008