FACTOR® BIOSCIENCE

Technology Catalog

2021

Introduction

Ten years ago, my co-founder, Dr. Christopher Rohde, and I founded Factor Bioscience to develop new technologies in a little-explored area that we believed had enormous potential: messenger RNA (“mRNA”). We started our company in a small biotech incubator space, which we filled with used lab equipment purchased with our limited personal savings.

Today, Factor’s innovations are protected by more than 100 patents, including patents covering key discoveries in the areas of mRNA-based cell reprogramming and gene editing. We engage in, and fund research projects with our university collaborators focused on generating scientific knowledge to enable the development of new mRNA-based therapies. We have established partnerships with companies working to use our technology to develop new treatments for inflammatory, infectious, and genetic diseases, as well as cancer. Most importantly, we have created and invested in new companies that are using our technology to develop the next generation of engineered cell therapies.

In addition to new mRNA technologies, in this year’s technology catalog, you will read about two members of our scientific team who made major contributions to our company, our industry, and the field of mRNA. You will also read about our new ISO Class 7 cleanroom facility, recently completed at our Cambridge headquarters in the heart of Greater Boston's biotech community.

While we have come a long way from our small incubator space filled with used lab equipment, we are proud to have maintained the entrepreneurial spirit of those early days, and we look forward to being a part of this exciting field for years to come.

At Factor, we support a model of unlimited discovery. At Factor, science is our business.

Matt Angel, Ph.D.
Co-Founder, Chairman and CEO

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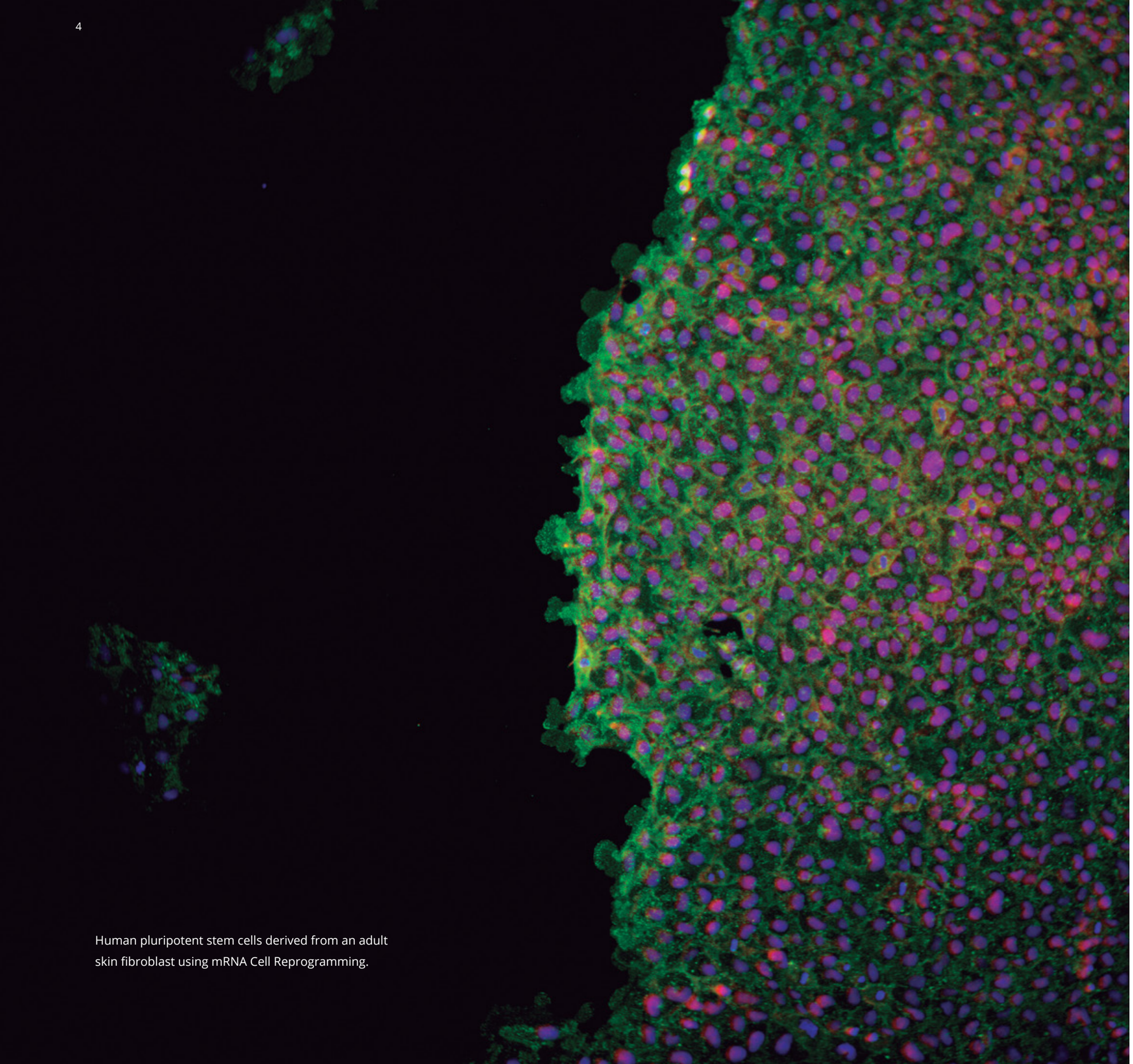
The Culture at Factor



Human pluripotent stem cells derived from an adult skin fibroblast using mRNA Cell Reprogramming.

Gene-Editing & Cell Reprogramming

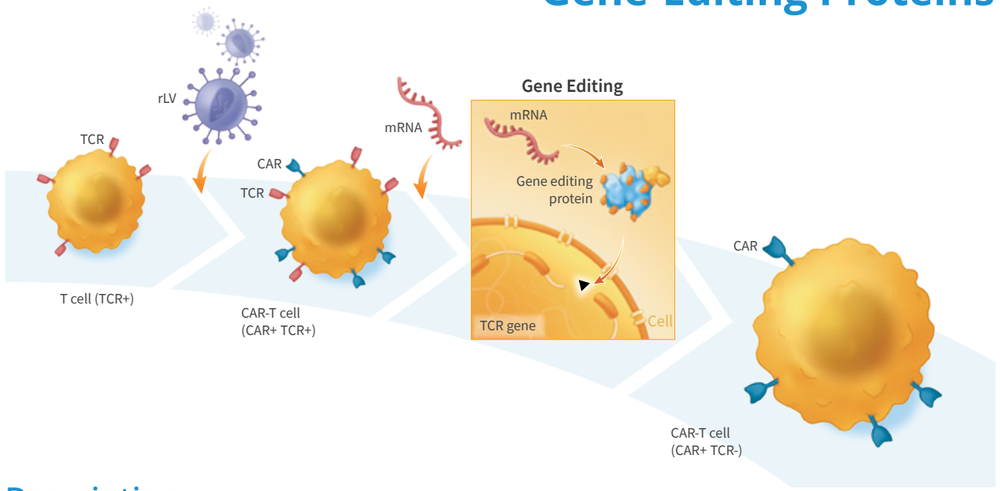
Cells contain two programs that work together to determine their behavior. A genetic program, written in the sequence of a cell's DNA, encodes information about each protein that the cell produces, while an epigenetic program not encoded in the sequence of a cell's DNA determines other heritable characteristics, including the amount of each protein produced. These two programs ensure that the trillions of cells that make up a complex multicellular organism act in concert to perform the many specialized functions needed for the organism to survive and grow.

We develop technologies to re-write these two cellular programs to treat disease and improve the way cells function.

Our gene-editing technologies enable the precise deletion, insertion, and repair of DNA sequences in living cells to correct disease-causing mutations, make cells resistant to infection and degenerative disease, modulate the expression of immunoregulatory proteins to enable the generation of durable allogeneic cell therapies, and engineer immune cells to more effectively fight cancer.

Our cell-reprogramming technologies enable the generation of clonal lines of pluripotent stem cells that can be expanded and differentiated into any desired cell type for the development of regenerative cell therapies.

mRNA Vectorization of Gene-Editing Proteins



Description

Gene-editing proteins can be used to inactivate, repair or insert sequences in living cells. Conventional approaches using plasmids or viruses to express gene-editing proteins can result in low-efficiency editing and unwanted mutagenesis when an exogenous nucleic acid fragment is inserted at random locations in the genome.

Our scientists developed a technology that uses mRNA to express gene-editing proteins. This technology can enable dramatically higher efficiency gene editing, including in primary cells, than other approaches, without using viruses or DNA-based vectors that may cause unwanted mutagenesis. This technology can be used, for example, to generate allogeneic CAR-T therapies for the treatment of cancer in which mRNA encoding gene-editing proteins are used to inactivate the endogenous T-cell receptor to prevent therapeutic T cells from causing graft-versus-host disease (GvHD), and/or to generate allogeneic stem cell-derived therapies in which mRNA encoding gene-editing proteins are used to inactivate one or more components of the human leukocyte antigen (HLA) complex to render the cells immuno-nonreactive or “stealth”.

mRNA Vectorization of Gene-Editing Proteins is protected by three U.S. patents (with additional patents pending in the U.S. and in other countries). Of note, certain granted patents include claims that are not limited by disease indication, cell type, target sequence, mRNA sequence or chemistry, or method of transfection.

Example Applications

- Ultra-high efficiency editing of T cells, fibroblasts, keratinocytes, and pluripotent stem cells
- Ultra-high specificity gene editing
- Virus-free and DNA-free gene editing
- Gene repair using a DNA-repair template
- Donor sequence insertion into a target genomic locus (e.g., TRAC, AAVS1 safe harbor, etc.)
- Gene-editing therapies (ex vivo and in vivo)
- Autologous and allogeneic engineered cell therapies (e.g., CAR-T, CAR-NK, stem cell-derived therapies, etc.)

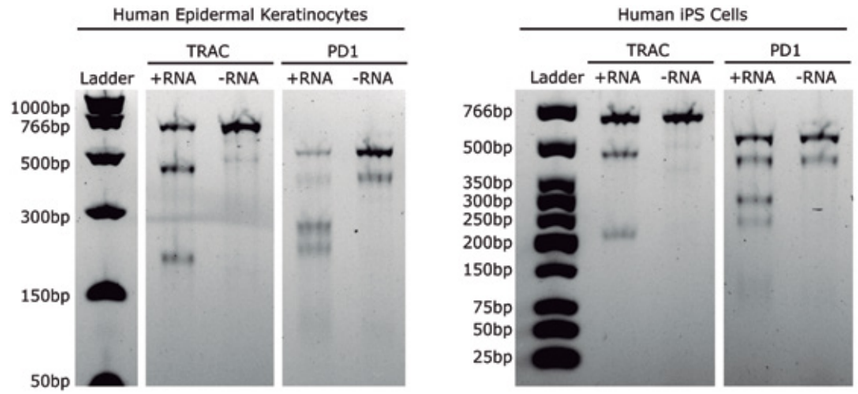


Figure 1. High-efficiency gene editing of TRAC and PD1 in human epidermal keratinocytes and human iPS cells.

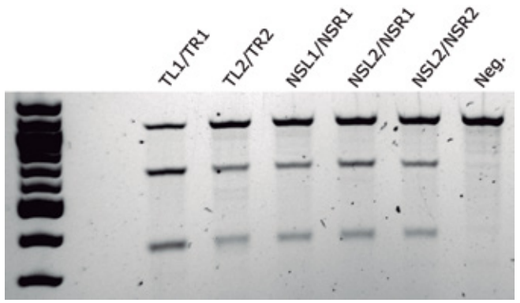


Figure 2. High-efficiency gene editing of the AAVS1 genomic safe harbor locus in human iPS cells.

Representative Claim

U.S. Pat. No. 10,662,410

A method for producing a gene-edited cell, comprising:

(a) providing a cell comprising a target DNA sequence;

(b) culturing the cell; and

(c) transfecting the cell with a plurality of synthetic RNA molecules, wherein the synthetic RNA molecules include:

i. a first synthetic RNA molecule encoding a first fusion protein comprising a DNA-binding domain and a catalytic domain of a nuclease; and

ii. a second synthetic RNA molecule encoding a second fusion protein comprising a DNA-binding domain and a catalytic domain of a nuclease; wherein:

the first fusion protein and the second fusion protein are independently a transcription activator-like effector nuclease (TALEN);

the transfecting results in the cell expressing the first fusion protein and the second fusion protein to result in a double-stranded break in the target DNA sequence; and

the first synthetic RNA molecule and the second synthetic RNA molecule are independently synthesized by in vitro transcription from a DNA template.

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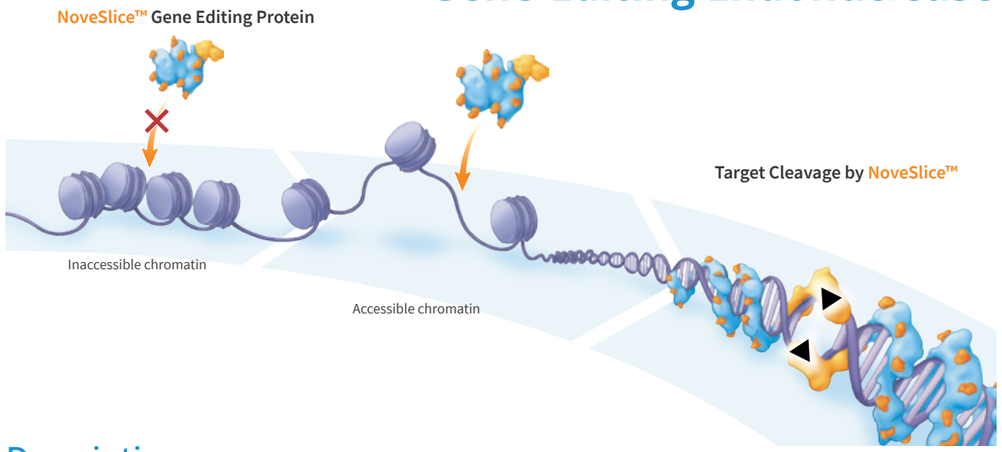
Chromatin Context-Sensitive Gene-Editing Endonuclease



Description

Many uses of gene-editing proteins are limited by their specificity ("off-target" effects), which can be of particular concern when these proteins are delivered or expressed in vivo.

