High-throughput screening platform for CRISPR

20 January 2016 | Laurie Winkless

US scientists have developed a new platform to rapidly screen formulations of biomaterials and molecular components for gene-editing systems.

Biologists have been editing genomes for decades, but in the past five years, only one route has made headlines – CRISPR. This powerful gene-editing tool is quick, cheap and easy to use, and may offer a way to treat genetic diseases. CRISPR relies on an enzyme called Cas9 that uses a short guide RNA molecule to target a specific faulty gene sequence. Once delivered to the genome, it can 'cut' through at that location, to prevent replication of the gene. But there are a vast number of possible ways to combine the RNA and delivery material, which makes identifying the optimal combination for a particular cell line (or patient) very challenging.

But researchers at the University of Wisconsin-Madison have developed a platform that can rapidly generate and screen many formulations of delivery materials and CRISPR-Cas9. And they believe that this approach, to be published in an upcoming issue of *Acta Biomaterialia* [DOI: 10.1016/j.actbio.2015.12.036], could help transition 'genome surgery' from the lab to the clinic.

Their platform is based on a number of techniques – *microcontact printing* was used to isolate cells, and *image cytometry* measured the optical properties of cells via fluorescent dyes. *High content image analysis*, which provides quantitative data on the presence of small molecules within a cell, could then be used to monitor CRISPR delivery and editing 'in action'. Four commercially available synthetic biomaterials were selected as the delivery media for this work. A range of different RNA molecules were added to these materials, forming a series of lipid formulations that were then delivered to human embryonic kidney cells.

The editing efficiency of the CRISPR-Cas9 system was found to be highly dependent on the choice of delivery material. And successful editing was detected in only a fraction of the cell population, which suggests some limitations to this lipid-based delivery approach. But there is real potential in the proposed screening platform – it was shown to be capable of screening hundreds of cell populations simultaneously, speeding up the processes of identifying an optimal molecular system. The delivery and editing process could also be monitored in real-time, and it is applicable to a variety of cell/tissue types. The team believe that the platform could ultimately advance and inform genomic medicine, regenerative biology and drug discovery.

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B. Steyer, J. Carlson-Stevermer, N. Angenent-Mari, A. Khalil, T. Harkness, K. Saha – *Acta Biomaterialia*, In Press, Available online 30 December 2015. "High content analysis platform for optimization of lipid mediated CRISPR-Cas9 delivery strategies in human cells" DOI: 10.1016/j.actbio.2015.12.036

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