High-Throughput Design and Engineering of Mammalian Cells

A novel approach for designing, building, and delivering large DNA vectors (>100kb) for highly customizable expression of multiple gene products.

Technology

Researchers at NYU Langone Health have developed a novel approach for designing, building, and delivering large DNA vectors (>100kb) for highly customizable expression of multiple gene products. Cellular behaviors, such as tolerance to perturbations including hypoxia, pH alteration, or shear stress, may require many genes, found in overlapping pathways, each of which is expressed at various levels. Assessing which permutations lead to the correct replication of a biological behavior is highly time-consuming when testing these combinations individually. By utilizing directed evolution and multiplexed libraries, this technology provides a fast method of discovering the appropriate promoters, genes, copy number, and localization sequences that confer the desired phenotype to a single cell.

Background

With the advent of gene therapies in the last decade, the usage of viral vectors to express specific target proteins has significantly increased. These therapies can be priced upwards of $1M for the product, excluding hospital costs and drug administration, due to the high manufacturing and development costs. Lowering patient costs will require effective cell culture technologies that maximize viral titer and protein production. Genetic engineering of mammalian cells can combat some of these issues by adapting cells to require fewer resources or increasing resilience to environmental stressors experienced at scale in bioreactors. However, current approaches to finding solutions that confer these properties are inefficient and lack the flexibility for fine-tuning. Failure to optimize our cell culture capabilities may lead to interruptions in therapeutics production during future periods of demand.

Applications

- This technology can be applied to developing biologics such as antibodies, cell and gene therapies, as well as the production of bacterial and viral vectors.
- Improving cellular fitness to allow further scaling in minimal media (i.e. lab-grown meats)
- Adapting primary cells for easier engineering in vitro by adding features such as immortalization potential and increased resistance to cryopreservation and thawing.
- Improving resilience of cellular therapies subject to harsh physiological contexts such as nutrient starvation in the tumor microenvironment.

Advantages

Technology ID

TRO02-01

Category

Life Sciences/Biologics
Life Sciences/Genetic Engineering
Life Sciences/Research tools/Gene Editing

Authors

Sudarshan Pinglay, PhD
Julie Trolle, PhD

Learn more

- This invention reduces the difficulty and time required for both designing and testing large DNA cargoes.
- This technology allows rapid genotyping and selection of cells with optimized cellular function using minimal infrastructure

Intellectual Property

Provisional patent pending

References

1. Trolle J, McBee RM, Kaufman A, Pinglay S, Berger H, German S, Liu L, Shen MJ, Guo X, Martin JA, Pacold ME, Jones DR, Boeke JD, Wang HH. , https://pubmed.ncbi.nlm.nih.gov/36165439/
2. Pinglay S, Bulajić M, Rahe DP, Huang E, Brosh R, Mamrak NE, King BR, German S, Cadley JA, Rieber L, Easo N, Lionnet T, Mahony S, Maurano MT, Holt LJ, Mazzoni EO, Boeke JD. , https://pubmed.ncbi.nlm.nih.gov/35771912
3. Brosh R, Laurent JM, Ordoñez R, Huang E, Hogan MS, Hitchcock AM, Mitchell LA, Pinglay S, Cadley JA, Luther RD, Truong DM, Boeke JD, Maurano MT , https://pubmed.ncbi.nlm.nih.gov/33649239