Our scientists developed a novel high-specificity gene-editing endonuclease that exhibits high efficiency on target cutting and enhanced sensitivity to the chromatin context of the target site[1]. The protein comprises an array of DNA-binding repeat sequences connected by flexible linkers. This technology can be used to target cutting activity to genes that are actively expressed, reducing off-target effects, minimizing cellular toxicity, and enabling enhanced safety for therapeutic applications.

The Chromatin Context-Sensitive Gene-Editing Endonuclease is protected by nine U.S. patents, as well as patents in Australia, Japan, and Mexico (with additional patents pending in the U.S. and in other countries). Of note, certain granted patents include claims that are not limited by disease indication, cell type, target sequence, or vector.

Example Applications

- Ultra-high efficiency editing of primary cells (up to 100% by IDAA assay[1])
- Ultra-high specificity gene editing (e.g., express gene-editing proteins with 36-40 base target sequences)
- Combine with Factor's mRNA Vectorization of Gene-Editing Proteins technology for virus-free and DNA-free gene editing
- Gene repair using a DNA-repair template
- Donor sequence insertion into a target genomic locus (e.g., TRAC, AAVS1 safe harbor, etc.)
- Gene-editing therapies (ex vivo and in vivo)
- Autologous and allogeneic engineered cell therapies (e.g., CAR-T, CAR-NK, stem cell-derived therapies, etc.)
- Combine with Factor's mRNA Cell Reprogramming technology to generate models of genetic disease, gene-corrected patient-specific cell therapies, and allogeneic (i.e., immuno-nonreactive or "stealth") cell therapies, including allogeneic pluripotent stem cell-derived CAR-T and CAR-NK cell therapies for the treatment of cancer, and engineered mesenchymal stem cell (MSC) therapies for regenerative medicine, wound-healing, inflammatory and auto-immune diseases, and tumor-targeting applications

[1]Kopacz, M., et al. Mol Ther, Vol 28 No 4S1, 2020.

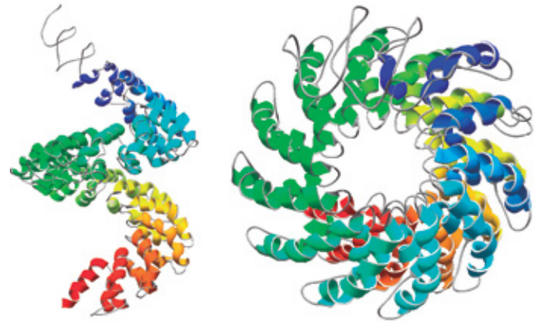


Figure 1. Example Chromatin Context-Sensitive Gene-Editing Endonuclease DNA-binding domain.

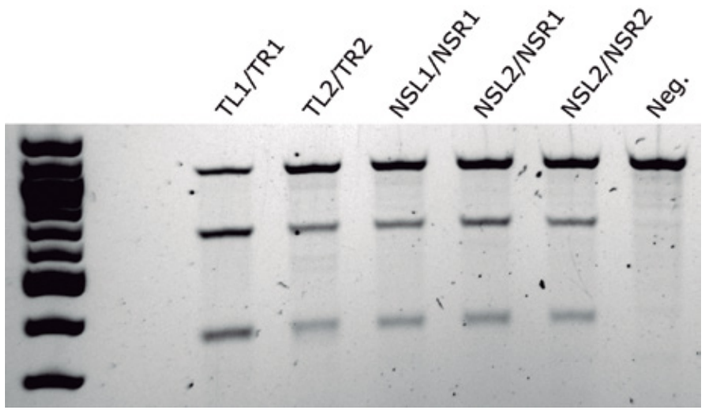


Figure 2. High-efficiency gene editing of the AAVS1 genomic safe harbor locus in human iPS cells.

Representative Claim

U.S. Pat. No. 9,758,797

A composition comprising a nucleic acid encoding a gene-editing protein, the gene-editing protein comprising: (a) a DNA-binding domain and (b) a nuclease domain, wherein:

(a) the DNA-binding domain comprises a plurality of repeat sequences and at least one of the repeat sequences comprises the amino acid sequence: LTPvQVVAIAwxyzGHGG (SEQ ID NO: 75) and is between 36 and 39 amino acids long, wherein:

"v" is Q, D or E,

"w" is S or N,

"x" is N,

"y" is D, A, H, N, K, or G, and

"z" is GGKQALETVQRLLPVLCQD (SEQ ID NO: 670) or

GGKQALETVQRLLPVLCQA (SEQ ID NO: 671); and

(b) the nuclease domain comprises a catalytic domain of a nuclease.

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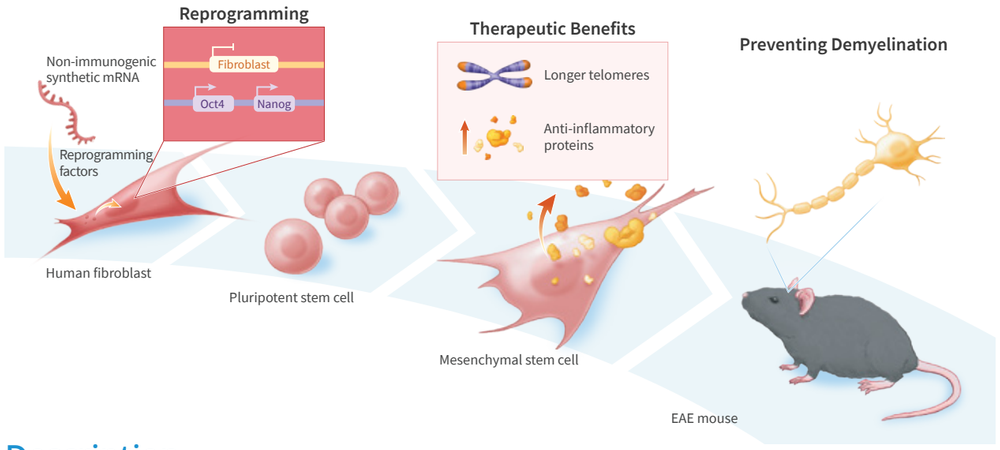
mRNA Cell Reprogramming



Description

Conventional reprogramming methods (e.g., using Sendai virus or episomal vectors) can result in very low-efficiency reprogramming, can select for cells with abnormal growth characteristics, and can leave traces of the vector in reprogrammed cells.

Our scientists developed a technology for reprogramming cells that uses mRNA to express reprogramming factors[2].

mRNA Cell Reprogramming is protected by nine U.S. patents, as well as patents in Australia, China, Europe, Japan, Mexico, and Russia (with additional patents pending in the U.S. and in other countries). Of note, certain granted patents include claims that are not limited by disease indication, cell type, reprogramming factor(s), mRNA sequence or chemistry, or method of transfection.

Example Applications

- Ultra-high efficiency reprogramming (e.g., reprogram single cells)
- Reprogram without using viruses or other potentially mutagenic vectors
- Reprogram cells quickly, and using a simple protocol (e.g., 4-6 transfections, pick colonies in 8-12 days)
- Reprogram without feeders, conditioning, passaging, immunosuppressants, demethylating agents or other toxic small molecules, pre-mixing or aliquoting of RNA solutions
- Reprogram using a completely animal component-free process
- Use for the development of allogeneic or autologous cell therapies
- Combine with Factor's Chromatin ContextSensitive Gene-Editing Endonuclease and/or Factor's Combined mRNA Gene Editing & Cell Reprogramming technology to generate models of genetic disease, gene-corrected patient-specific cell therapies, and allogeneic (i.e., immunononreactive or "stealth") cell therapies, including allogeneic pluripotent stem cell-derived CAR-T and CAR-NK cell therapies for the treatment of cancer, and engineered mesenchymal stem cell (MSC) therapies for regenerative medicine, wound-healing, inflammatory and auto-immune diseases, and tumor-targeting applications

[2]Harris, J., et al. Mol Ther, Vol 28 No 4S1, 2020.

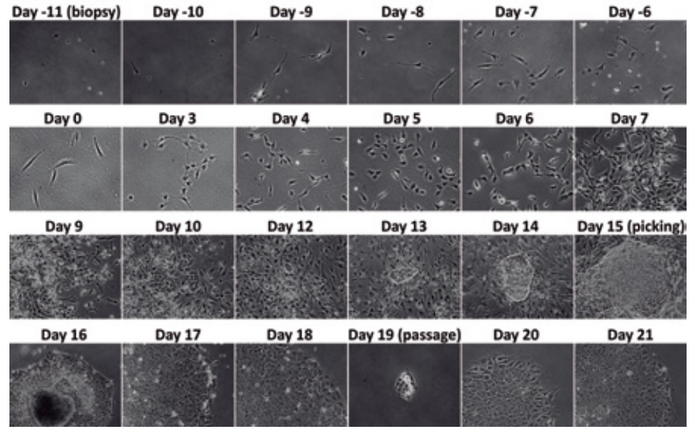


Figure 1. mRNA Cell Reprogramming from biopsy to pluripotent stem cell line.

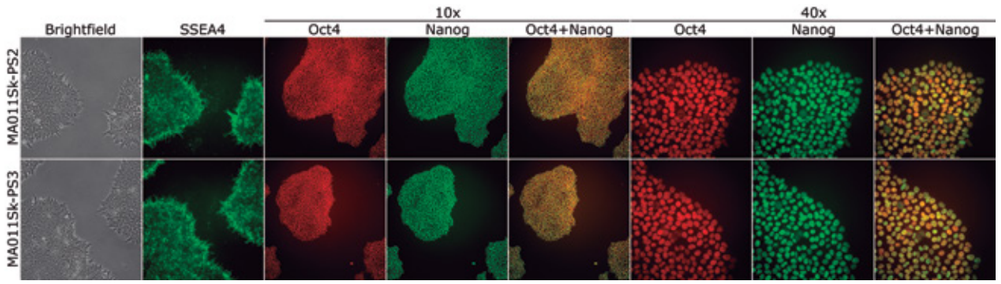


Figure 2. Characterization of human pluripotent stem cells generated using mRNA Cell Reprogramming.

Representative Claim

U.S. Pat. No. 10,443,045

A method for reprogramming a non-pluripotent cell, comprising:

(a) providing a non-pluripotent cell;

(b) culturing the non-pluripotent cell; and

(c) transfecting the non-pluripotent cell with one or more synthetic RNA molecules,

wherein the one or more synthetic RNA molecules include at least one RNA molecule encoding one or more reprogramming factors;

wherein the transfecting results in the cell expressing the one or more reprogramming factors to result in the cell being reprogrammed; and

wherein step (c) is performed at least twice and the amount of one or more synthetic RNA molecules transfected in one or more later transfections is greater than the amount transfected in one or more earlier transfections to result in the non-pluripotent cell being reprogrammed and occurs in the presence of a medium containing ingredients that support reprogramming of the non-pluripotent cell.

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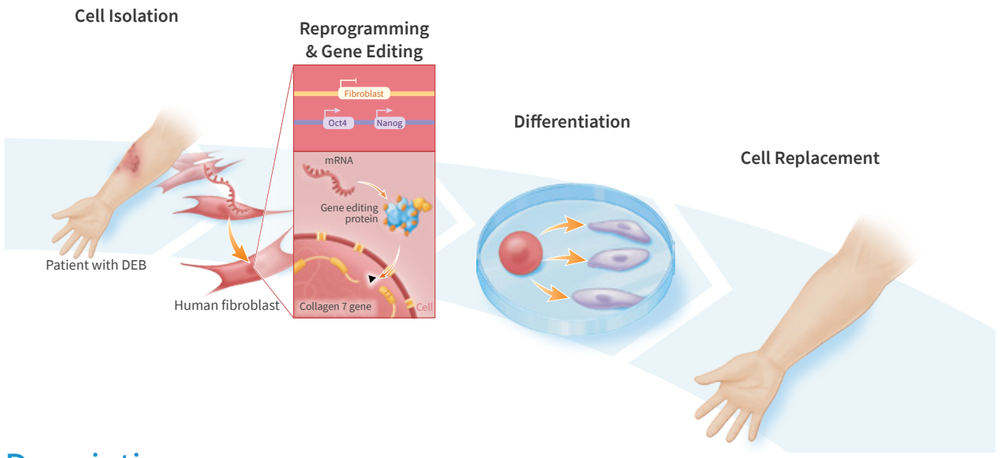
Combined mRNA Gene-Editing & Cell Reprogramming



Description

Combining gene editing with cell reprogramming enables the generation of gene-corrected personalized cell therapies, models of genetic disease, engineered cell therapies, including allogeneic (i.e., immuno-nonreactive or "stealth") cell therapies, including CAR-T, CAR-NK, and engineered mesenchymal stem cell (MSC) therapies for regenerative medicine, wound-healing, inflammatory and auto-immune diseases, and tumor-targeting applications.

Our scientists developed a technology that uses mRNA to express both gene editing proteins and reprogramming factors.

Combined mRNA Gene Editing & Cell Reprogramming is protected by U.S. Patent Number 10,472,611 (with additional patents pending in the U.S. and in other countries). Of note, the granted patent includes claims that are not limited by disease indication, cell type, reprogramming factor(s), mRNA sequence or chemistry, transfection method, target sequence, or type of gene-editing protein.

