

Century Therapeutics

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Engineered stem cells power expansive range of cancer therapies

Century Therapeutics' deliberate, high-caliber approach to generating induced pluripotent stem cell-derived products has the potential to significantly expand the effectiveness and accessibility of cell therapies for both blood and solid cancers.

Induced pluripotent stem cells (iPSCs) derived from adult somatic cells are becoming an increasingly important tool for developing novel cell therapies. iPSCs can be used to create cell types or tissue that the body may need to counter disease, from diabetes to neurodegeneration and cancer.

Philadelphia-based, biotech Century Therapeutics is applying its expertise in cellular reprogramming, genetic engineering and manufacturing to generate an army of cancer-attacking immune cells from iPSCs. "iPSCs provide an unparalleled opportunity to advance cancer treatment," said Osvaldo (Lalo) Flores, Chief Executive Officer of Century Therapeutics. "Our aim is to become a leading developer of allogeneic iPSC-derived natural killer (NK) and T cell products that offer superior efficacy and are safer and available on demand for patients," he added.

To date, most cancer cell therapies have been based on patient derived (autologous) or healthy-donor-derived (allogeneic) terminally differentiated T cells that are activated to recognize cancer cells and expanded before they are re-infused into patients. Genetically modified T cells expressing chimeric antigen receptors (CARs) that target tumor-associated molecules have shown impressive efficacy in hematological malignancies, but their ability to infiltrate and attack solid tumors has been less promising.

The impact of autologous cell therapies is also limited by the durability of response and a complex manufacturing process. "Developing autologous CAR-T therapies is time consuming, costly, and can lead to variable cell product quality and treatment failures. In contrast, iPSC-derived cell therapies offer the advantages of generating highly uniform, off-the-shelf cell products with multiple gene edits designed to improve efficacy, safety and cell persistence," said Luis Borges, Chief Scientific Officer.

Century Therapeutics' technology—which is platform agnostic because of its ability to flexibly generate CAR-NK, CAR-T and other engineered immune cells that seek out and destroy tumors—can improve the clinical effects of existing cell therapies by generating more homogeneous, effective and persistent cancer-killing cells at a reduced cost. Furthermore, the Century team has the unique ability to incorporate gene edits that help their cells avoid rejection by the host. The company expects to start clinical testing of its first iPSC-derived genetically engineered NK and T cell products in 2022. "The strength of our platform is the ability to provide off-the-shelf, uniform products at any hospital or clinic that will be more effective and more accessible to patients," Flores explained.

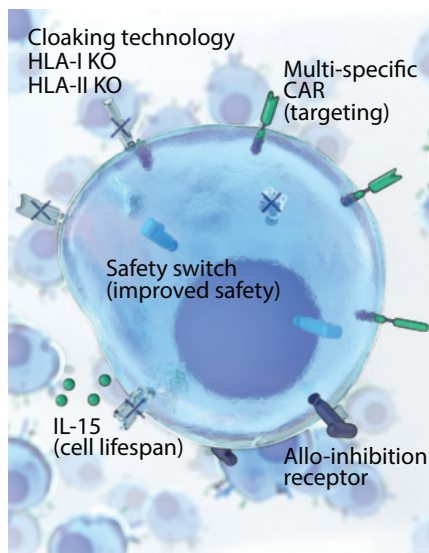


Fig. 1 | Century's engineered, iPSC-derived product.

Preeminent, end-to-end iPSC platform

The self-renewing capacity of pluripotent stem cells means that they are easier to manipulate and expand than differentiated cells. "iPSCs are a blank canvas from which we can generate, through multiple rounds of thoughtful and precise cellular engineering, master cell banks of modified cells that can be developed into cancer fighting immune cells," Borges explained.

The company's foundational iPSC technology is licensed from Fujifilm Cellular Dynamics (FCDI) and has been optimized over the last 15 years, translating into institutional know-how and faster in-house product iteration with capacity to support a growing pipeline of cellular products.

Clinical grade iPSC lines that are capable of generating high yields of immune cells are genetically engineered using the CRISPR/MAD7 system to target cancer cells, avoid rejection by the host immune system and provide durable responses. "Our engineered cells express T cell receptors and/or CARs that have been optimized to target multiple cancer antigens specifically, and to trigger enhanced cancer-killing responses. Because these CARs are designed to be multi-specific, they may offer a viable strategy to target tumor heterogeneity and antigen loss, and improve therapeutic efficacy," added Borges.

Moreover, through sequential gene editing, it is possible to make further modifications that increase the cells' lifespan, such as inducing the expression

of IL-15, reducing immunogenicity and improving safety. By knocking out the expression of human leukocyte antigen (HLA) I/II and introducing the expression of HLA-E, which acts an allo-inhibition receptor, Century Therapeutics is creating cells that evade the immune system and therefore can help prevent host versus graft disease and the rejection of allogeneic drug products (Fig. 1).

"We believe that our cloaking technology will allow us to generate hypoimmunogenic products that can be delivered in repeated doses, which in turn offer the potential to enhance the efficacy, persistence, durability and safety profile of our products compared to existing CAR-T therapies," noted Flores. "This unique capability, along with our NK and T cell agnostic approach, set us apart as the company with one of the most advanced, end-to-end iPSC platforms which positions us well to lead the way advancing allogeneic iPSC-derived cell therapies for cancer."

The engineered iPSCs are expanded to generate master cell banks that become the starting point for the manufacturing process and can then be differentiated to generate a rich pipeline of uniform, high-quality products in a scalable and cost-effective manner. In addition to privileged access to the FCDI facilities, the company's own in-house manufacturing facility will be operational later this year. Century Therapeutics' pipeline already comprises 10 iPSC-derived T or NK cell products that have shown potent and reliable effects in preclinical models for solid and hematological cancers.

With a proven leadership team at the helm, Century Therapeutics is primed to continue building upon the tremendous accomplishments of the last year and anticipates generating multiple INDs annually in the coming years.

"We look forward to fully realizing our platform's potential and becoming one of the preeminent cell therapy companies developing off-the-shelf iPSC-based therapies to improve patient lives," Flores concluded.

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