CRISPR GENE-EDITED CELL LIBRARIES: RAPID VALIDATION OF RESEARCH

A conversation with **DR. DANIELLA STEEL**, Senior Product Manager, Horizon Discovery Ltd

As part of its role as a fully-integrated life science company providing research tools and services to academia, biopharma and diagnostics companies, Horizon has created a library of ready-made isogenic human cell line pairs edited using CRISPR-Cas9 technology. With 10,000 gene targets available — 3,000 of them off-the-shelf — the knockout cell lines can be used as a model system to study the role of genes in cellular processes and drug responses, and to validate and provide quality control for research projects.

What is the function of CRISPR gene-edited cell lines in research?
In order to understand the role that different genes play in disease pathways, researchers need to be able to modify levels of gene expression. RNA interference (RNAi) technology is well established as a tool to modify expression, but because it knocks down rather than knocks out the gene, validation is required.

There are a number of different validation methods. Scientists can use pharmacological agents to inhibit the protein or receptor, but the results can be dose dependent, and there may be a lack of specificity. Standardized patient-derived cell lines also play a role, but may not have control cell lines available.

The advantage of using CRISPR-edited cell lines to validate results is that they provide a gene knock-out, rather than a knockdown, and the modified cells can be paired with unmodified cells from the same line, providing a matched control.

What are the advantages of ready-made cell lines?
There are a lot of benefits of CRISPR technology for research. However, while the principle seems simple, CRISPR editing is a complex and lengthy process with a steep learning curve. Particularly for postgraduates and postdocs working within a limited timeframe and budget, the time spent learning and applying the technology may outweigh the benefits. There are service providers that can custom-make knockout cell lines, but the process is still lengthy – up to 15 weeks – and the costs can add up. By using ready-made cell lines, researchers can spend their precious time and money on research, rather than getting to grips with a new technology.

What makes Horizon's library of gene-edited cell lines different?
There is a small number of companies that provide a library of CRISPR-edited cell lines but we believe we are the largest and have the broadest spread of coverage. We have access to 10,000 gene targets, and at any one time, more than 3,000 edited cell lines are in stock. The cell lines come with a matched wild-type parental cell line as a control. This means that any phenotypic changes can be directly attributed to the genetic modification. We also can produce two clones for each gene knockout, which is the recommended control for off-target effects.

Our libraries are based on highly characterized and quality controlled clonal human cell lines with conserved biology.

BY USING READY-MADE GENE-EDITED CELL LINES, RESEARCHERS CAN SPEND THEIR PRECIOUS TIME AND MONEY ON RESEARCH.

We know which genes and proteins are critical to cell survival and proliferation, and therefore we save researchers time because we won't attempt to develop cell lines that won't survive. Our catalog includes common cancer cell lines such as DLD1, MCF10 and HCT116, as well as our proprietary HAP1 cell line.

Our customers can find the gene targets available on our website. For those cell lines that are in stock, we can deliver within seven days, depending on destination. For gene knockouts that aren't in stock, we can deliver in around 12 weeks. This is quicker than custom cell line production as we already have the cells characterized, genes identified and systems for editing in place.

Do you have an example of an application?
We worked with a researcher who was trying to understand the biology of the differences in patient responses to chemotherapy. He had shown that high and low responders had different profiles of expressed proteins, and backed this up with research showing that a cell line from a bank of patient-derived cells had similar genetic and protein signatures. He submitted a paper, but the journal wanted data from a second independent model to indicate more clearly the role of specific proteins.

The researcher was approaching his grant deadline, and so had limits on both time and money. We had knockout cells relating to the family of proteins he was working on in stock. He used these and found a yes/no response for the genes. Adding CRISPR gives researchers the quality and precision they need.

Where is Horizon Discovery going next?
Horizon's vision is to enable the future of cell-based research. As a principle supplier of gene modulation technologies, including RNAi and CRISPR reagents and arrayed libraries, Horizon works with researchers from the beginning of the gene interrogation process to the end, continuously supporting the process with innovative high quality products.

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