FACTOR®
BIOSCIENCE

Technology Catalog

2024

Introduction

From the production of basic biologic medicines like insulin to the development of state-of-the-art allogeneic CAR-T therapies for the treatment of cancer, biotechnology gives patients suffering from debilitating disease real hope of health and longevity. As you will read throughout this year's Technology Catalog, at Factor, we are working to create the future of biotechnology – a future that we believe is even more exciting.

My co-founder, Dr. Christopher Rohde, and I founded Factor thirteen years ago to pursue our vision of harnessing the power of mRNA to control the way cells function. We discovered how to use mRNA to reprogram and gene edit cells, work that has led to a pipeline of advanced cell-engineering therapies under development at Factor, including for the treatment of Parkinson's disease, muscular dystrophies, and solid tumors.

In this year's Technology Catalog, you will read about new technologies that we have developed at Factor for engineering cells – technologies that we are now employing in our cleanroom facility to produce engineered cells for eventual testing in humans. This year, I am also proud to highlight three members of our scientific team who have contributed to advancing these programs. Their stories give insight into how we have created a vibrant community of scientists at Factor who are collaborating to unleash the power of mRNA.

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

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

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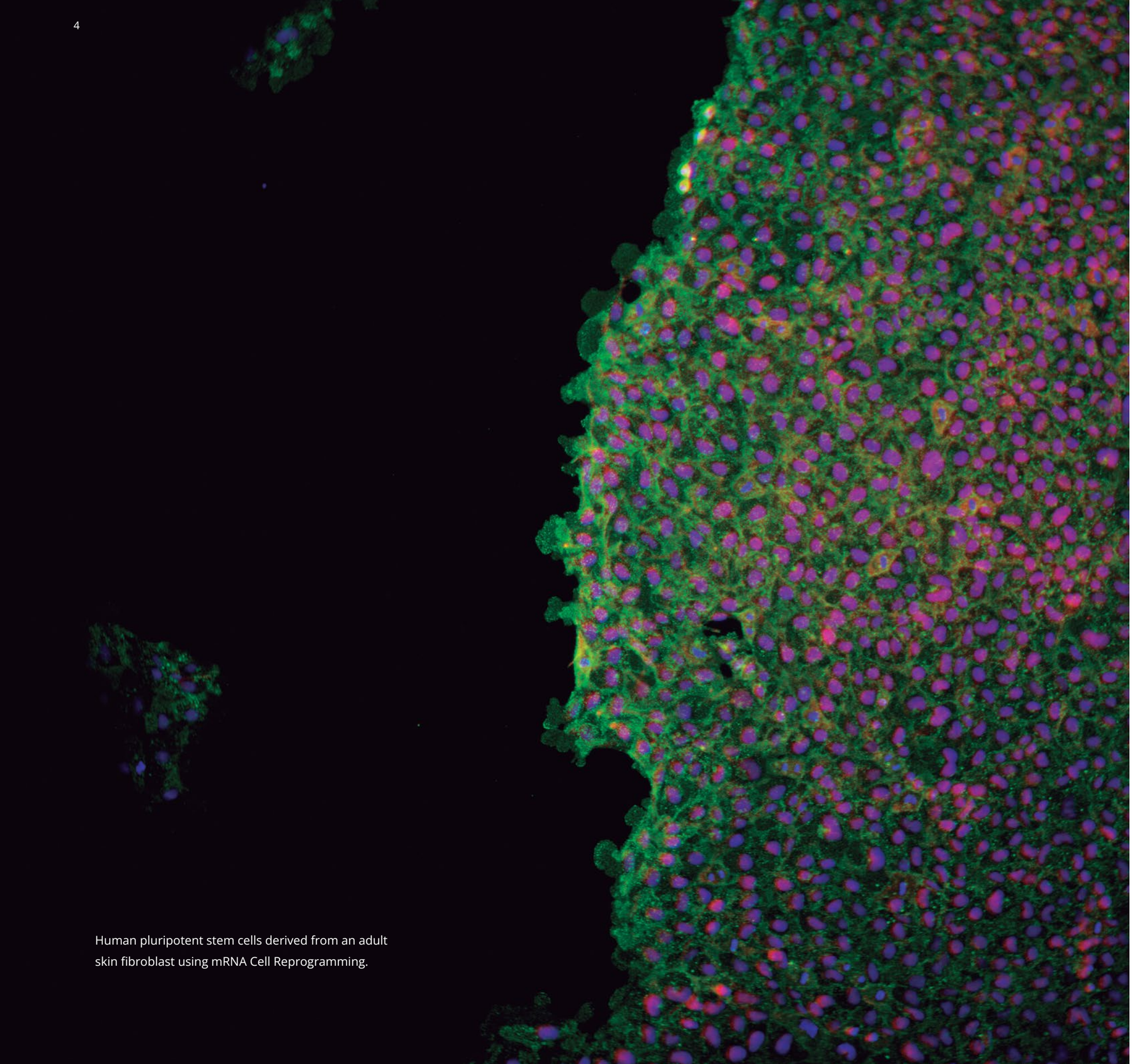


