Curr Synthetic Sys Biol 2015, 3:3
http://dx.doi.org/10.4172/2332-0737.C1.003

OMICS International
conferenceseries.com

Synthetic microRNAs to boost cellular production of biopharmaceuticals

Kerstin Otte
University of Applied Sciences, Germany

Recently, microRNAs (miRNAs) have been discovered as innovative instruments for cell engineering of biopharmaceutical production cells to minimize existing bottlenecks of eukaryotic expression systems. As small non-coding RNAs, miRNAs do not add any translational burden to the cell and several miRNAs can be exploited in parallel as polycystronic clusters thereby acting concertedly to regulate hundreds of different target genes and regulate entire pathways within the cell. miRNAs are involved in virtually all cellular processes such as apoptosis, proliferation, development or protein biosynthesis. The revelation of the Chinese hamster ovary (CHO) genome and transcriptome as well as the CHO miRNome substantially accelerated miRNA research in this industrially relevant cell type.To elucidate miRNA function and usability as engineering tools in recombinant CHO cells, we performed a genome-wide high-content miRNA screen assaying for phenotypic changes regarding productivity, cell proliferation, viability, necrosis and apoptosis. Among many novel 'engimiRs' which have been found within the screen we discovered a whole miRNA family to strongly contribute to enhanced protein production in CHO cells. Stable overexpression gave rise to superior cell lines outperforming the parental cell line. Moreover, detailed analysis of screening data revealed a novel redundant mechanism of action for miRNAs in eukaryotic cell systems. Our results highlight the application of miRNAs as powerful tools for cell engineering and will shed additional light on these tiny but mighty regulators of gene expression.

Otte@hochschule-bc.de

DNA recombination engineering for improved and more reliable protein expression from DNA vectors

Nicolas Mermod
University of Lausanne, Switzerland

Epigenetic regulatory DNA elements can be added to expression vectors to increase transgene genomic integration to dampen silencing and to provide overall a more reliable expression in cultured mammalian cells. Nevertheless, expression remains variable from one cell clone to the next. We have sequenced the genomes of CHO cell clones expressing recombinant proteins yielding information on the molecular mechanisms that allowed the genomic integration of the plasmid vectors. This provided an approach to transiently silence unwanted recombination pathways so as to favor a microhomology-based recombination mechanism that mediates integration into expression-permissive genomic loci. When combined to MAR epigenetic regulatory elements, this provides much more predictable and homogeneous levels of transgene expression in polyclonal cell populations expressing a gene of interest.

Nicolas.Mermod@unil.ch