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Application of Thermoplastic Microbioreactor to the Single Cell Study of Budding Yeast to Decipher the Effect of 5-Hydroxymethylfurfural on Growth

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Abstract : Yeast cells are generally used as a model system of eukaryotes due to their complex genetic structure, rapid growth ability in optimum conditions, easy replication and well-defined genetic system properties. Thus, yeast cells increased the knowledge of the principal pathways in humans. During fermentation, carbohydrates (hexoses and pentoses) degrade into some toxic by-products such as 5-hydroxymethylfurfural (5-HMF or HMF) and furfural. HMF influences the ethanol yield, and ethanol productivity; it interferes with microbial growth and is considered as a potent inhibitor of bioethanol production. In this study, yeast single cell behavior under HMF application was monitored by using a continuous flow single phase microfluidic platform. Microfluidic device in operation is fabricated by hot embossing and thermo-compression techniques from cyclo-olefin polymer (COP). COP is biocompatible, transparent and rigid material and it is suitable for observing fluorescence of cells considering its low auto-fluorescence characteristic. The response of yeast cells was recorded through Red Fluorescent Protein (RFP) tagged Nop56 gene product, which is an essential evolutionary-conserved nucleolar protein, and also a member of the box C/D snoRNP complexes. With the application of HMF, yeast cell proliferation continued but HMF slowed down the cell growth, and after HMF treatment the cell proliferation stopped. By the addition of fresh nutrient medium, the yeast cells recovered after 6 hours of HMF exposure. Thus, HMF application suppresses normal functioning of cell cycle but it does not cause cells to die. The monitoring of Nop56 expression phases of the individual cells shed light on the protein and ribosome synthesis cycles along with their link to growth. Further computational study revealed that the mechanisms underlying the inhibitory or inductive effects of HMF on growth are enriched in functional categories of protein degradation, protein processing, DNA repair and multidrug resistance. The present microfluidic device can successfully be used for studying the effects of inhibitory agents on growth by single cell tracking, thus capturing cell to cell variations. By metabolic engineering techniques, engineered strains can be developed, and the metabolic network of the microorganism can thus be manipulated such that chemical overproduction of target metabolite is achieved along with the maximum growth/biomass yield.

Keywords : COP, HMF, ribosome biogenesis, thermoplastic microbioreactor, yeast
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