Example Applications

- Generate gene-corrected personalized cell therapies
- Simplify manufacturing of engineered cell therapies by eliminating serial gene-editing and cell-reprogramming steps
- Take advantage of the clonality of mRNA Cell Reprogramming to generate defined clonal populations of gene-edited cells
- Generate allogeneic pluripotent stem cell-derived CAR-T and CAR-NK cell therapies for the treatment of cancer, and engineered mesenchymal stem cell (MSC) therapies for regenerative medicine, wound-healing, inflammatory and auto-immune diseases, and tumor-targeting applications

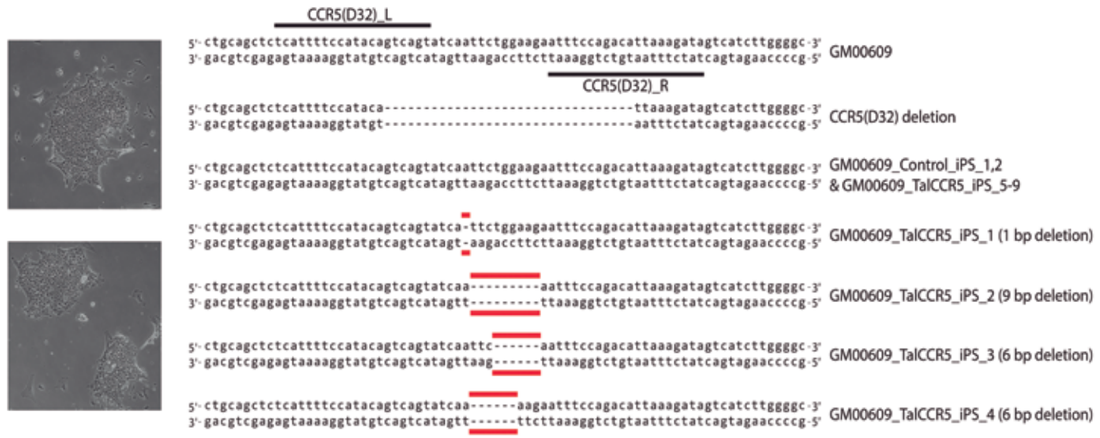


Figure 1. Combined mRNA Gene Editing & Cell Reprogramming to create clonal pluripotent stem cell lines containing defined deletions in the CCR5 gene.

Representative Claim

U.S. Pat. No. 10,472,611

A method for producing a gene-edited, reprogrammed cell, comprising:

(a) providing a non-pluripotent cell;

(b) culturing the non-pluripotent cell; and

(c) transfecting the non-pluripotent cell with one or more synthetic RNA molecules, wherein the one or more synthetic RNA molecules include:

(i) at least one RNA molecule encoding one or more reprogramming factors, and

(ii) at least one RNA molecule encoding one or more gene-editing proteins;

wherein the transfecting results in the cell expressing the one or more reprogramming factors and the one or more gene editing proteins to result in a gene-edited, reprogrammed cell;

wherein step (c) is performed without using irradiated human neonatal fibroblast feeder cells and occurs in the presence of a medium containing ingredients that support reprogramming of the cell.

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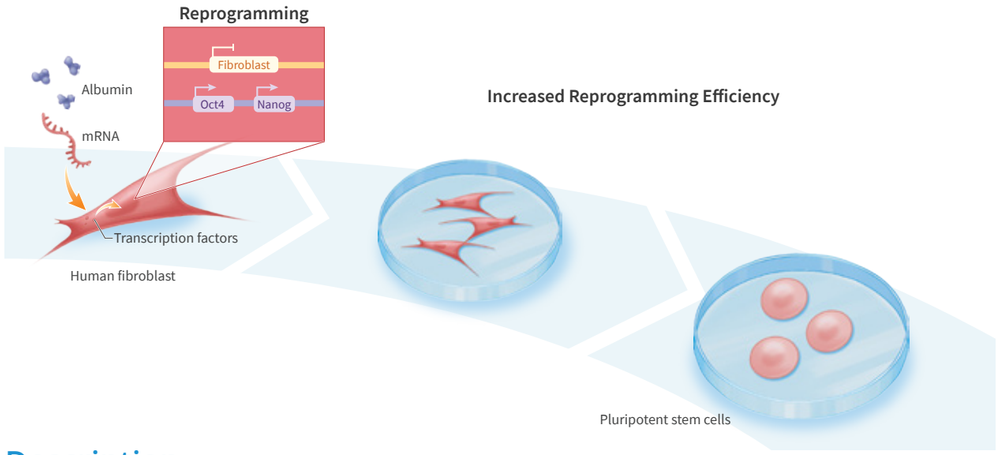
Cell Reprogramming Medium



Description

Conventional cell-culture media, including serum-free and animal component-free media, can result in very low efficiency cell reprogramming.

Our scientists developed a novel cell-culture medium that can enable dramatically higher efficiency cell reprogramming than conventional media, including when mRNA is used to express reprogramming factors[3].

The Cell Reprogramming Medium is protected by U.S. Patent Number 9,127,248, as well as patents in Australia, China, Japan, The Republic of Korea, and Mexico (with additional patents pending in the U.S. and in other countries). Of note, the granted U.S. patent includes claims that are not limited by disease indication, cell type, or method of reprogramming.

Example Applications

- Ultra-high efficiency reprogramming (e.g., reprogram single cells)
- Reprogram without using viruses or other potentially mutagenic vectors
- Reprogram cells quickly, and using a simple protocol (e.g., 4-6 transfections, pick colonies in 8-12 days)
- Reprogram without feeders, conditioning, passaging, immunosuppressants, demethylating agents or other toxic small molecules, pre-mixing or aliquoting of RNA solutions
- Reprogram using a completely animal component-free process
- Use for the development of allogenic or autologous cell therapies
- Combine with Factor's Chromatin Context-Sensitive Gene-Editing Endonuclease and/or Factor's Combined mRNA Gene Editing & Cell Reprogramming technology to generate models of genetic disease, gene-corrected patient-specific cell therapies, and allogeneic (i.e., immuno-nonreactive or "stealth") cell therapies, including allogeneic pluripotent stem cell-derived CAR-T and CAR-NK cell therapies for the treatment of cancer, and engineered mesenchymal stem cell (MSC) therapies for regenerative medicine, wound-healing, inflammatory and auto-immune diseases, and tumor-targeting applications

[3]Harris, J., et al. Mol Ther, Vol 29, No 4S1, 2021.

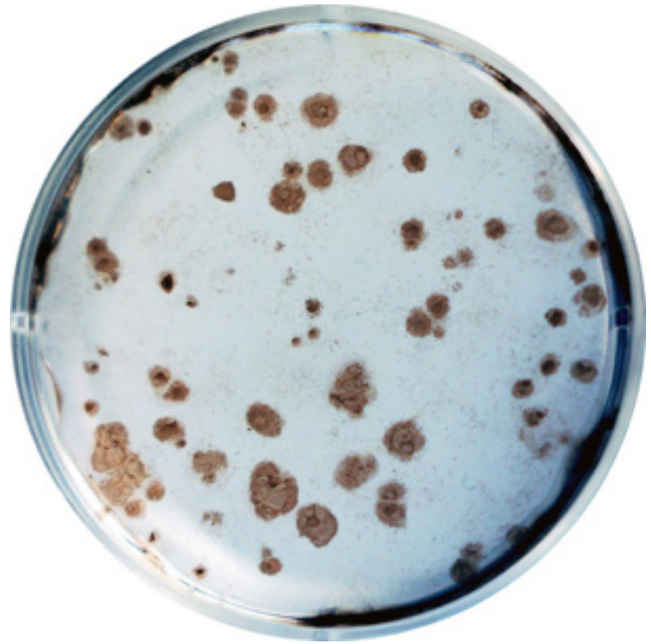


Figure 1. High-efficiency mRNA cell reprogramming of primary human fibroblasts (colonies stained for SSEA4).

Representative Claim

U.S. Pat. No. 9,127,248

A cell-culture medium comprising: DMEM/F12, 10 µg/mL insulin, 5.5 µg/mL transferrin, 6.7 ng/mL sodium selenite, 20 ng/mL bFGF, and 5 mg/mL albumin, wherein less than 0.65% of the albumin's dry weight comprises lipids and/or less than 0.35% of the albumin's dry weight comprises free fatty acids.

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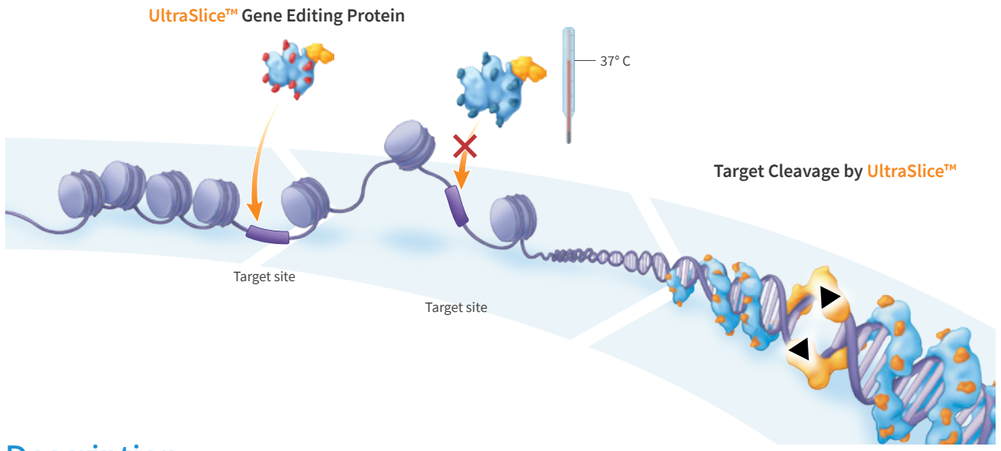
Temperature-Tunable Gene-Editing Endonuclease



Description

Conventional approaches to in vivo gene editing using viral vectors or lipid nanoparticles can result in limited tissue-targeting.

Our scientists developed a novel high-specificity gene-editing endonuclease that exhibits high-efficiency on-target cutting at sub-physiological temperatures[4]. This technology can be used to target cutting activity to specific organs and tissues, allowing higher doses, minimizing systemic effects, and enabling enhanced safety for therapeutic applications.

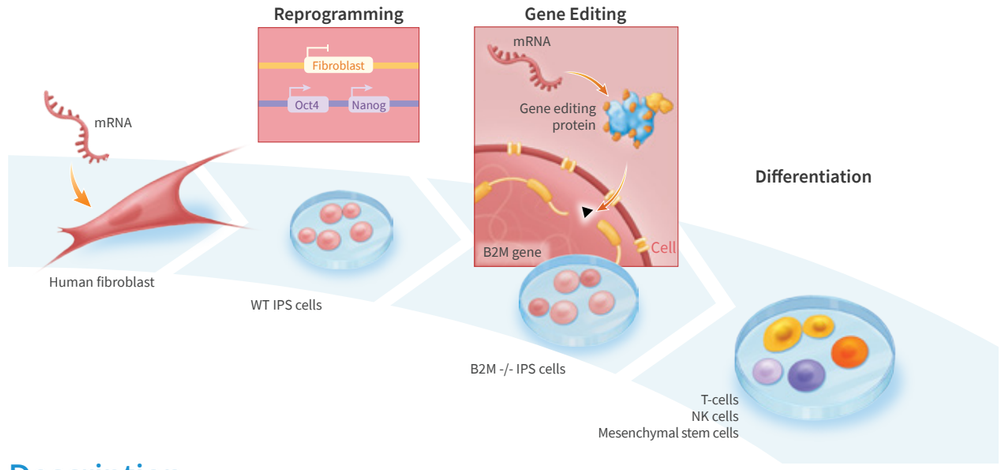
The Temperature-Tunable Gene-Editing Endonuclease is protected by a pending U.S. patent (with additional patents pending in other countries).

Example Applications

- Ultra-high efficiency editing of primary cells and pluripotent stem cells
- Ultra-high specificity gene editing
- Virus-free and DNA-free gene editing
- Gene repair using a DNA-repair template
- Donor sequence insertion into a target genomic locus (e.g., TRAC, AAVS1 safe harbor, etc.)
- Gene-editing therapies (ex vivo and in vivo)
- Autologous and allogeneic engineered cell therapies (e.g., CAR-T, CAR-NK, stem cell-derived therapies, etc.)
- Combine with Factor's mRNA Cell Reprogramming technology to generate models of genetic disease, gene-corrected patient-specific cell therapies, and allogeneic (i.e., immuno-nonreactive or "stealth") cell therapies, including allogeneic pluripotent stem cell-derived CAR-T and CAR-NK cell therapies for the treatment of cancer, and engineered mesenchymal stem cell (MSC) therapies for regenerative medicine, wound-healing, inflammatory and auto-immune diseases, and tumor-targeting applications

[4]Osayame, Y., et al. Mol Ther, Vol 29 No 4S1, 2021.

Gene-Edited Allogeneic Cell Therapies



Description

Allogeneic cell therapies can enable "off-the-shelf" treatment options. Conventional allogeneic cell therapy approaches can result in rejection, low potency, and in the case of allogeneic immune cell therapy, graft-versus-host disease.

Our scientists developed a technology that uses gene editing to address limitations of conventional approaches to allogeneic cell therapy[5]. This technology can be used to generate allogeneic cell therapies with high potency and enhanced targeting.

The Gene-Edited Allogeneic Cell Therapies technology is protected by a pending U.S. patent (with additional patents pending in other countries).

Example Applications

- Ultra-high efficiency editing of T cells, fibroblasts, keratinocytes, and pluripotent stem cells
- Ultra-high specificity gene editing
- Virus-free and DNA-free gene editing
- Gene repair using a DNA-repair template
- Donor sequence insertion into a target genomic locus (e.g., TRAC, AAVS1 safe harbor, etc.)
- Gene-editing therapies (ex vivo and in vivo)
- Allogeneic engineered cell therapies (e.g., CAR-T, CAR-NK, stem cell-derived therapies, etc.)

[5]Kopacz, M., et al. Mol Ther, Vol 29, No 4S1, 2021.

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The Culture at Factor

Our culture is one of curiosity and discovery, driven by a desire to invent new technologies to treat disease and improve health.

At Factor, we strive to immerse our scientists in an environment that provides all of the resources they need to be successful.

In this environment, we have assembled a vibrant and diverse community of people collaborating to produce outstanding results.

Jasmine Harris, Associate Scientist

"For two years, I was sort of off in a corner, differentiating these cells, testing out and characterizing them, and writing up procedures for animal studies. And then COVID happened, and suddenly there was high interest in anti-inflammatory therapies."

Finding Passion and Purpose in Her Work

When Jasmine Harris graduated with a bachelor's degree in Materials Science and Engineering from MIT and began her job search, she hadn't taken a biology course since her freshman year. She was seeking a research position that would give her independence, responsibility, and allow her to learn a new scientific discipline. And, while Jasmine had worked for two years in a biological conservation lab in high school, she was determined not to pursue a career in biology. "I'm also very stubborn," she said. "I never wanted to fit into expectations based on my gender identity. I felt the need to defy expectations and show I could do anything my male peers could do. So, biology was out because that's the science I was told to go into," she stated.

