#### **CUSTOMER SUCCESS STORY**

# Cellistic is using the CYTENA UP.SIGHT to generate monoclonal gene-edited iPSCs



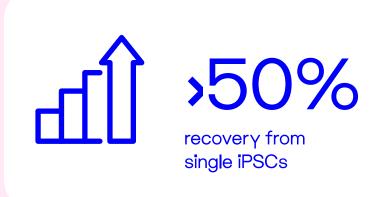
## Cellistic is using the CYTENA UP.SIGHT to generate monoclonal gene-edited iPSCs

Cellistic specializes in developing and manufacturing allogeneic iPSC-derived cell therapies. Utilizing their Pulse and Echo platform, they create custom iPSC lines differentiated at scale into immune cells, this simplifies, de-risks, and speeds up the development and manufacture of therapeutic candidates. The Pulse platform covers the entire iPSC process, from reprogramming to high-efficiency gene editing, ensuring monoclonality and optimizing recoverability. This integrated approach accelerates the development of next-generation cell therapies, making them more accessible to patients.



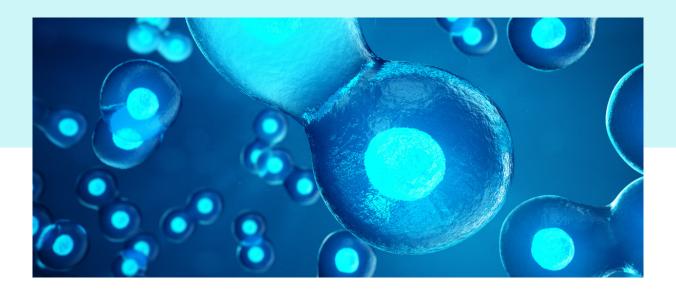
#### Key Results





#### BACKGROUND

Allogeneic iPSCs continue to transform healthcare across various fields. Modern gene editing techniques facilitate the "immune cloaking" of donor iPSCs, which has helped overcome issues with immune rejection. This allows iPSCs to be used as universal donor cells, which are accepted by all patients. Gene editing also helps increase the safety and utility of these cell-based therapies by disabling oncogenes, inserting genetic safety switches, and allowing for application-specific customization. iPSCs are a medical revolution with applications in genetic disorders like cystic fibrosis, cardiovascular disease, neurological disorders, and cancer immunotherapy.



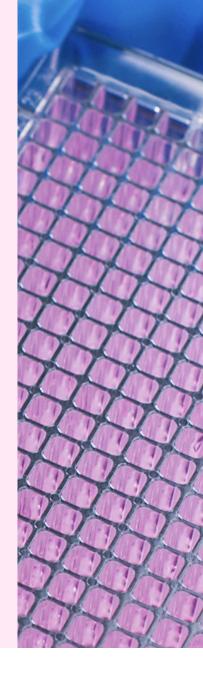
Despite the compelling potential of "off-the-shelf" allogeneic cell therapies, gene editing of monoclonal iPSCs is laden with potential risks. Inefficiencies in workflows lead to compliance issues, missed deadlines, and unfulfilled commitments to clients and patients. Particular challenges include the sensitivity of iPSCs to handling techniques and multiple genetic manipulations, particularly with Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR). However, gentle single-cell seeding poses significant technical challenges that must be solved to ensure cell viability, monoclonality, and traceability. Moreover, researchers must be able to demonstrate clonality and use handling devices that support workflows in a GMP environment and offer single-use consumables that satisfy regulatory requirements. Overcoming these challenges is essential for iPSCs to reach their full potential and expedite the treatment of a wide range of diseases.

#### CHALLENGE

From previous experience the Cell Line Development (CLD) team at Cellistic is aware of the numerous challenges in generating high quality monoclonally-derived gene-edited iPSCs.

Techniques such as limiting dilution, where 0.5 cells per well are used, are inefficient and can take weeks to perform. Limiting dilution often results in some wells being empty and others containing multiple clones, which increases the risk of false positives. This approach necessitated a prolonged time investment for manual pipetting of test plates, which increased the risk of error, contamination, and repetitive strain injury to the operator. Furthermore, it required using more reagents than necessary and manually monitoring individual wells for successful clones.

These challenges lead to regulatory compliance concerns due to difficulties verifying cell line monoclonality. Suzanne Snellenberg, PhD, VP of Cell Line Development at Cellistic noted that:



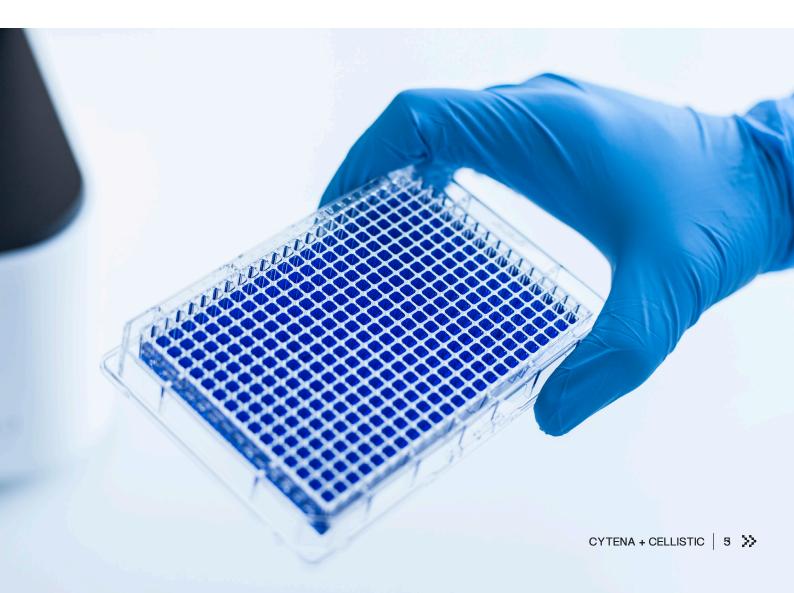
## "Limiting dilution involves subjective judgment, which can be difficult to document comprehensively."

Achieving compliance required them to invest in expensive imaging and next-generation sequencing techniques to demonstrate monoclonality. This led to increased operating costs and slower workflows.

### SOLUTION

The issues inherent to their workflow led Cellistic to search for alternative solutions and evaluate systems that minimize shear stress. Dr. Snellenberg indicated that:

"iPSCs are very sensitive to shear stress and pressure changes during sorting which affects the viability and functionality."



#### SOLUTION

Cellistic then tested the UP.SIGHT system from CYTENA, which provided an immediate solution to their challenges.

The UP.SIGHT's microfluidics system gave Cellistic the gentle sorting capabilities that a FACS cannot provide. Furthermore, dual imaging ensured monoclonality without the need for serial dilution and inefficient use of reagents. The UP.SIGHT promised and delivered on the core problem areas Cellistic experienced, helping them achieve:



High recovery rates of iPSCs



Highest assurance of monoclonality



Regulatory-standard monoclonality reports



Minimized need for manual input and higher ease of use

Another key factor that convinced Cellistic that the UP.SIGHT system was a wise strategic purchase, was its automation compatibility and proven best-in-class monoclonality scores. CYTENA's instruments offer fully integratable and easy-to-use automation solutions with pre-configured workflows, to jumpstart cell line development.

## **IMPACT**

The UP.SIGHT single-cell dispenser and imager had an immediate transformative impact on Cellistic's workflows. Straight away, they achieved high iPSC recovery rates (>50%) and saved time and resources due to automated single-cell dispensing.



Furthermore, the UP.SIGHT's single-cell seeding eliminated the need for manual pipetting and screening, removing the chance for false positives and saving researchers from labor-intensive and error-prone workflows. While limiting dilution is very labor-intensive, the UP.SIGHT performed isolation in minutes in addition to providing monoclonality assurance, single-use dispensing cartridges, and software data management for data traceability. Due to its all-in-one capabilities, the UP.SIGHT not only streamlined single-cell dispensing, but also covered imaging and clone selection. This saved Cellistic time and money that would have been spent on other less advanced support equipment.



"In combination with Cellistic's proprietary gene editing capabilities and CYTENA's UP.SIGHT, we have to screen fewer clones and also plate fewer cells, making the work less labor-intensive"



After training, Cellistic researchers found the UP.SIGHT easy to use and praised the exceptional and timely support they received from the CYTENA team. Today, Cellistic recommends the UP.SIGHT to anyone looking for a streamlined and reliable solution for cell line development applications.

Cellistic now boasts a 90% gene editing efficiency in iPSCs using its STAR-CRISPR(TM) gene editing technology, which sets it apart from competitors and establishes it as a pioneer in facilitating the next generation of iPSC cell therapies.

>> Note: Cellistic and STAR-CRISPR are trademarks of Cellistic SA or its affiliates.

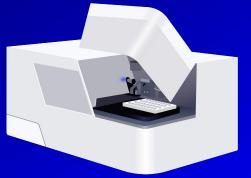
#### **GET STARTED**

# Connect with our experts to learn more about the UP.SIGHT.



>>> Book a demo

## Check Out The UPSIGHT 2nd Generation





#### We create the future of health.



#### CYTENA, A BICO COMPANY

CYTENA is a leading provider of high-precision instruments for isolating, dispensing, imaging, analyzing and handling biological cells. The company continues to build on the success of the single-cell dispensing technology it patented as a spin-off from the University of Freiburg, Germany, in 2014. Today, as part of BICO, the world's leading bio convergence company, CYTENA's award-winning devices are still manufactured in Germany and used at prestigious academic and pharmaceutical labs around the world to automate workflows in numerous application areas, including stable cell line development, single-cell omics, high-throughput screening and drug discovery. CYTENA's breakthrough innovations for the lab combine advanced automation, state-of-the-art software engineering and the latest insights in cell biology to maximize efficiencies in the life sciences and create the future of health. Learn more at www.cytena.com