Human pluripotent stem cells derived from an adult skin fibroblast using mRNA Cell Reprogramming.

Cell Reprogramming & Gene Editing

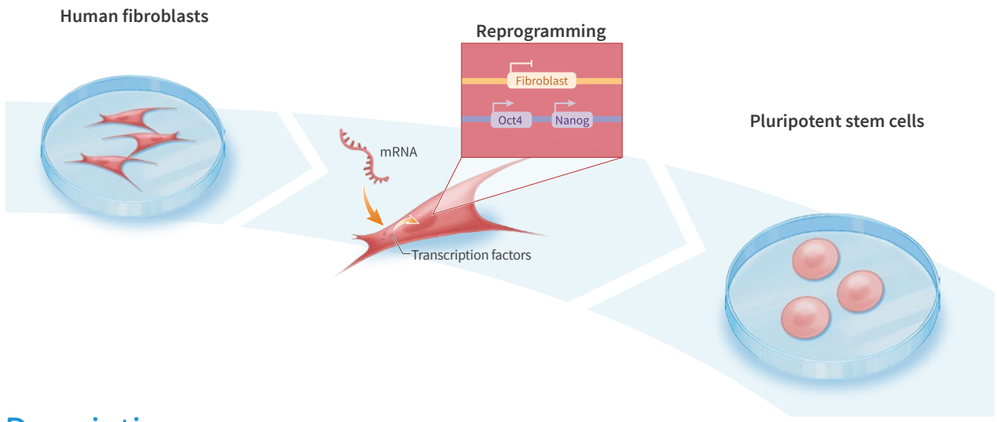
Cells contain two programs that work together to determine their behavior. A genetic program, written in the sequence of a cell's DNA, encodes information about each protein that the cell produces, while an epigenetic program not encoded in the sequence of a cell's DNA determines other heritable characteristics, 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 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[1].

mRNA Cell Reprogramming is protected by ten U.S. patents, as well as patents in Canada, 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 methods 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 Context-Sensitive Gene-Editing Endonuclease and/or Factor's Combined mRNA Cell Reprogramming & Gene Editing 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]Harris, J., et al. Mol Ther, Vol 28 No 4S1, 2020.

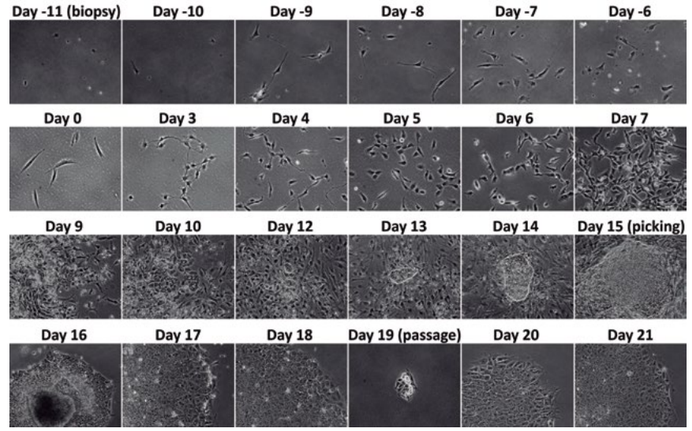


Figure 1. mRNA Cell Reprogramming from biopsy to pluripotent stem cell line.

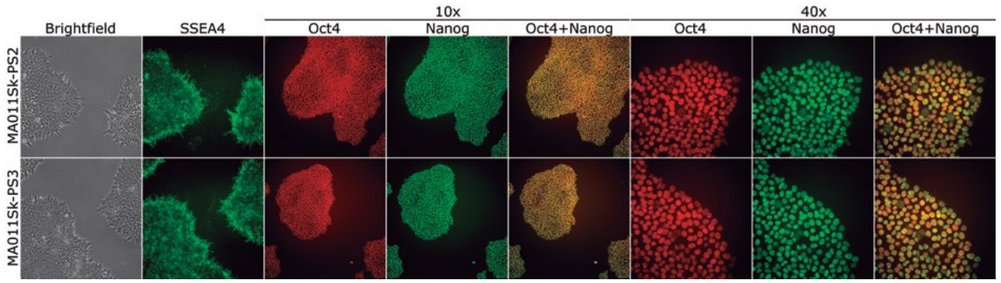


Figure 2. Characterization of human pluripotent stem cells generated using mRNA Cell Reprogramming.