After starting in chemistry at MIT, she discovered MIT's undergraduate program in Materials Science and Engineering, seeing it as an opportunity to learn many different aspects of science and engineering. "That worked for me because, while I love to learn different things, I'm very non-committal. I just realized I'm sort of like stem cells in that I'm very non-committal. I want to be everything," she said.

Most biotechnology companies require candidate researchers to have a bachelor's or master's degree in biology or a related field or to have experience in biological research. But Jasmine was offered, and accepted, an Associate Scientist position with Novellus Therapeutics, a company created by Factor Bioscience to develop therapeutic products based on Factor's mRNA, gene-editing, and cell-reprogramming technologies. "I ended up choosing this company over other companies because it granted me the most agency—and it also gave me the most opportunity to learn something new," she said. "I guess someone might call it a risky decision," she said. "But I saw the potential in the technology, and I was very curious to learn a new field. I knew it was a unique opportunity."

Beginning a Career in Science

In entering a new scientific field, Jasmine faced many challenges. But her new employers, Dr. Matt Angel and Dr. Christopher Rohde, worked closely with her, mentoring her through the ups and downs of her early days. "When I joined the company, the first project that I led dealt with uncoded regions of mRNA," said Jasmine. "At the same time, I started to learn how to reprogram cells from Matt, turning fibroblasts into stem cells. And I was doing those two things simultaneously to figure out if I wanted to be on the molecular biology side or the cell biology side," she explained. "I was learning a new field on the fly while I also was expected to produce viable research for the company."

An Opportunity Arises to Address a Global Challenge

Jasmine found that she liked cell biology and wanted to focus on cell work. So, after a meeting with Dr. Angel, they decided to differentiate the in-house produced pluripotent stem cells into mesenchymal stem cells (MSCs). "For two years, I was sort of off in a corner, differentiating these cells, testing out and characterizing them, and writing up procedures for animal studies. And then COVID happened, and suddenly there was high interest in anti-inflammatory therapies."

In 2020, only two years after she had started work, Jasmine's research fundamentally transformed her company. Jasmine presented the results of her work on generating MSCs using advanced mRNA cell reprogramming technology at the American Society of Gene & Cell Therapy 2020 Annual Meeting. Later that year, her work resulted in a multimillion-dollar contract with a public pharmaceutical company to develop an MSC-based treatment for acute respiratory distress syndrome (ARDS), including in COVID-19 patients, and Novellus shifted to focus entirely on developing MSC-based therapies. In April 2021, Novellus secured a second multimillion-dollar contract with another public company, and in July 2021, Novellus was acquired by that company for $125 million.

"Jasmine is one of those rare individuals with both the capacity to perform challenging scientific research and the drive to push through the challenges and achieve success. It is difficult to convey the magnitude of the impact that Jasmine has had on our company, our industry, and the field of regenerative medicine in only three short years. I am incredibly grateful for having had the opportunity to work with Jasmine," said Dr. Angel, CEO and Co-Founder of Factor Bioscience and Co-Founder of Novellus Therapeutics.

"I have found a field of study I'm passionate about," said Jasmine. "That's a huge takeaway for me. I started as someone who had minimal direction regarding where I wanted to go for my research, and now I feel very directed and focused. I know that I want to do regenerative medicine. I know I want to work with stem cells. I know the cellular lineage that I want to go into. This is a huge takeaway for me," said Jasmine.

Jasmine recommends anyone going from undergrad to grad school take a couple of years to work in industry. "I feel more equipped for grad school. I've had to deal with high-pressure timelines that go with multimillion-dollar research projects." When asked what she would advise a job seeker in biotech today, she paused. "Don't settle for something because it's what you initially got into or thought you wanted. If I had pursued a career in materials science, I would have been miserable," she stated emphatically.

"At the end of the day, if you're unhappy, it's not going to be worth it because you're not going to be able to do as much research that will have an impact as you would if you were passionate about your work." And Jasmine's passion and hard work have paid off. She has been accepted into the Developmental & Stem Cell Biology Graduate Program at the University of California San Francisco, one of the top graduate programs globally for stem cell research, and leaves Factor Bioscience to start her Ph.D. program in the fall.

Franklin Kostas, Associate Scientist

"I spent five months banging my head against the wall, trying a million things that didn't work at all," said Franklin. "So, to have this actually work was really, really great, and it was very encouraging. My experience at Factor has helped put me on the track toward science."

Realizing Achievement and Direction through Research

Franklin Kostas joined one of Factor Bioscience's spinoffs, Novellus Therapeutics, as an Associate Scientist after graduating with a Bachelor of Science degree in chemistry from Haverford College in 2018. Many from his graduating class went straight into graduate school or took technician positions in university labs, but Franklin decided to work in industry before pursuing his Ph.D.

"Even though I loved chemistry, I didn't want to jump right into five to seven more years of school," Franklin said. "What drew me to this particular job was the small, tight-knit team. They had me present my research, and they were engaged with it. It was just clear that they were very, very smart and also warm and receptive. And it felt like a group of people that I would fit in with," he stated. Franklin described leaving the interview, deciding that if he were offered the job, he would take it no matter what. He was thrilled when he received the offer letter. He accepted the job immediately and moved to Cambridge.

A Promising Scientist Given Freedom and Responsibility

Initially, Dr. Matt Angel, CEO and Co-Founder of Factor Bioscience and Co-Founder of Novellus Therapeutics, and Dr. Christopher Rohde, Chief Technology Officer and Co-Founder of Factor Bioscience and Co-Founder of Novellus Therapeutics, presented Franklin with the challenge of developing a formulation to deliver mRNA to cells in vivo. Dr. Angel worked closely with Franklin as he designed his research strategy. Franklin described his early days at the company as almost entirely self-directed. "Matt and Chris have a very hands-off management style, which I have come to prefer," he said. "They were happy to provide assistance and talk things through with me, but I was also given a lot of freedom and responsibility to find some of the directions that we were going to take."

Franklin described long hard months spent trying to find a solution after discovering that many of the molecules he was working with were inhibited by serum. And he took note of Dr. Angel and Dr. Rohde's approach to research when things aren't going as planned. "I learned something from them. When things don't work right, Matt and Chris have this incredible capability to redouble their efforts and keep trying," he stated. "It's counterintuitive. You want to pull back if you're not getting good results out of your work. At that point, you don't want to put hard work in, but Matt and Chris actually will increase their efforts," he said. "That's something that I've tried to apply to other parts of my life."

A Discovery at the Interface of Chemistry and Biology

Franklin designed and executed many rounds of experiments using both panels of lipid and polymer-based reagents that he selected for this purpose as well as molecules that he designed and synthesized himself. His results led him to develop a family of novel chemical substances, including a group of ionizable fusogenic lipids, which he synthesized for the first time in the company's lab. Through in vitro and in vivo experiments, Franklin discovered that his new lipids allowed superior mRNA delivery to cells, including delivery of gene-editing mRNA and mRNA encoding COVID-19 antigens.

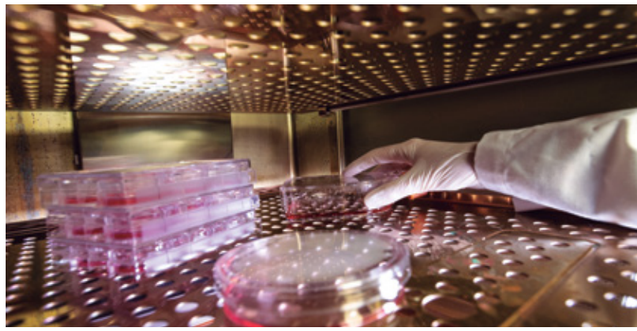
Franklin's discovery has so far resulted in four granted U.S. patents, a presentation at the American Society of Gene & Cell Therapy 2020 Annual Meeting, and a sponsored research collaboration with the National University of Ireland, Galway. More recently, Franklin's work has yielded two multimillion-dollar contracts under which Factor's partners will use Franklin's lipids to develop new therapies for the treatment of various genetic diseases and cancers.

"In addition to his work on mRNA delivery, Franklin has made meaningful contributions to many other areas of our company, including the development of gene-editing proteins comprising novel DNA-binding domains," said Dr. Angel. "Franklin is an incredibly talented scientist, and his achievements clearly reflect his extraordinary aptitude for independent research."

A Solid Foundation for a Career in Science

"I spent five months banging my head against the wall, trying a million things that didn't work at all," said Franklin. "So, to have this actually work was really, really great, and it was very encouraging. My experience at Factor has helped put me on the track toward science. And it feels like something that I could do for a career."

When asked what he would advise someone considering science as a career, he replied, "For someone who is in college and contemplating a career in scientific research, I would definitely recommend taking some time to work in industry. For me, it's been beneficial in terms of finding a direction and understanding the type of science that I want to do. You know, I once thought I wanted to be a doctor. And then I discovered science, and moved away from medicine. But my time at Factor has helped me understand that I want to do something much closer to therapeutic development, much more directed towards solving a problem."



Franklin leaves Factor to begin his Ph.D. program at the Massachusetts Institute of Technology's Department of Chemistry in the fall.

ISO Class 7 Cleanroom Facility

This year, we completed the construction of an ISO Class 7 cleanroom facility at our headquarters in Cambridge, Massachusetts. Our new facility is designed to produce cutting-edge mRNA and cellular medicines for all phases of clinical testing.

In this facility, we will produce cells that have been reprogrammed and gene-edited using mRNA for anti-inflammatory, anti-cancer, and regenerative-medicine applications. We will also produce next-generation mRNA vaccines designed to elicit a robust and durable immune response against diverse pathogens.

In addition to supporting our own projects, we are pleased to provide our partners with access to our cleanrooms to support and accelerate their clinical programs.

Disease-Focused Technologies

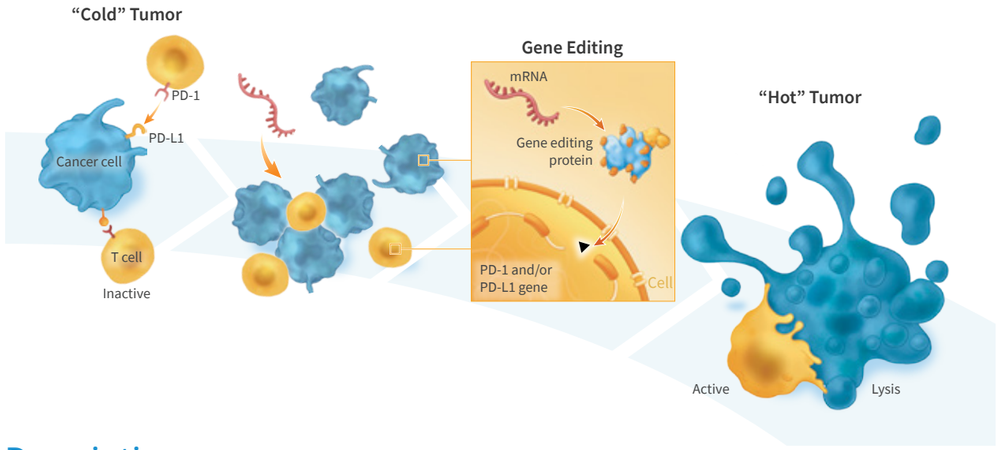
Human disease is caused by cellular dysfunction. Genetic diseases and cancer result from errors in a cell's genetic program that are introduced during cell division (either in the organism itself or its ancestors), while infectious, autoimmune, and degenerative diseases result from cells' susceptibility to pathogenic, environmental, and metabolic factors. While every disease is unique, the link to cellular function provides opportunities to intervene in the disease state using cell engineering technologies.

We develop technologies that can be used to create treatments for cancer, genetic, infectious, and degenerative diseases.

Our cell engineering technologies enable the unmasking of immunosuppressive (i.e., "cold") tumors, correction of disease-causing mutations, inactivation of cell surface receptors to generate infection-resistant cells, inactivation of genes responsible for degenerative proteopathies, and inactivation of ion channels responsible for aberrant neuronal activity associated with chronic pain.

Human neurons derived from an adult skin fibroblast using mRNA Cell Reprogramming.

Gene-Editing Checkpoint Molecule Genes for the Treatment of Cancer



Description

Checkpoint molecule genes act to prevent the immune system from attacking normal cells. In many cancers, the expression of checkpoint molecule genes by cancer cells prevents their destruction by the immune system (a "cold" tumor).

Our scientists developed a method for treating cancer by inactivating checkpoint molecule genes in cancer cells using mRNA encoding gene-editing proteins to unmask the cancer cells to the immune system, and thus turn a "cold" tumor "hot".

Gene Editing Checkpoint Molecule Genes for the Treatment of Cancer is protected by six U.S. patents (with additional patents pending in the U.S. and in other countries). Of note, certain granted patents include claims that are not limited by type of cancer, specific checkpoint molecule gene, mRNA sequence or chemistry, or type of gene-editing protein.

