Abstract Submitted
for the MAR12 Meeting of
The American Physical Society

Sorting Category: 04.1.9 (E)

Decreasing the stochasticity of mammalian gene expression by a synthetic gene circuit[1] DMITRY NEVOZHAY, Department of Systems Biology, The University of Texas MD Anderson Cancer Center, TOMASZ ZAL, Department of Immunology, The University of Texas MD Anderson Cancer Center, GABOR BALAZSI, Department of Systems Biology, The University of Texas MD Anderson Cancer Center — Gene therapy and functional genetic studies usually require precisely controlled and uniform gene expression in a population of cells for reliable level of protein production. Due to this requirement, stochastic gene expression is perceived as undesirable in these fields and ideally has to be minimized. The number of approaches for decreasing gene expression stochasticity in mammalian cells is limited. This creates an unmet need to develop new gene expression systems for this purpose. Based on earlier synthetic constructs in yeast, we developed and assessed a negative feedback-based mammalian gene circuit, with uniform and low level of stochasticity in gene expression at different levels of induction. In addition, this new synthetic construct enables highly precise gene expression control in mammalian cells, due to the linear dependence of gene expression on the inducer concentration applied to the system. This mammalian gene expression circuit has potential applicability for the development of new treatment modalities in gene therapy and research tools in functional genetics. In addition, this work creates a roadmap for moving synthetic gene circuits from microbes into mammalian cells.

[1]This research was supported by the NIH Director's New Innovator Award Program [1DP2 OD006481-01] and a UT MD Anderson Cancer Center Institutional Research Grant [ORA 3002623] to Gabor Balazsi

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[X] Prefer Oral Session
[ ] Prefer Poster Session

Date submitted: 13 Dec 2011 Electronic form version 1.4