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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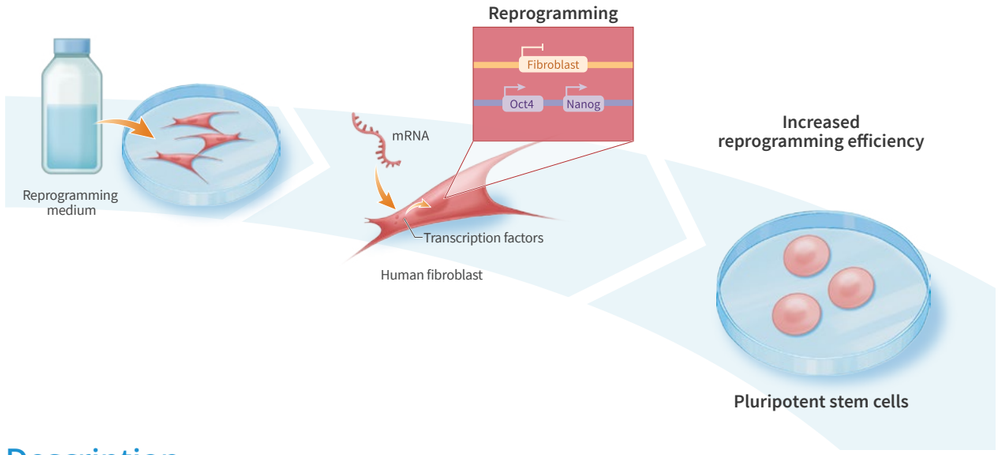
Cell Reprogramming Medium



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[2].

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 Cell Reprogramming & Gene Editing 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

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

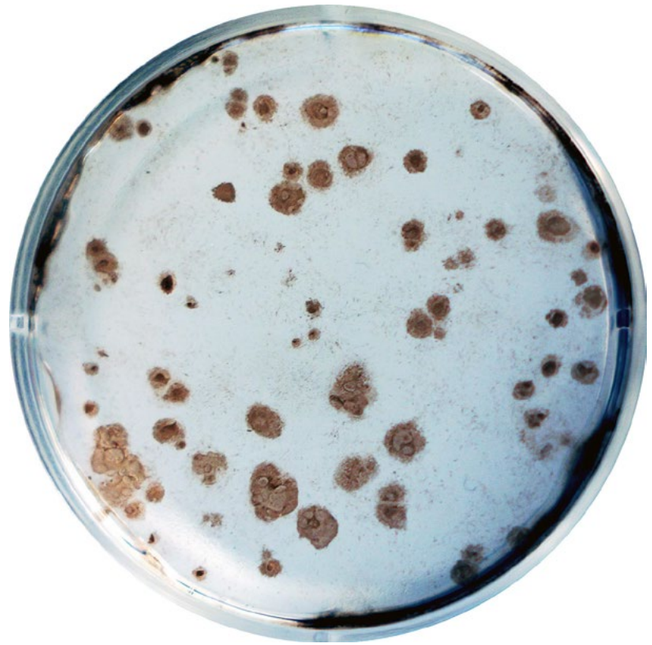


Figure 1. High-efficiency mRNA cell reprogramming of primary human fibroblasts (colonies stained for SSEA4).