Example Applications

- Inactivate checkpoint molecule genes in tumor cells to unmask them to the immune system
- Treat metastatic disease by training the immune system on unmasked tumor cells
- Combine with Factor's Chromatin Context-Sensitive Gene-Editing Endonuclease for high-specificity inactivation of target checkpoint molecule genes
- Combine with Factor's ToRNAdo™ Nucleic-Acid Delivery System for high-efficiency delivery to tumor cells in vivo
- Inactivate multiple checkpoint molecule genes to unmask multi-pathway-resistant tumor cells

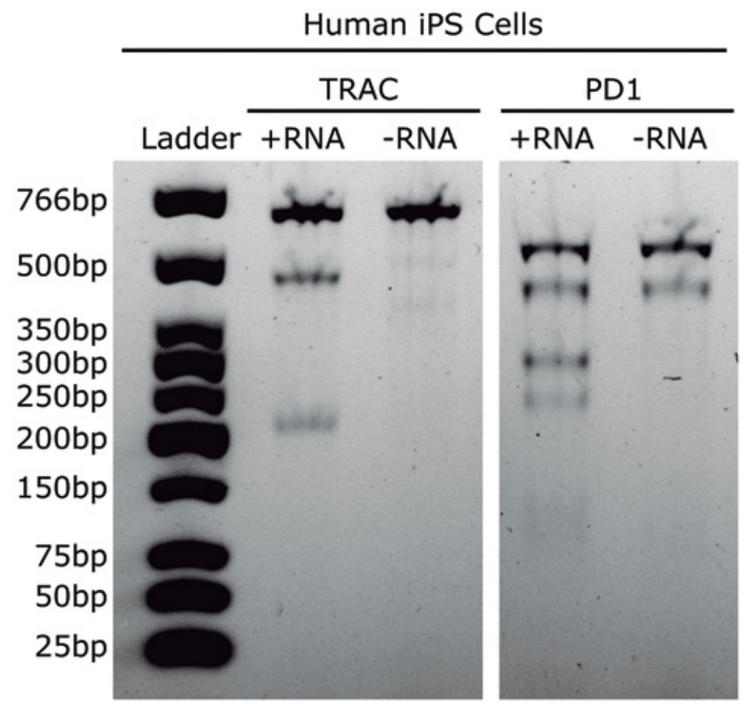


Figure 1. Gene editing the TRAC gene and the checkpoint molecule gene PD1 in human iPS cells.

Representative Claim

U.S. Pat. No. 10,363,321

An in vivo method for treating cancer in a subject comprising:

administering to the subject by intratumoral injection a non-viral, cell-free composition comprising a synthetic messenger RNA (mRNA) encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, and

causing a single-strand or double-strand break in the DNA of a tumor cell, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the tumor cell in the subject, resulting in the stimulation or enhancement of an immune response in the subject;

thereby treating cancer in the subject.

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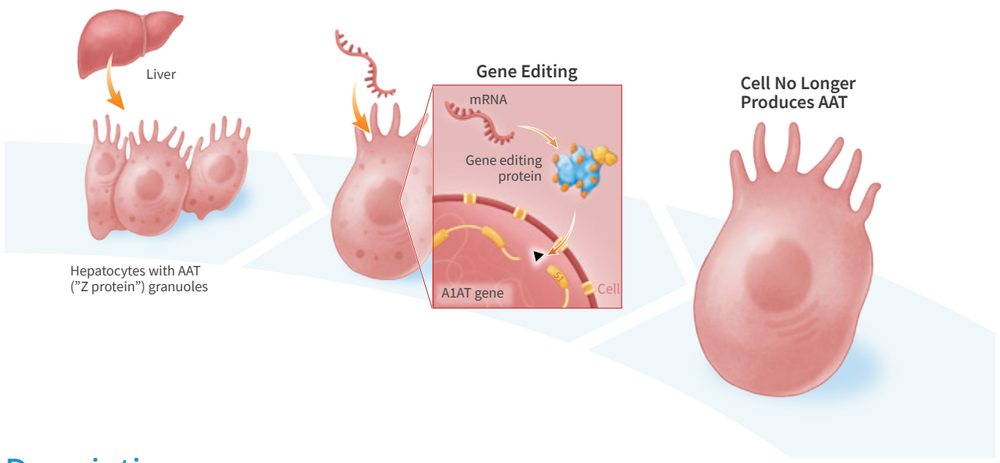
Gene-Editing Therapies for Alpha-1-Antitrypsin Deficiency



Description

Alpha-1-antitrypsin deficiency is a disease caused by mutations in the A1AT gene. Patients with this disease experience progressive liver failure, as well as lung irritation and damage. Most patients with AAT deficiency are homozygous for the Glu342Lys mutation, which causes cells to produce a form of AAT that aggregates into toxic intracellular polymers.

Our scientists developed a method for treating AAT deficiency by editing the A1AT gene using mRNA to express gene-editing proteins.

Gene-Editing Therapies for Alpha-1-Antitrypsin Deficiency is protected by U.S. Patent Number 10,576,167 (with additional patents pending in the U.S. and in other countries). Of note, certain claims of the granted patent are not limited by specific target sequence, formulation, or route of administration.

Example Applications

- Develop a single therapy for the majority of patients – most AAT deficiency patients share the same mutation (Glu342Lys)
- Avoid gene repair or gene insertion by using a combination therapy that includes AAT protein replacement
- Express gene-editing proteins in vivo or harvest cells, gene-edit ex vivo and infuse gene-edited cells
- Combine with Factor's mRNA Cell Reprogramming technology to generate a clonal line of gene-corrected pluripotent stem cells

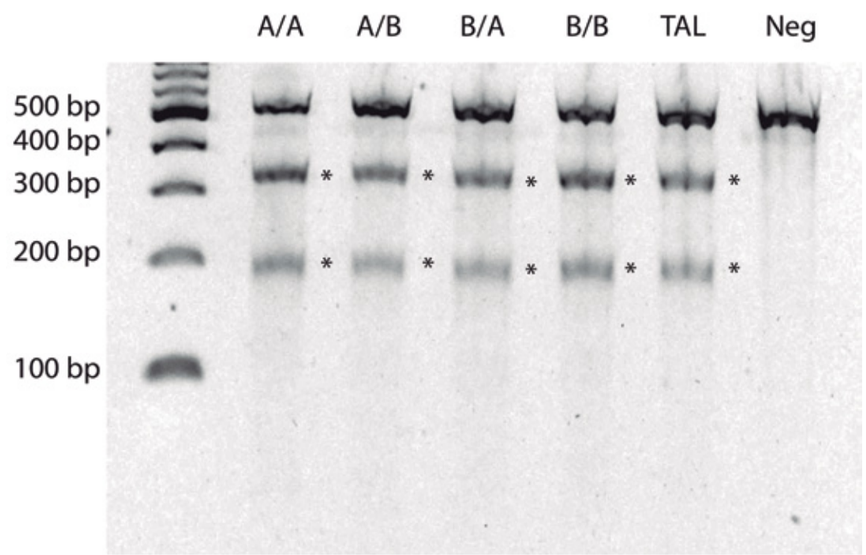


Figure 1. Gene editing of the A1AT gene in primary human cells using mRNA encoding gene-editing proteins.

Representative Claim

U.S. Pat. No. 10,576,167

A method for treating alpha-1 antitrypsin (A1AT) deficiency comprising administering an effective amount of a synthetic RNA encoding a gene-editing protein capable of creating a double strand break in A1AT to a subject, wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity, and

wherein the gene-editing protein comprises:

(i) a DNA-binding domain comprising a plurality of repeat sequences and at least one of the repeat sequences comprises the amino acid sequence: LTPvQVVAIAwxyzGHGG (SEQ ID NO: 629) and is between 36 and 39 amino acids long, wherein:

"v" is Q, D or E,

"w" is S or N,

"x" is H, N, or I,

"y" is D, A, I, N, G, H, K, S, or null, and

"z" is GGKQALETVQRLLPVLCQD (SEQ ID NO: 630) or GGKQALETVQRLLPVLCQA (SEQ ID NO: 631); and

(ii) a nuclease domain comprising a catalytic domain of a nuclease.

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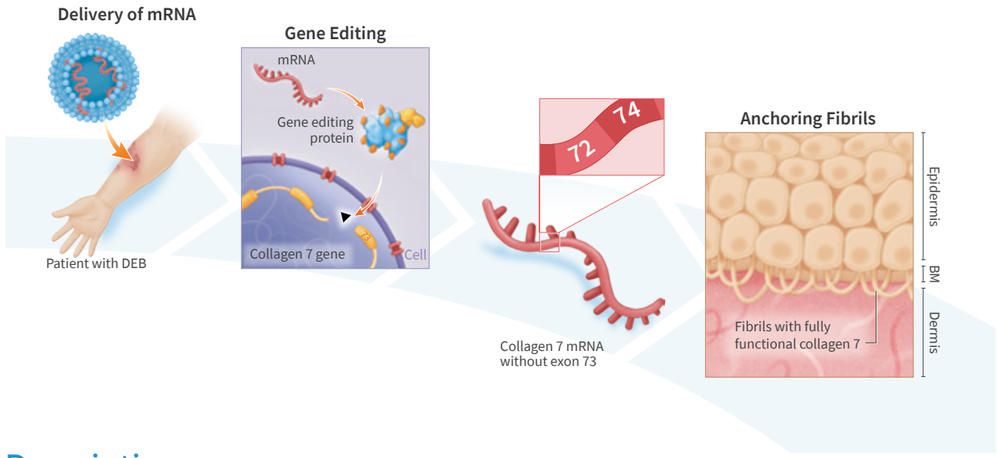
Gene-Editing Therapies for Epidermolysis Bullosa (EB)



Description

Epidermolysis Bullosa (EB) is a collection of genetic diseases caused by mutations in genes that are important for normal skin function. Many EB patients have extremely delicate skin, and in the most severe cases, live with painful blisters and open wounds over large areas of their bodies.

Our scientists developed a method for treating epidermolysis bullosa by using mRNA to express gene-editing proteins directly in a patient's skin.

Gene-Editing Therapies for Epidermolysis Bullosa (EB) is protected by two U.S. patents (with additional patents pending in the U.S. and in other countries). Of note, certain granted patents include claims that are not limited by specific target sequence, mRNA sequence or chemistry, or type of gene-editing protein.

Example Applications

- Repair individual mutations or alter collagen 7 mRNA splicing, e.g., ablate the exon 73 splice acceptor site to generate functional collagen 7 in patients with a disease-causing mutation in exon 73[6]
- Deliver the therapy directly to the patient's skin – avoid ex vivo cell manipulation and skin grafts
- Combine with Factor's Chromatin Context-Sensitive Gene-Editing Endonuclease for high-specificity in vivo gene editing
- Combine with Factor's ToRNAdo™ Nucleic-Acid Delivery System for high efficiency in vivo delivery – proven delivery to human skin in vivo

[6]Mealmaker, C., et al. Mol Ther, Vol 28 No 4S1, 2020

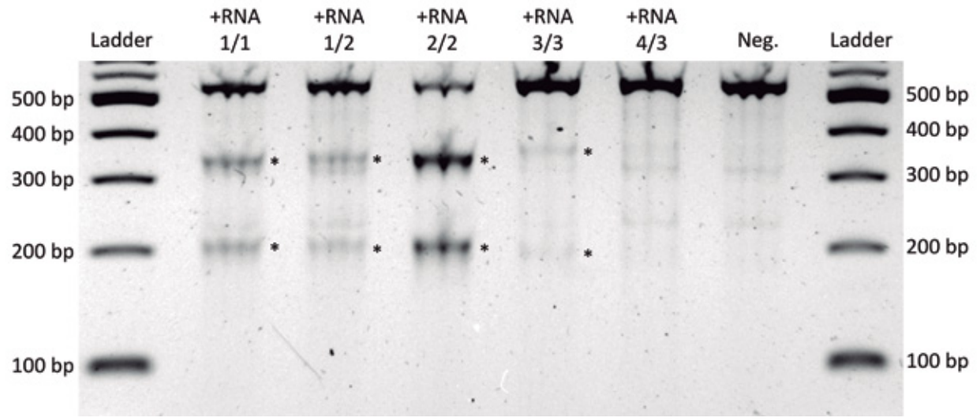


Figure 1. Gene editing of the COL7A1 gene in primary human cells using mRNA encoding gene-editing proteins.

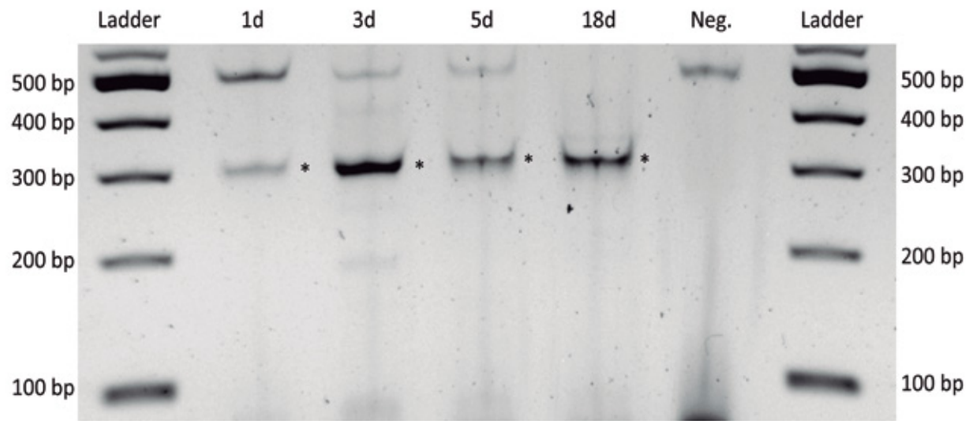


Figure 2. Durable exclusion of exon 73 in collagen 7 mRNA of treated cells.

Representative Claim

U.S. Pat. No. 10,124,042

An in vivo method for treating epidermolysis bullosa, comprising

delivering a synthetic RNA encoding a gene-editing protein that targets a COL7 gene to a patient in need thereof and

inducing a single-strand or double-strand break in the COL7 gene of the patient's keratinocytes,

thereby eliminating a mutation that is at least partially responsible for a disease phenotype, wherein:

the synthetic RNA is delivered to the patient's keratinocytes by injection to the epidermis and

the gene-editing protein comprises a DNA-binding domain and a nuclease domain.

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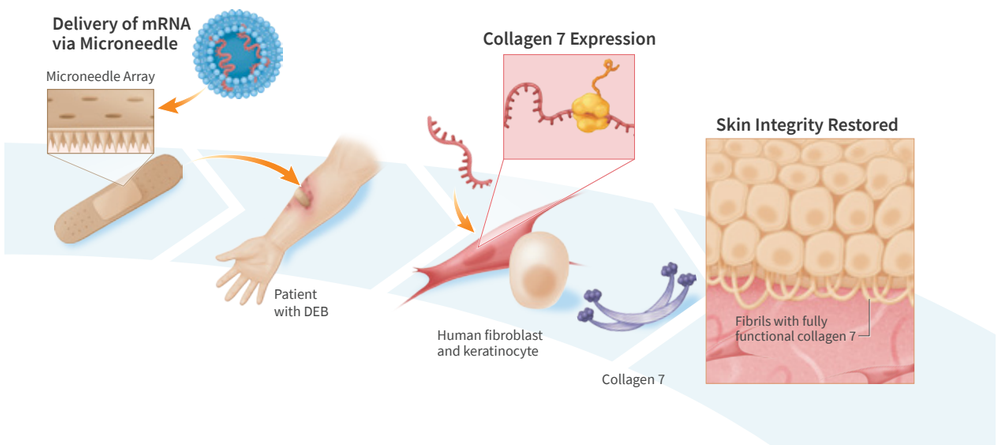
mRNA Therapies for Dystrophic Epidermolysis Bullosa (DEB)



Description

Dystrophic Epidermolysis Bullosa (DEB) is a disease caused by mutations in the COL7A1 gene, which encodes collagen 7. Many DEB patients have extremely delicate skin, and in the most severe cases, live with painful blisters and open wounds over large areas of their bodies.

