



Study Published in Nature Biotechnology Demonstrates Ability of Moderna's Novel Therapeutic Paradigm to Repair and Regenerate Damaged Heart Tissue

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Messenger RNA therapeutics™ successfully induced high-level, transient expression of VEGF-A protein in the heart, stimulating the growth of cardiovascular cells and improving heart function and survival in an animal model of myocardial infarction

CAMBRIDGE, Mass., Sept. 8, 2013—Moderna Therapeutics, the pioneering company developing [messenger RNA therapeutics™](#), a revolutionary new treatment modality to enable the *in vivo* production of therapeutic proteins, announced today that two of its academic co-founders published a [study in Nature Biotechnology](#) demonstrating that Moderna's messenger RNA therapeutics™ platform induced *in vivo* production of proteins to stimulate blood vessel growth, repair damaged heart tissue, and improve outcomes in a mouse model of myocardial infarction (MI).

The research, led by Moderna's academic co-founder Kenneth Chien, M.D., Ph.D., with the help of academic co-founder Derrick Rossi, Ph.D., provides proof-of-concept that messenger RNA therapeutics™ provide an effective and robust platform for gene transfer that could be applicable across a number of diseases. The *Nature Biotechnology* paper is the first peer-reviewed scientific publication describing the ability of messenger RNA therapeutics™ to stimulate *in vivo* production of human proteins and to achieve a long-term therapeutic effect.

Researchers injected mice with a single dose of VEGF-A-coded messenger RNA in the heart shortly following myocardial infarction to trigger production of the VEGF-A protein. VEGF-A (vascular endothelial growth factor-A) is an important angiogenic factor protein that mediates the growth of blood vessels. Mice injected with messenger RNA went on to generate new cardiovascular cells and show improvements on measures of cardiac function and survival when compared with controls.

"Regeneration of heart tissue through the mobilization of heart progenitor cells holds tremendous potential for the treatment of myocardial infarction and other forms of heart injury but has remained an elusive goal for over a decade," said Dr. Chien. "Over the past 20 years, many labs have attempted to repair damaged heart muscle in animal models by delivering VEGF-A and other factors to the heart using recombinant proteins, DNA plasmids, and engineered viruses—with little if any clinical success. The results we have seen using messenger RNA therapeutics™ mark the start of a new and exciting phase of drug development with potentially profound implications for patients."

In the study, the mice injected with VEGF-A-coded messenger RNA produced a "pulse-like" expression of a significant quantity of VEGF-A near the injection site. The production of VEGF-A in turn mobilized heart progenitor cells to produce functional, intact blood vessels in the heart and led to marked improvements in heart function and improved long-term survival of the mice for at least one year post-MI. Researchers attribute these effects to a reduction in the size of infarct region and an increase in capillary density in the affected region. In this way, the high-level, transient production of VEGF-A led to a sustained therapeutic improvement by altering the behavior of heart progenitor cells.

Introduction of modRNA was not associated with an innate immune response, further supporting the safety and effectiveness of this novel approach.

"We are extremely proud that our messenger RNA therapeutics™ platform enabled Ken to realize his vision and clinical intuition of the last 20 years," said Stéphane Bancel, president and founding CEO of Moderna. "Beyond the considerable implications for the treatment of heart injury, this publication provides an important validation of the potential of messenger RNA therapeutics™ across a wide range of diseases. The ability to stimulate protein production within cells will enable the treatment of many diseases that cannot be addressed today. What is also exciting is the fact that the Moderna team has considerably improved our technology since its performance for this groundbreaking study. The current generation of our technology is capable of producing 50 times more protein per dose, and our R&D team has many new improvements in the making, further increasing the potential of messenger RNA therapeutics™ to transform drug development and improve patients' lives."

Moderna in March announced an exclusive strategic option agreement with AstraZeneca to discover, develop, and commercialize messenger RNA therapeutics™ for the treatment of serious cardiovascular, metabolic, and renal diseases as well as selected targets in oncology. Targets covered under the agreement included the use of VEGF in the treatment of cardiovascular disease.

"Cardio-metabolic medicine is a core therapy area for AstraZeneca, and part of our research focuses on identifying novel therapies that will activate progenitor cells within the heart to turn into healthy heart cells. Recent findings by Dr. Chien and his team will play an important role in our work with Karolinska Institutet to advance cardiac regenerative therapy and our collaboration with Moderna Therapeutics to discover and develop messenger RNA therapeutics™," said Dr. Marcus Schindler, Head of the AstraZeneca Cardiovascular and Metabolic Disease Innovative Medicines Unit.

About Moderna Therapeutics

Moderna is pioneering [messenger RNA Therapeutics™](#), an entirely new *in vivo* drug modality that produces human proteins or antibodies inside patient cells, which are in turn active intracellularly or secreted. This breakthrough platform addresses currently undruggable targets and offers a superior alternative to existing drug modalities for a wide range of disease conditions. Moderna has developed a broad intellectual property estate, including 144 patent applications with 6,910 claims ranging from novel nucleotide chemistries to specific drug compositions. The company plans to develop and commercialize its innovative messenger RNA drugs—initially for rare diseases and oncology—while partnering drug candidates in other therapeutic areas in order to rapidly deliver this innovation to patients. Moderna is a privately held company based in Cambridge, Mass. Visit www.modernatx.com to learn more.