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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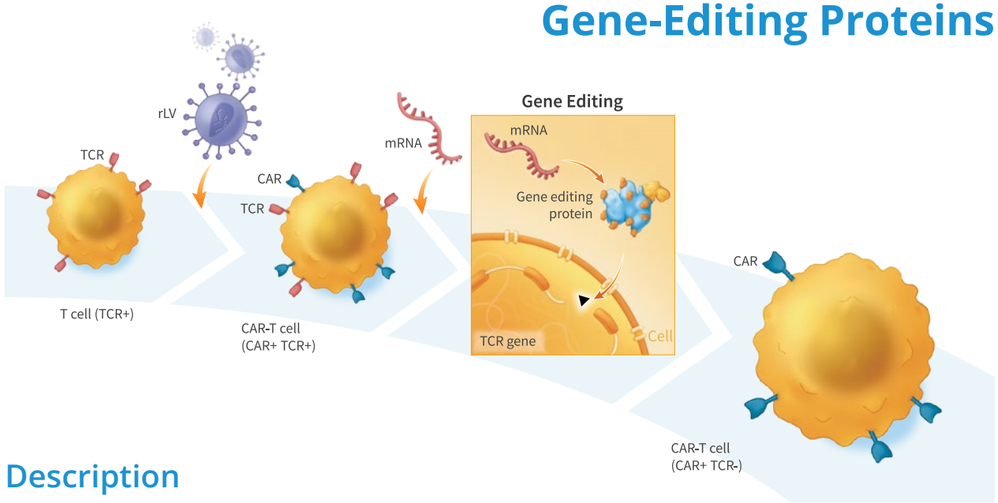
mRNA Vectorization of Gene-Editing Proteins



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 five U.S. patents, as well as patents in Australia, Korea, 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, 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.)

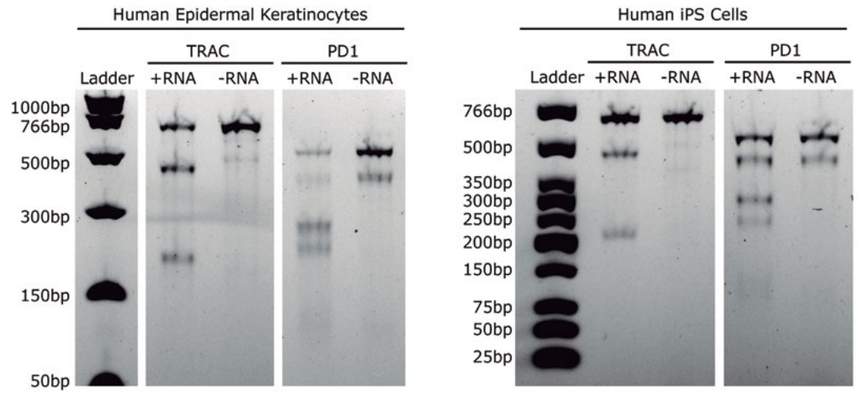


Figure 1. High-efficiency gene editing of TRAC and PD1 in human epidermal keratinocytes and human iPS cells.

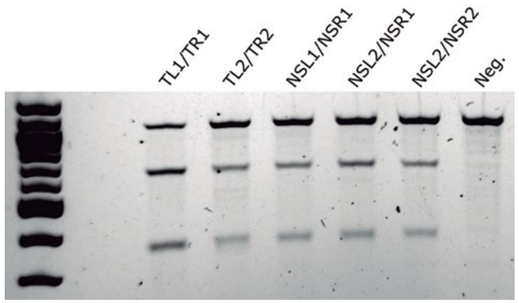


Figure 2. High-efficiency gene editing of the AAVS1 genomic safe harbor locus in human iPS cells.

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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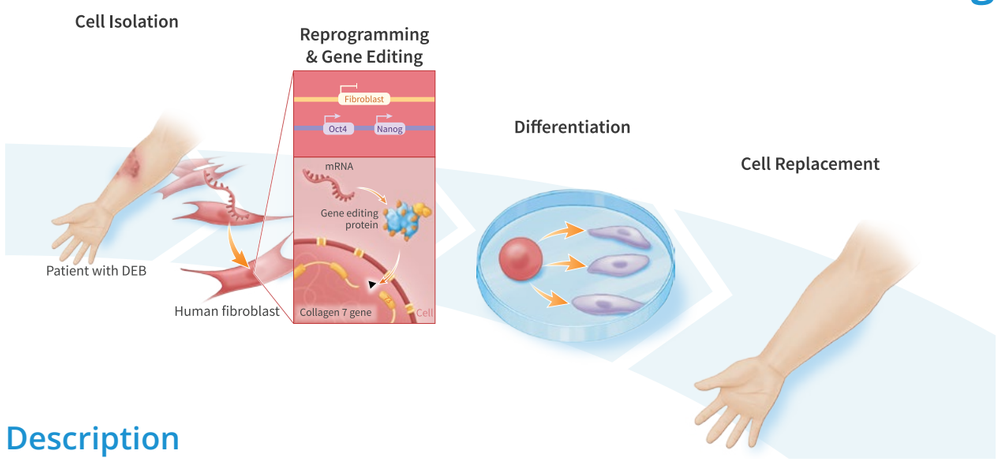
Combined mRNA Cell Reprogramming & Gene Editing



