The m6A reader YTHDF2 and m1A eraser ALKBH3 fine-tune mRNA transgene expression in CHO cells

Nga Lao[1] and Niall Barron[2]

[1]NIBRT
[2]National Institute for Bioprocessing Research and Training

April 28, 2020

Abstract

N6-methylated adenosine (m6A) and N1-methylated adenosine (m1A) are two epi-transcriptomic modifications on eukaryotic mRNA which have recently been rediscovered and are generating considerable interest. M6A methylation impacts on all aspects of cellular RNA metabolism and numerous physiological processes. Although less abundant than the m6A epitranscriptomic mark, m1A methylation has recently also attracted interest due to its dynamic nature in response to physiological changes. We investigated the role of the m6A and m1A methylation regulators on the expression of a transgene in Chinese Hamster Ovary (CHO) cells - the host cell of choice in producing biopharmaceutical proteins commercially. Using siRNA-mediated gene depletion and methylation-specific RNA immunoprecipitation with anti-m6A or m1A-antibodies, we show that (i) knock-down of the m6A 'reader' YTHDF2 or the m1A 'eraser' ALKBH3 dramatically impacts transgene expression; (ii) the effects of YTHDF2 and ALKBH3 depletion on transgene expression are m6A- and m1A-mediated. We conclude that the expression of transgenes in CHO cells can be subjected to regulation by both m6A and m1A regulators. These findings open up the prospect of previously unexplored epi-transcriptomic-based approaches to CHO cell line engineering for improved recombinant protein production.

Hosted file

`Main document_Biotech and Bioenginnering_NLao_20 April 20.pdf` available at https://authorea.com/users/313781/articles/444213-the-m6a-reader-ythdf2-and-m1a-eraser-alkbh3-fine-tune-mrna-transgene-expression-in-cho-cells

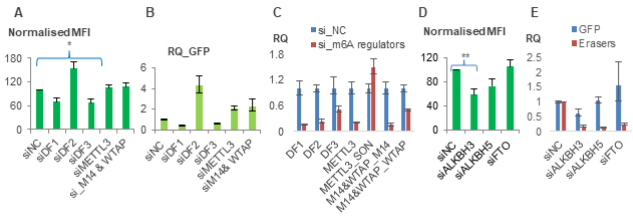

Figure 1

Hosted file

Figures_NLao_20 April 20.pdf available at https://authorea.com/users/313781/articles/444213-the-m6a-reader-ythdf2-and-m1a-eraser-alkbh3-fine-tune-mrna-transgene-expression-in-cho-cells