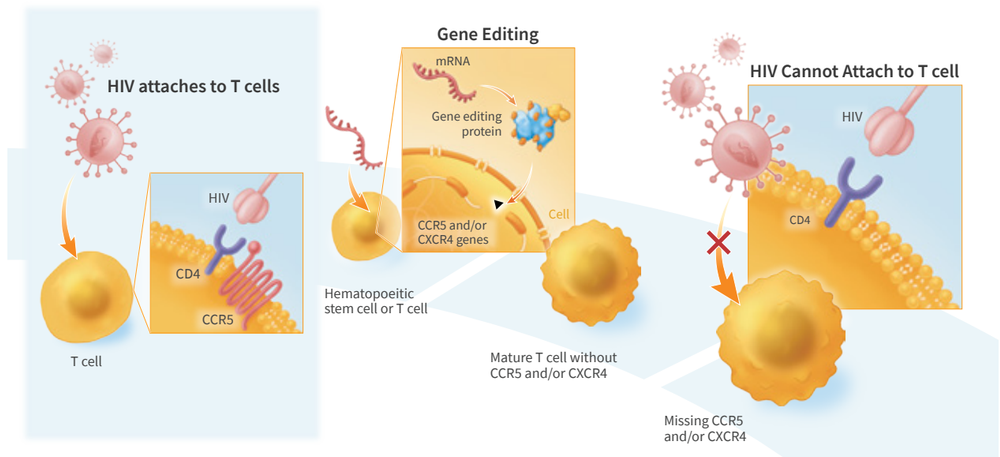
Our scientists developed a method for treating dystrophic epidermolysis bullosa by using mRNA to express collagen 7 directly in a patient's skin.

The mRNA Therapies for Dystrophic Epidermolysis Bullosa (DEB) technology is protected by AU Patent Number 2015210769 (with additional patents pending in the U.S. and in other countries). Of note, the granted patent includes claims that are not limited by specific mRNA sequence, chemistry or formulation.

Example Applications

- Directly express collagen 7 in DEB patient skin
- Develop a single product to treat a complex population with hundreds of disease-causing mutations
- Treat large areas using a microneedle array
- Dose infrequently – collagen 7 has a long in vivo half-life (>30 days)
- Combine with Factor's ToRNAdo™ Nucleic-Acid Delivery System for high efficiency in vivo delivery – proven delivery to human skin in vivo

Gene-Editing Therapies for HIV



Description

Human Immunodeficiency Virus uses surface proteins such as CCR5 to infect immune cells. People with a rare natural variant of the CCR5 gene exhibit resistance to HIV infection.

Our scientists developed a method for treating HIV using mRNA encoding gene-editing proteins to inactivate CCR5 and/or CXCR4 in hematopoietic cells.

Gene-Editing Therapies for HIV is protected by three U.S. patents (with additional patents pending in the U.S. and in other countries). Of note, certain granted patents include claims that are not limited by specific target sequence, mRNA sequence or chemistry, or type of gene-editing protein.

Example Applications

- Replicate natural HIV resistance using site-specific genome engineering of a patient's cells
- Achieve high-efficiency delivery of mRNA encoding gene-editing proteins to hematopoietic cells ex vivo using electroporation
- Target T cells and/or HSCs for persistent HIV immunity
- Gene edit somatic cells to avoid the risk of germline transmission
- Combine with Factor's Chromatin Context-Sensitive Gene-Editing Endonuclease for high-specificity ex vivo gene editing

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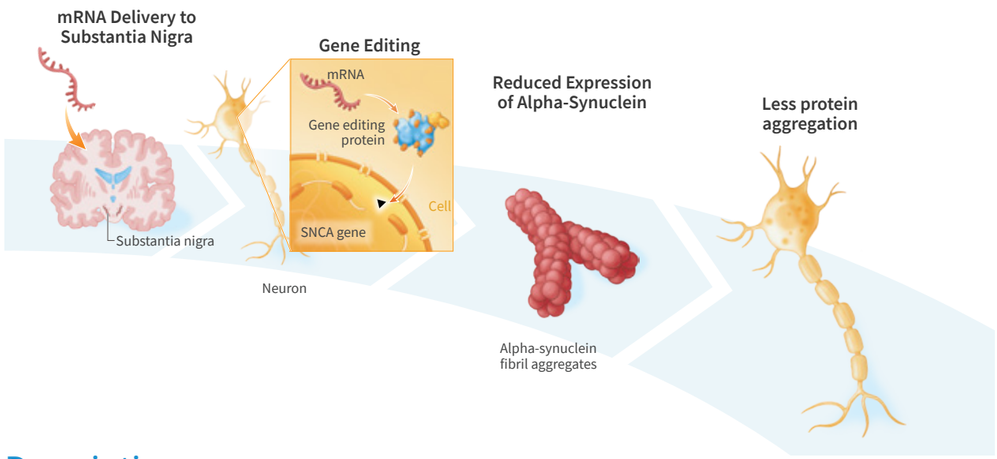
Gene-Editing Therapies for Parkinson's Disease



Description

Parkinson's disease is associated with the accumulation of alpha-synuclein aggregates in dopaminergic neurons of the substantia nigra pars compacta, leading to cell death, and resulting loss of motor control.

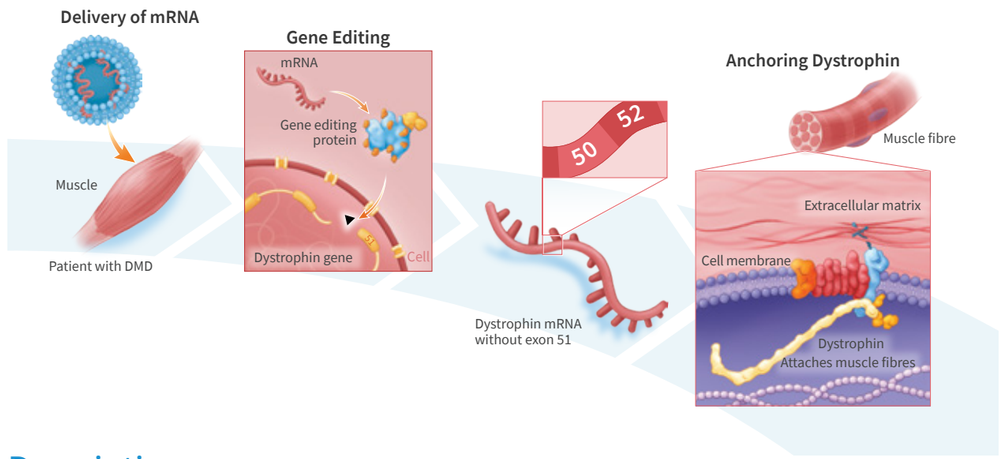
Our scientists developed a method for treating Parkinson's disease by editing the gene that encodes alpha-synuclein to prevent aggregation of the encoded protein in affected cells.

Gene-Editing Therapies for Parkinson's Disease is protected by U.S. Patent Number 10,752,919 (with additional patents pending in the U.S. and in other countries). Of note, certain claims of the granted patent are not limited by type of nucleic acid or formulation.

Example Applications

- Employ multiple therapeutic strategies – monoallelic or biallelic inactivation of alpha-synuclein in vulnerable cells, altering alpha-synuclein mRNA splicing to generate non-aggregating forms by ablating splice acceptor/donor sites, etc.
- Combine with Factor's Chromatin Context-Sensitive Gene-Editing Endonuclease for high-specificity in vivo gene editing
- Combine with Factor's ToRNAdo™ Nucleic-Acid Delivery System for high efficiency in vivo delivery – proven delivery to brain in vivo

Gene-Editing Therapies for Duchenne Muscular Dystrophy (DMD)



Description

Duchenne muscular dystrophy (DMD) is caused by mutations in the DMD gene, which encodes dystrophin, a protein normally expressed in skeletal muscle.

Our scientists developed a method for treating DMD by using gene-editing proteins to edit the DMD gene to result in the production of a functional form of dystrophin protein.

Gene-Editing Therapies for Duchenne Muscular Dystrophy (DMD) is protected by U.S. Patent Number 10,752,918 (with additional patents pending in the U.S. and in other countries). Of note, certain claims of the granted patent are not limited by type of nucleic acid or formulation.

Example Applications

- Alter dystrophin mRNA splicing, e.g., ablate the splice acceptor site upstream of a mutation-containing exon to generate functional dystrophin protein
- Deliver the therapy directly to the patient's skeletal muscle – avoid ex vivo cell manipulation
- Combine with Factor's Chromatin Context-Sensitive Gene-Editing Endonuclease for high-specificity in vivo gene editing
- Combine with Factor's ToRNAdo™ Nucleic-Acid Delivery System for high efficiency in vivo delivery – proven delivery to various cells and tissues ex vivo and in vivo

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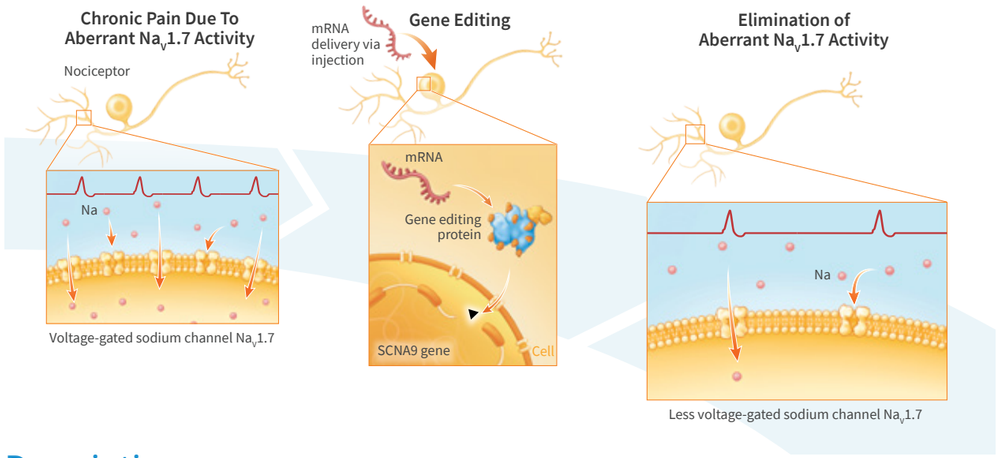
Gene-Editing Therapies for Chronic Pain



Description

Chronic pain is a debilitating disorder associated with aberrant neuronal activity.

Our scientists developed a method for treating chronic pain by editing genes encoding voltage-gated sodium channels in cells of the central nervous system or peripheral nervous system.

Gene-Editing Therapies for Chronic Pain is protected by a pending international patent application (with plans to pursue patents in the U.S. and in other countries).

Example Applications

- Achieve direct, persistent treatment of affected neurons – monoallelic or biallelic inactivation of the SCN9A gene (encoding Nav1.7) in vulnerable cells of the dorsal root ganglia
- Combine with Factor's Chromatin Context-Sensitive Gene-Editing Endonuclease for high-specificity in vivo gene editing
- Combine with Factor's ToRNAdo™ Nucleic-Acid Delivery System for high efficiency in vivo delivery – proven delivery to primary neurons ex vivo and CNS in vivo

Nucleic-Acid Delivery

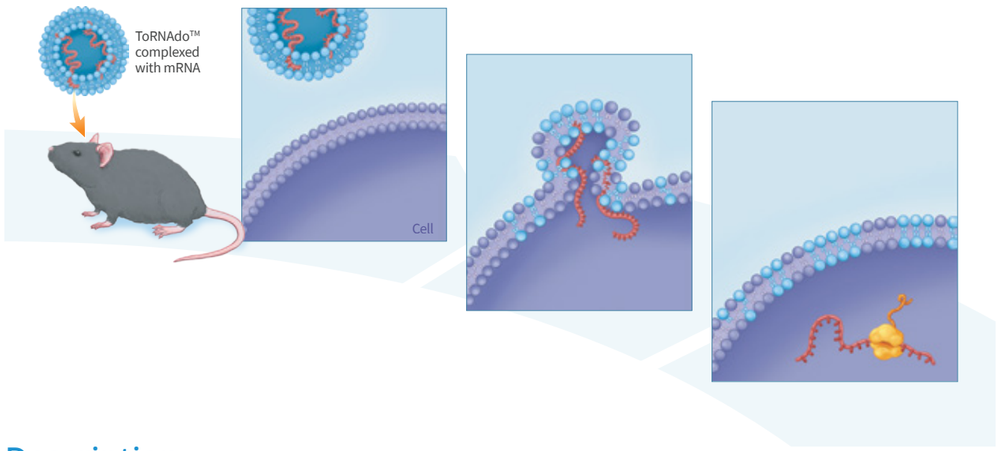
Nucleic acids, such as mRNA, can be used to induce cells to express proteins, including proteins that are capable of re-writing genetic and epigenetic cellular programs. However, the plasma membrane normally protects cells from exogenous nucleic acids, preventing efficient uptake and protein translation.

We develop technologies for delivering nucleic acids to cells ex vivo and in vivo.

Our nucleic-acid delivery technologies enable efficient ex vivo delivery of mRNA encoding gene-editing proteins and reprogramming factors, including to primary cells, insertion of exogenous sequences into genomic safe-harbor loci, and efficient in vivo delivery of mRNA to the brain, eye, skin, and lung.

