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Re-programming CHO cell metabolism using miR-23 tips the balance towards a highly productive phenotype

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microRNA-mediated engineering of CHO cells is an attractive method for enhancing various industrially relevant phenotypes, ultimately boosting recombinant protein titres. A single miRNAs ability to interact with multiple mRNA targets allows their regulatory capacity to extend to processes such as cellular metabolism. Various metabolic states have previously been associated with particular CHO cell phenotypes such as glycolytic or oxidative metabolism accommodating growth and productivity, respectively. miR-23 has previously been demonstrated to play a role in glutamate metabolism resulting in enhanced oxidative phosphorylation through the TCA cycle. Re-programming cellular bioenergetics through miR-23 could tip the balance, forcing mammalian production cells to be more productive by favouring metabolic channelling into oxidative metabolism.

CHO clones depleted of miR-23 using a miR-sponge decoy demonstrated an average ~3-fold enhanced specific productivity with no impact on cell growth. Mitochondrial activity was found to be enhanced by ~30% at Complex I and II of the electron transport system. Additionally, label-free proteomic analysis uncovered various potential novel targets of miR-23 including *LETM1* and *IDH1*, both implicated in oxidative metabolism and mitochondrial activity.