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Tune Therapeutics Unveils Breakthrough Data Showing Stable and Durable Epigenetic Regulation in Non-Human Primates

Method targets the epigenome, makes no changes to the underlying DNA sequence
First example of lasting repression after transient epi-editor delivery in a non-human primate

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DURHAM, N.C. & SEATTLE--(BUSINESS WIRE)--Last week, at the 26th Annual Meeting of the American Society of Gene & Cell Therapy (ASGCT), leading epigenetic editing company Tune Therapeutics showcased the power and potential of its TEMPO ™ genetic tuning platform, by presenting data showing the stable repression of the PCSK9 gene and the effective reduction of LDL-cholesterol levels in non-human primates (NHPs). This data marks a significant waypoint on the path to epigenetic medicine, in that it represents the first demonstration of durable epigenetic gene regulation, in a large animal model, following transient delivery of an epi-editor.

A common therapeutic target for the prevention of cardiovascular disease, it is well established that repressing the PCSK9 gene reduces elevated LDL-cholesterol levels, in turn associated with the formation of artery-clogging plaques. The non-human primate data presented at the ASGCT conference showed that epigenome editing (or genetic tuning) can drive the stable repression of *PCSK9* (ongoing past four months) following a single treatment, and without cutting or nicking the DNA, or altering its coding sequence in any way.

Tune's TEMPO platform is based on decades of foundational research by company Co-Founders Charles Gersbach and Fyodor Urnov. The versatile, modular platform incorporates a DNA-binding Domain (DBD) that binds to DNA without cutting it, tethered to one or more effector proteins, which produce the required epigenetic effect. Depending on the effector selected, this can mean repressing genes that actively drive disease, or activating genes for which deficiency is the problem. Moreover, the TEMPO platform itself can be used to screen for unique gene regulation targets – providing an integrated, high-throughput process that accelerates the initial phases of drug discovery and development.

In the live data presentation, entitled "Transient Delivery of Epigenome Editors Stably Represses PCSK9 and Lowers LDL Cholesterol in Non-Human Primates", Senior Scientist Jennifer Kwon described how Tune developed a TEMPO epi-repressor targeting the *PCSK9* gene, encoded it into RNA, and delivered it to cells and large animal subjects via lipid nanoparticle (LNP). Initial experiments in rapidly dividing liver cells showed gene repression levels of up to 98% with effects maintained for over 6 months, suggesting a stable, heritable, and highly durable mechanism.

When a single dose of the same epi-repressor was delivered intravenously to three NHPs, researchers recorded:

- ~75% drop in serum PCSK9 past 120 days of observation
- ~56% reduction in LDL-cholesterol levels

- Methylation patterns around the PCSK9 target site that were practically unchanged between day 7 and day 85 of the study

Taken together, these results show a potent and persistent genetic tuning effect, well tolerated by the animals, and validate epigenetic DNA methylation as the core mode of action. The study is ongoing, and the durability of gene repression will continue to be monitored.

“In our journey to develop genetic tuning into a precise and robust therapeutic modality, these results are incredibly promising,” said Derek Jantz, Ph.D., Chief Scientific Officer at Tune Therapeutics. “Safe and durable gene silencing following the transient delivery of an epi-repressor in primates represents a major milestone for the field and a significant step toward enacting meaningful change for millions of patients suffering from common and chronic diseases.”

“This data is highly encouraging for the field,” added Matt Kane, CEO of Tune Therapeutics, “as it presents a broad proof-of-concept for liver-directed epi-editing and attests to the potential for genetic tuning to unlock common disease and regenerative medicine.”

At the same ASGCT meeting, Tune also showed new data on the application of epi-editing to cell therapies and immuno-oncology. In a detailed poster presentation, Tune scientists showed that HER2-targeting human CAR T-cells could be epigenetically modified *ex vivo* to enhance their ability to proliferate, persist, and control the growth of solid tumors in engrafted mice. This exciting data suggested that multiplexing (targeting and tuning two genes simultaneously) had a combined effect that surpassed that of each gene targeted in isolation – in effect remodeling the cell to create a more robust, tumor-killing phenotype.

“The progress we’ve seen over the last six months has been momentous,” says Kane. “It’s an exciting time for the field, and we’re thrilled to be leading it.”

ASGCT Presentation Details

Title: *Transient Delivery of Epigenome Editors Stably Represses PCSK9 and Lowers LDL Cholesterol in Non-Human Primates*
Date & Time: Friday May 19th, 9:00-9:15AM PT
Location: Los Angeles Convention Center, Room 515AB
Link to Abstract: https://annualmeeting.asgct.org/abstracts/abstract-details?abstractId=15223

Title: *Precision-Targeted Epigenome Editing Enhances CAR T Functional Profiles and Anti-Tumor Activity*
Date & Time: Thursday May 18th, 12:00-2:00PM PT
Location: Los Angeles Convention Center Exhibit Hall, Board # 1096
Link to Abstract: https://annualmeeting.asgct.org/abstracts/abstract-details?abstractId=13716

Both presentations are available on the Tune Therapeutics website, at: https://tunetx.com/tune-therapeutics-unveils-breakthrough-data-showing-stable-and-durable-epigenetic-regulation-in-non-human-primates/

About Tune Therapeutics

With its versatile and powerful TEMPO epigenomic control platform, Tune Therapeutics is pioneering a new therapeutic modality that has the potential to fine-tune any gene network and unlock the full power and potential of regenerative medicine.

With deep experience and a passionate commitment to exploration and innovation, Tune is driving through an inflection point in the history of genetic medicine: from targeting a limited range of rare conditions, to addressing thousands of common and complex diseases for which no curative treatment is available.

Contacts

E: media@tunetx.com