Human skin containing cells expressing red fluorescent protein after intradermal injection of ToRNAdo™-mRNA complexes.

ToRNAdo™ Nucleic-Acid Delivery System



Description

Delivery systems can be used to enhance the uptake of nucleic acids by cells. Conventional delivery systems often suffer from endosomal entrapment and toxicity, which can limit their therapeutic use.

Our scientists developed a novel chemical substance that is exceptionally effective at delivering nucleic acids, including mRNA, to cells both ex vivo and in vivo.

The ToRNAdo™ Nucleic-Acid Delivery System is protected by four U.S. patents (with additional patents pending in the U.S. and in other countries). Of note, certain granted patents include claims that are not limited by disease indication, cell type, route of administration, or type of nucleic acid.

Example Applications

- Use fusogenic lipid/nucleic-acid particles made with ToRNAdo™ to avoid endocytosis pathways that require “endosomal escape”
- Generate non-toxic formulated nucleic-acid products (ToRNAdo™ is made using omega-6 unsaturated tails derived from sunflower seed oil)
- Achieve ultra-high-efficiency transfection in up to 100% serum
- Protect cargo from nuclease attack
- Efficient delivery of mRNA, siRNA, and plasmid to a variety of cell types
- Deliver nucleic acids, including mRNA, in vivo – proven delivery to brain, eye, skin, and lung[7]
- Use Factor’s high-yield synthesis protocol to streamline nucleic-acid therapy manufacturing
- Combine with Factor’s mRNA Cell Reprogramming technology to generate footprint-free pluripotent stem cells
- Combine with Factor’s Chromatin Context-Sensitive Gene-Editing Endonuclease for high-specificity in vivo gene editing

[7]Kostas, F., et al. Mol Ther, Vol 28 No 4S1, 2020.

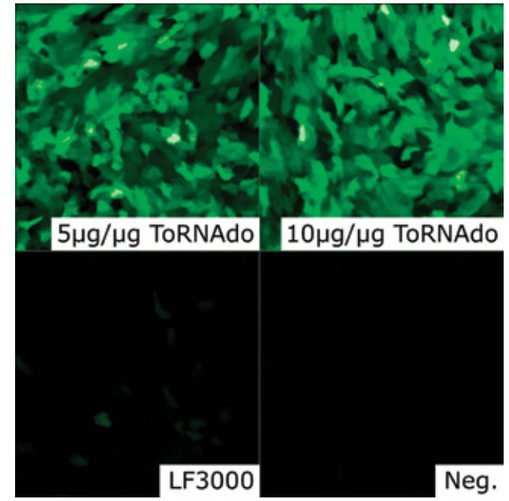


Figure 1. ToRNAdo™ delivery of GFP mRNA to human epidermal keratinocytes in vitro.

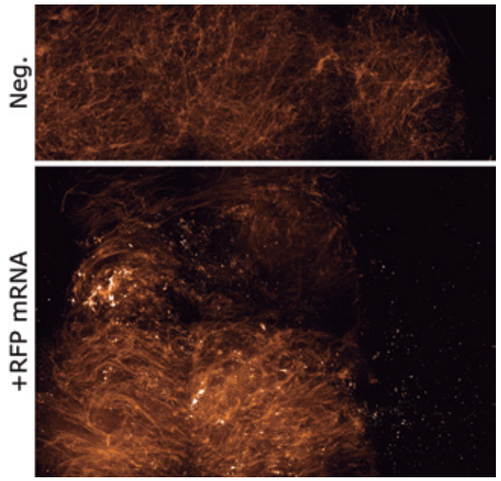
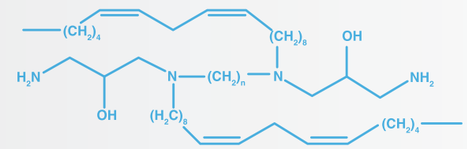


Figure 2. ToRNAdo™ delivery of RFP mRNA to human skin in vivo.

Representative Claim

U.S. Pat. No. 10,501,404

A compound of Formula (I)



wherein n is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15.

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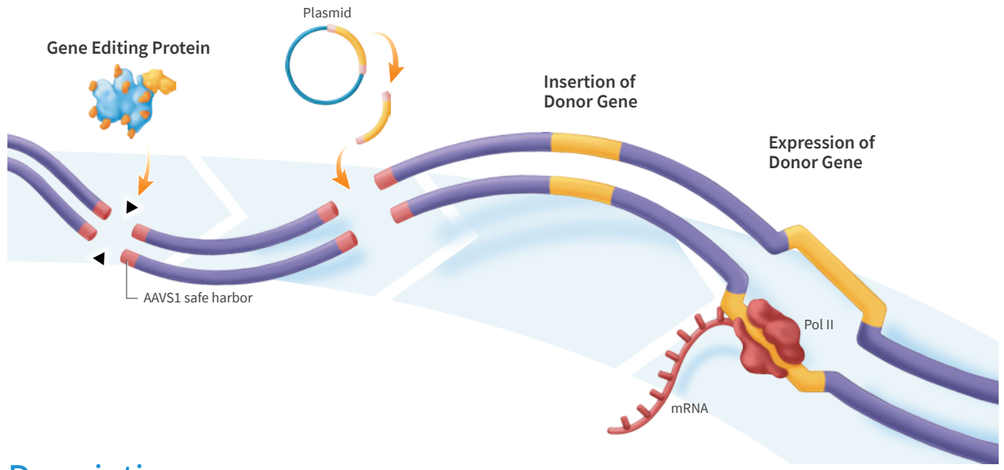
Insertion of Sequences into Safe-Harbor Loci



Description

Safe-harbor loci are regions of the genome that can be disrupted in a wide variety of cell types without causing adverse effects. These safe-harbor loci are thus ideal sites for inserting exogenous nucleic-acid sequences.

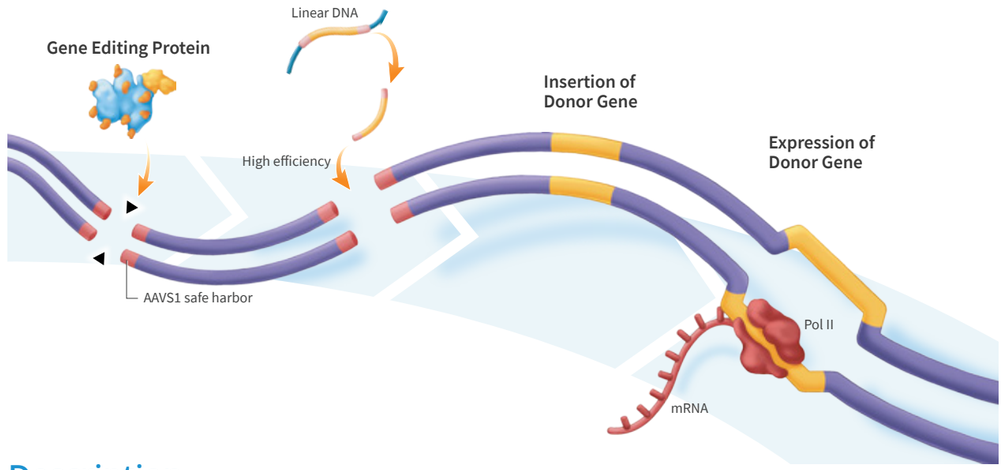
Our scientists developed a method for inserting sequences in safe harbor loci using mRNA encoding gene-editing proteins.

Insertion of Sequences into Safe-Harbor Loci is protected by U.S. Patent Number 10,724,053 (with additional patents pending in the U.S. and in other countries). Of note, certain claims of the granted patent are not limited by type of nucleic acid or formulation.

Example Applications

- Achieve high-efficiency insertion into the AAVS1 safe-harbor locus
- Combine with Factor's Chromatin Context-Sensitive Gene-Editing Endonuclease for high-specificity in vivo gene editing
- Combine with Factor's ToRNAdo™ Nucleic-Acid Delivery System for high efficiency in vivo delivery – proven delivery to various cells and tissues ex vivo and in vivo

End-Modified Linear DNA Donors



Description

Gene-editing proteins can be used to inactivate, repair, or insert sequences in living cells. Conventional approaches using plasmids or viruses to encode donor DNA sequences for insertion can result in low-efficiency insertion and unwanted mutagenesis when an exogenous nucleic acid fragment is inserted at random locations in the genome.

Our scientists developed a technology that uses end-modified linear DNA donors to enable high-specificity on-target insertion[8]. This technology can be used, for example, to generate allogeneic CAR-T therapies for the treatment of cancer in which an end-modified linear DNA donor is used to insert a CAR sequence into a safe-harbor locus, and/or to generate allogeneic stem cell-derived therapies in which an end-modified linear DNA donor is used to insert a non-classical MHC class I sequence into the B2M gene to render the cells immuno-nonreactive or "stealth."

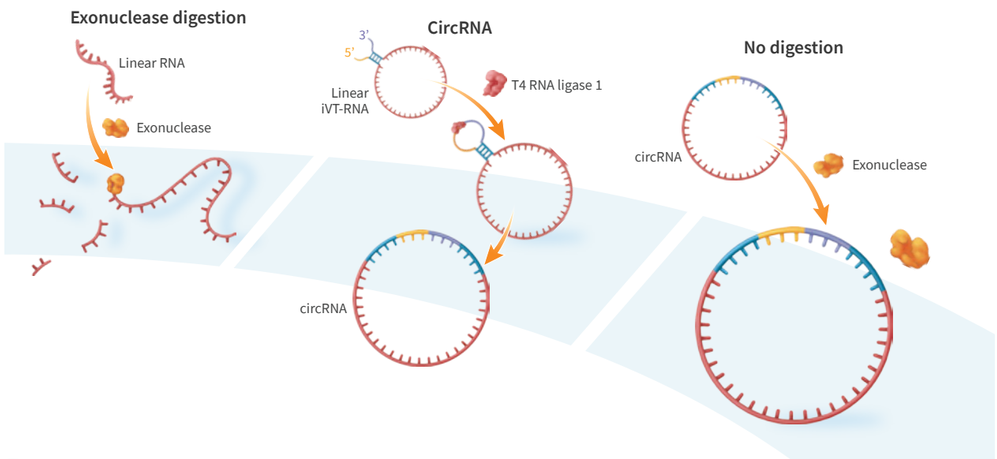
The End-Modified Linear DNA Donors technology is protected by a pending U.S. patent (with additional patents pending in other countries).

Example Applications

- High-efficiency, high-specificity insertion of donor sequences into target genomic loci (e.g., TRAC, AAVS1 safe harbor, etc.)
- Virus-free gene editing
- Gene repair using a DNA-repair template
- Gene-editing therapies (ex vivo and in vivo)
- Autologous and allogeneic engineered cell therapies (e.g., CAR-T, CAR-NK, stem cell-derived therapies, etc.)
- Combine with Factor's ToRNAdo™ Nucleic-Acid Delivery System for high efficiency in vivo delivery

[8]Simpson, A., et al. Mol Ther, Vol 29, No 4S1, 2021.

Splint and Ribozyme-Independent Circular RNA Synthesis



Description

RNA molecules can be used to express proteins in cells, both ex vivo and in vivo. Conventional approaches using linear RNA molecules can result in exonuclease degradation, which can lead to low protein expression.

Our scientists developed a technology for synthesizing circular RNA molecules that does not require splints or ribozymes[9]. This technology can enable durable protein expression in cells and can be used, for example, to generate low-dose RNA vaccines, and for in vivo epigenetic reprogramming.

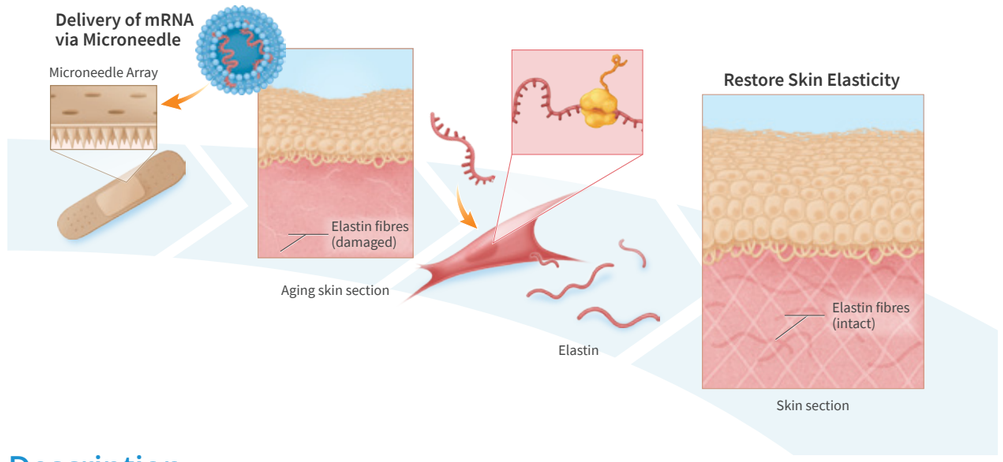
Splint and Ribozyme-Independent Circular RNA Synthesis is protected by a pending U.S. patent (with additional patents pending in other countries).

Example Applications

- Ultra-high efficiency editing of T cells, fibroblasts, keratinocytes, and pluripotent stem cells
- Ultra-high specificity gene editing
- Virus-free and DNA-free gene editing
- Gene repair using a DNA-repair template
- Donor sequence insertion into a target genomic locus (e.g., TRAC, AAVS1 safe harbor, etc.)
- Gene-editing therapies (ex vivo and in vivo)
- Autologous and allogeneic engineered cell therapies (e.g., CAR-T, CAR-NK, stem cell-derived therapies, etc.)
- Low-dose RNA vaccines

[9]Svihla, A., et al. Mol Ther, Vol 29, No 4S1, 2021.

mRNA Delivery to Skin



Description

In addition to being the largest and most accessible organ of the body, the skin contains large numbers of highly active cells that have a high capacity for protein synthesis. These characteristics make the skin an ideal platform for expressing therapeutic proteins both locally, for the treatment of dermatological conditions, and systemically, for the treatment of a wide range of diseases and conditions.

Our scientists developed a method for expressing therapeutic proteins, including circulating proteins, by administering ultra-low doses of mRNA to the skin.

mRNA Delivery to Skin is protected by a pending U.S. patent (with additional patents pending in other countries).

