

PRESS RELEASE

Cellectis Publishes Manuscript in Frontiers Bioengineering and Biotechnology Unveiling Efficient Multitool/Multiplex Gene Engineering combining TALEN® and TALE Base Editors (TALE-BE)

November 10, 2022 - New York, NY — Cellectis (the "Company") (Euronext Growth: ALCLS - NASDAQ: CLLS), a clinical-stage biotechnology company using its pioneering gene-editing platform to develop life-saving cell and gene therapies, today published a manuscript in *Frontiers Bioengineering and Biotechnology* demonstrating the feasibility of efficient multiplex gene engineering using a combination of two different molecular tools: Cellectis' TALEN® gene editing technology (TALE nuclease) and a TALE-BE (TALE Base editor).

TALE base editors are a recent and very important addition to the gene editing landscape. This approach does not create DNA double strand breaks as does CRISPR/Cas9, or other engineered nucleases, and is a promising therapeutic strategy for genetic diseases. A key aspect to broaden the scope of possible applications is our comprehension of design rules.

Cellectis used a screening approach to gain in-depth insights into the editing rules driving TALE-BE activity and applied this knowledge to design highly efficient TALE-BE compatible with potential therapeutic application. Moreover, TALE-BE show insignificant levels of by-products such as indels.

Cellectis scientists combined two molecular tools, a TALEN® and a TALE-BE, to perform a double gene Knock Out (KO) of *TRAC* and CD52, a combination of target genes used for allogeneic CAR T-cell adoptive therapies. This combination of molecular tools paves the way to simultaneous multiplex gene engineering with more controllable outcomes.

"A multiplex/multitool strategy presents several advantages: firstly, it prevents the creation of translocations often observed with the simultaneous use of several nucleases. Secondly, it allows for the possibility of going beyond multiple knock-outs while still allowing gene knock-in at the nuclease target site, altogether extending the scope of possible application," said Alex Juillerat, Ph.D., Vice President Gene Editing & New York Lab Head at Cellectis. "The precise positional rules we have determined for TALE-BE will allow Cellectis to unleash the full potential of these technologies for future applications."

Research data showed that:

- Employing a medium/high throughput strategy, Cellectis gained in-depth insight of the editing rules in cellulo, while excluding confounding factors.
- Designed TALE-BE targeting CD52 achieved very high frequency of gene knock-out (up to 80% of phenotypic CD52 knock out).
- When TALE-BE was combined with a TALEN® targeting the *TRAC* locus, very high frequency of double gene knock-out (up to 75% of phenotypic double gene knock-out) was achieved without the creation of translocations between the two targeted loci.

This article is available on *Frontiers in Bioengineering and Biotechnology* website by clicking on this link.

About Cellectis

Cellectis is a clinical-stage biotechnology company using its pioneering gene-editing platform to develop life-saving cell and gene therapies. Cellectis utilizes an allogeneic approach for CAR-T immunotherapies in oncology, pioneering the concept of off-the-shelf and ready-to-use gene-edited CAR T-cells to treat cancer patients, and a platform to make therapeutic gene editing in hemopoietic stem cells for various diseases. As a clinical-stage biopharmaceutical company with over 22 years of experience and expertise in gene editing, Cellectis is developing life-changing product candidates utilizing TALEN[®], its gene editing technology, and PulseAgile, its pioneering electroporation system to harness the power of the immune system in order to treat diseases with unmet medical needs. Cellectis' headquarters are in Paris, France, with locations in New York, New York and Raleigh, North Carolina. Cellectis is listed on the Nasdaq Global Market (ticker: CLLS) and on Euronext Growth (ticker: ALCLS).

For more information, visit www.cellectis.com. Follow Cellectis on social media: @cellectis, LinkedIn and YouTube.

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Forward-looking Statements

This press release contains "forward-looking" statements within the meaning of applicable securities laws, including the Private Securities Litigation Reform Act of 1995. Forward-looking statements may be identified by words such as "anticipate," "believe," "intend", "expect," "plan," "scheduled," "could," "may" and "will," or the negative of these and similar expressions. These forward-looking statements, which are based on our management's current expectations and assumptions and on information currently available to management. Forward-looking statements

include statements about the potential of our innovation programs. These forward-looking statements are made in light of information currently available to us and are subject to numerous risks and uncertainties, including with respect to the numerous risks associated with biopharmaceutical product candidate development. With respect to our cash runway, our operating plans, including product development plans, may change as a result of various factors, including factors currently unknown to us. Furthermore, many other important factors, including those described in our Annual Report on Form 20-F and the financial report (including the management report) for the year ended December 31, 2021 and subsequent filings Cellectis makes with the Securities Exchange Commission from time to time, as well as other known and unknown risks and uncertainties may adversely affect such forward-looking statements and cause our actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.