Example Applications

- Express proteins locally for the treatment of dermatologic conditions (e.g., elastin for the rare genetic disease cutis laxa and aesthetic applications)
- Express proteins systemically for the treatment of a wide range of diseases and conditions (e.g., BMP7 for diabetic nephropathy)
- Deliver the therapy directly to the patient's skin – avoid ex vivo cell manipulation
- Combine with Factor's Chromatin Context-Sensitive Gene-Editing Endonuclease for high-specificity in vivo gene editing
- Combine with Factor's ToRNAdo™ Nucleic-Acid Delivery System for high efficiency in vivo delivery – proven delivery to human skin in vivo

licensing@factorbio.com

Patent Portfolio

Our technologies are protected by a portfolio of patents, which we actively license to entities wishing to conduct commercial research, sell tools, reagents, and other products, perform commercial services for third parties, and develop human and veterinary therapeutics. Our goal is to deploy our technologies as broadly as possible through collaborations and the granting of non-exclusive and field-limited exclusive licenses, to promote scientific research and the successful development of therapeutic products.

Contact us today to explore licensing opportunities for your application.

Rat brain cells expressing a reporter protein after intracerebroventricular injection of mRNA.

Case	Country	Application	Patent	Status
FAB-001AU	Australia	2012347919 Dec-05-2012	2012347919 May-18-2017	PATENTED
FAB-001AUD1	Australia	2016277545 Dec-05-2012	2016277545 Sep-28-2017	PATENTED
FAB-001AUD2	Australia	2017225124 Dec-05-2012	2017225124 Jun-13-2019	PATENTED
FAB-001AUD3	Australia	2019203662 May-24-2019	2019203662 May-14-2020	PATENTED
FAB-001CN	China	201280068223.0 Dec-05-2012	ZL201280068223.0 Nov-25-2015	PATENTED
FAB-001CND1	China	201510852019.3 Dec-05-2012	ZL201510852019.3 May-29-2017	PATENTED
FAB-001CND2	China	201510853689.7 Dec-05-2012	ZL201510853689.7 Aug-13-2019	PATENTED
FAB-001CND3	China	201510853690.X Dec-05-2012	ZL201510853690.X Apr-17-2020	PATENTED
FAB-001EP	Europe	12813595.1 Dec-05-2012	2788033 May-31-2017	PATENTED
FAB-001CH	Switzerland	12813595.1 Dec-05-2012	2788033 May-31-2017	PATENTED
FAB-001DE	Germany	12813595.1 Dec-05-2012	2788033 May-31-2017	PATENTED
FAB-001FR	France	12813595.1 Dec-05-2012	2788033 May-31-2017	PATENTED
FAB-001GB	United Kingdom	12813595.1 Dec-05-2012	2788033 May-31-2017	PATENTED
FAB-001IE	Ireland	12813595.1 Dec-05-2012	2788033 May-31-2017	PATENTED
FAB-001EPD1	Europe	17170810.0 May-02-2017	3260140 Feb-03-2021	PATENTED
FAB-001BED1	Belgium	17170810.0 May-02-2017	3260140 Feb-03-2021	PATENTED
FAB-001CHD1	Switzerland	17170810.0 May-02-2017	3260140 Feb-03-2021	PATENTED
FAB-001DED1	Germany	17170810.0 May-02-2017	3260140 Feb-03-2021	PATENTED
FAB-001DKD1	Denmark	17170810.0 May-02-2017	3260140 Feb-03-2021	PATENTED
FAB-001FRD1	France	17170810.0 May-02-2017	3260140 Feb-03-2021	PATENTED
FAB-001GBD1	United Kingdom	17170810.0 May-02-2017	3260140 Feb-03-2021	PATENTED
FAB-001IED1	Ireland	17170810.0 May-02-2017	3260140 Feb-03-2021	PATENTED
FAB-001NLD1	Netherlands	17170810.0 May-02-2017	3260140 Feb-03-2021	PATENTED
FAB-001HK	Hong Kong	15103141.5 Dec-05-2012	1202443 Mar-23-2018	PATENTED
FAB-001HKD1	Hong Kong	16108558.9 Dec-05-2012	220490 Feb-23-2018	PATENTED
FAB-001HKD2	Hong Kong	16110473.7 Dec-05-2012	1222203 Sep-11-2020	PATENTED

Case	Country	Application	Patent	Status
FAB-001HKD3	Hong Kong	16110474.6 Dec-05-2012	1222204 Mar-19-2021	PATENTED
FAB-001JP	Japan	2014-546024 Dec-05-2012	6073916 Jan-13-2017	PATENTED
FAB-001JPD1	Japan	2016-213019 Oct-31-2016	6294944 Feb-23-2018	PATENTED
FAB-001KR	Republic of Korea	10-2014-7018569 Dec-05-2012	10-2196339 Dec-22-2020	PATENTED
FAB-001MX	Mexico	MX/a/2014/006663 Dec-05-2012	354995 Mar-27-2018	PATENTED
FAB-001MXD1	Mexico	MX/a/2018/003987 Mar-28-2018	N/A	ALLOWED
FAB-001RU	Russian Federation	2014127505 Dec-05-2012	2624139 Jun-30-2017	PATENTED
FAB-001RUD1	Russian Federation	2017118312 Dec-05-2012	2691027 Jun-07-2019	PATENTED
FAB-001C1	USA	14/296,220 Jun-04-2014	9,422,577 Aug-23-2016	PATENTED
FAB-001C10	USA	16/857,894 Apr-24-2020	10,829,738 Nov-10-2020	PATENTED
FAB-001C3	USA	15/207,167 Jul-11-2016	9,605,277 Mar-28-2017	PATENTED
FAB-001C4	USA	15/222,453 Jul-28-2016	9,605,278 Mar-28-2017	PATENTED
FAB-001C7	USA	16/402,175 May-02-2019	10,472,611 Nov-12-2019	PATENTED
FAB-001C9	USA	16/776,765 Jan-30-2020	10,662,410 May-26-2020	PATENTED
FAB-001C11	USA	16/869,232 May-7-2020	10,982,229 Apr-20-2021	PATENTED
FAB-003	USA	13/465,490 May-07-2012	8,497,124 Jul-30-2013	PATENTED
FAB-003C1	USA	13/931,251 Jun-28-2013	9,127,248 Sep-08-2015	PATENTED
FAB-003C2	USA	14/810,123 Jul-27-2015	9,399,761 Jul-26-2016	PATENTED
FAB-003C3	USA	15/178,190 Jun-9-2016	9,562,218 Feb-07-2017	PATENTED
FAB-003C4	USA	15/358,818 Nov-22-2016	9,695,401 Jul-04-2017	PATENTED
FAB-003C5	USA	15/605,513 May-25-2017	9,879,228 Jan-30-2018	PATENTED
FAB-003C6	USA	15/844,063 Dec-15-2017	9,969,983 May-15-2018	PATENTED
FAB-003C7	USA	15/947,741 Apr-06-2018	10,131,882 Nov-20-2018	PATENTED
FAB-003C8	USA	16/037,597 Jul-17-2018	10,301,599 May-28-2019	PATENTED
FAB-003C9	USA	16/374,482 Apr-03-2019	10,443,045 Oct-15-2019	PATENTED
FAB-005AU	Australia	2013337651 Nov-01-2013	2013337651 Mar-28-2019	PATENTED

Case	Country	Application	Patent	Status
FAB-005AUD1	Australia	2018264115 Nov-16-2018	N/A	ALLOWED
FAB-005EP	Europe	13850281.0 Nov-01-2013	2914728 Jul-08-2020	PATENTED
FAB-005CH	Switzerland	13850281.0 Nov-01-2013	2914728 Jul-08-2020	PATENTED
FAB-005DE	Germany	13850281.0 Nov-01-2013	2914728 Jul-08-2020	PATENTED
FAB-005FR	France	13850281.0 Nov-01-2013	2914728 Jul-08-2020	PATENTED
FAB-005GB	United Kingdom	13850281.0 Nov-01-2013	2914728 Jul-08-2020	PATENTED
FAB-005IE	Ireland	13850281.0 Nov-01-2013	2914728 Jul-08-2020	PATENTED
FAB-005HK	Hong Kong	16102376.2 Nov-01-2013	1214304B Apr-23-2021	PATENTED
FAB-005JP	Japan	2015-540833 Nov-01-2013	6510416 Apr-12-2019	PATENTED
FAB-005JPD1	Japan	2018-073676 Apr-06-2018	6890565 May-27-2021	PATENTED
FAB-005JPD2	Japan	2018-073677 Apr-06-2018	6793146 Nov-11-2020	PATENTED
FAB-005KR	Republic of Korea	10-2015-7013918 Nov-01-2013	10-2121086 Jun-03-2020	PATENTED
FAB-005MX	Mexico	MX/a/2015/005346 Nov-01-2013	363017 Mar-04-2019	PATENTED
FAB-005RU	Russian Federation	2015120524 Nov-01-2013	2711249 Jan-15-2020	PATENTED
FAB-005	USA	14/701,199 Apr-30-2015	9,447,395 Sep-20-2016	PATENTED
FAB-005C1	USA	14/735,603 Jun-10-2015	9,376,669 Jun-28-2016	PATENTED
FAB-005C2	USA	15/156,806 May-17-2016	9,464,285 Oct-11-2016	PATENTED
FAB-005C3	USA	15/156,829 May-17-2016	9,487,768 Nov-08-2016	PATENTED
FAB-005C4	USA	15/270,469 Sep-20-2016	9,657,282 May-23-2017	PATENTED
FAB-005C5	USA	15/487,088 Apr-13-2017	9,758,797 Sep-12-2017	PATENTED
FAB-005C6	USA	15/670,639 Aug-07-2017	10,415,060 Sep-17-2019	PATENTED
FAB-005C7	USA	16/523,558 Jul-26-2019	10,590,437 Mar-17-2020	PATENTED
FAB-005C9	USA	16/654,536 Oct-16-2019	10,752,917 Aug-25-2020	PATENTED
FAB-005C11	USA	16/655,744 Oct-17-2019	10,724,053 Jul-28-2020	PATENTED
FAB-005C13	USA	16/655,766 Oct-17-2019	10,767,195 Sep-08-2020	PATENTED
FAB-005C15	USA	16/657,321 Oct-18-2019	10,752,918 Aug-25-2020	PATENTED

Case	Country	Application	Patent	Status
FAB-005C16	USA	16/657,325 Oct-18-2019	10,752,919 Aug-25-2020	PATENTED
FAB-008	USA	14/761,461 Jul-16-2015	9,770,489 Sep-26-2017	PATENTED
FAB-008EP	Europe	15743915.9 Jan-30-2015	3099801 Mar-18-2020	PATENTED
FAB-008CH	Switzerland	15743915.9 Jan-30-2015	3099801 Mar-18-2020	PATENTED
FAB-008DE	Germany	15743915.9 Jan-30-2015	3099801 Mar-18-2020	PATENTED
FAB-008ES	Spain	15743915.9 Jan-30-2015	3099801 Mar-18-2020	PATENTED
FAB-008FR	France	15743915.9 Jan-30-2015	3099801 Mar-18-2020	PATENTED
FAB-008GB	United Kingdom	15743915.9 Jan-30-2015	3099801 Mar-18-2020	PATENTED
FAB-008IE	Ireland	15743915.9 Jan-30-2015	3099801 Mar-18-2020	PATENTED
FAB-008HK	Hong Kong	17105411.1 Jan-30-2015	1231917 Feb-11-2021	PATENTED
FAB-008MX	Mexico	MX/a/2016/009771 Jan-30-2015	372651 Jun-16-2020	PATENTED
FAB-008RU	Russian Federation	2016131251 Jan-30-2015	2714404 Feb-14-2020	PATENTED
FAB-008AU	Australia	2015210769 Jan-30-2015	2015210769 May-23-2015	PATENTED
FAB-008C1	USA	15/678,491 Aug-16-2017	10,124,042 Nov-13-2018	PATENTED
FAB-010A	USA	15/748,132 Jan-26-2018	10,576,167 Mar-03-2020	PATENTED
FAB-010B	USA	15/881,721 Jan-26-2018	10,137,206 Nov-27-2018	PATENTED
FAB-010C1	USA	16/030,670 Jul-09-2018	10,350,304 Jul-16-2019	PATENTED
FAB-010C2	USA	16/030,674 Jul-09-2018	10,363,321 Jul-30-2019	PATENTED
FAB-010C3	USA	16/030,675 Jul-09-2018	10,369,233 Aug-06-2019	PATENTED
FAB-010C4	USA	16/441,563 Jun-14-2019	10,888,627 Jan-12-2021	PATENTED
FAB-010C5	USA	16/441,622 Jun-14-2019	10,894,092 Jan-19-2021	PATENTED
FAB-012A	USA	16/526,621 Aug-12-2019	10,501,404 Dec-10-2019	PATENTED
FAB-012AC1	USA	16/660,299 Oct-22-2019	10,556,855 Feb-11-2020	PATENTED
FAB-012AC2	USA	16/660,317 Oct-22-2019	10,611,722 Apr-07-2020	PATENTED
FAB-012AC3	USA	16/746,279 Jan-17-2020	10,752,576 Aug-25-2020	PATENTED

Patented Technologies Available for Licensing

- mRNA Vectorization of Gene-Editing Proteins
- Chromatin Context-Sensitive Gene-Editing Endonuclease
- mRNA Cell Reprogramming
- Combined mRNA Gene Editing & Cell Reprogramming
- Cell Reprogramming Medium
- AAT Deficiency, EB, HIV, and Cancer-Focused Technologies
- ToRNAdo™ Nucleic-Acid Delivery System
- Parkinson's Disease and DMD-Focused Technologies
- Insertion of Sequences into Safe-Harbor Loci

Patent-Pending Technologies Available for Licensing

- Temperature-Tunable Gene-Editing Endonuclease
- Gene-Edited Allogeneic Cell Therapies
- End-Modified Linear DNA Donors
- Splint and Ribozyme-Independent Circular RNA Synthesis
- Chronic Pain-Focused Technologies
- mRNA Delivery to Skin

Notes

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