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 Cell Reprogramming & Gene Editing is protected by two U.S. patents, as well as a patent in Japan (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, 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

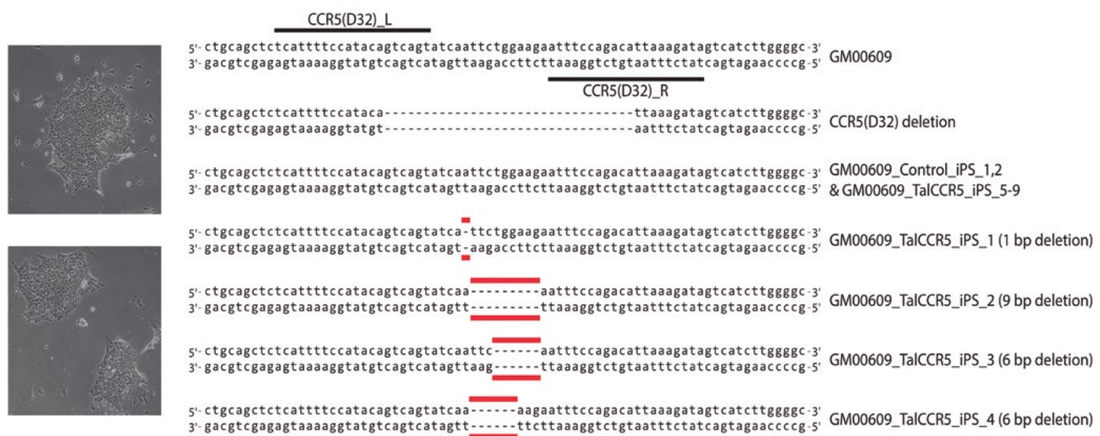


Figure 1. Combined mRNA Cell Reprogramming & Gene Editing to create clonal pluripotent stem cell lines containing defined deletions in the CCR5 gene.

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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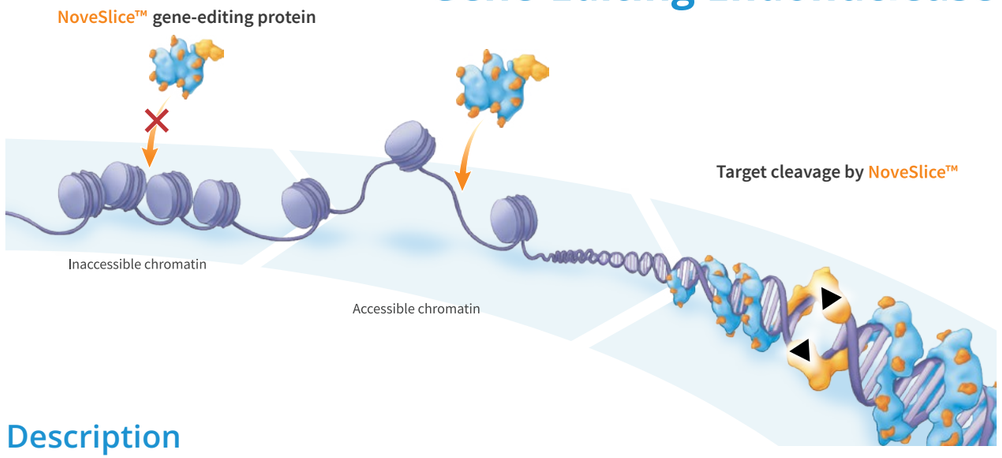
Chromatin Context-Sensitive Gene-Editing Endonuclease



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[3]. 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 ten U.S. patents, as well as patents in Europe, Canada, Australia, Japan, Korea, Brazil, Russia, 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[3])
- 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

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

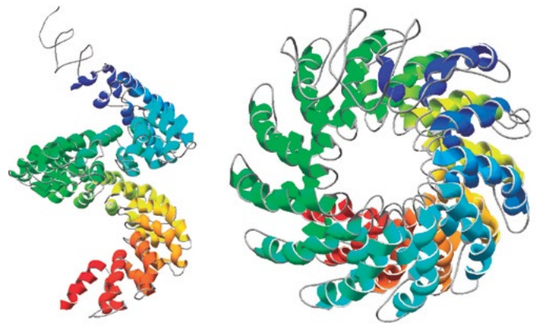


Figure 1. Example Chromatin Context-Sensitive Gene-Editing Endonuclease DNA-binding domain.

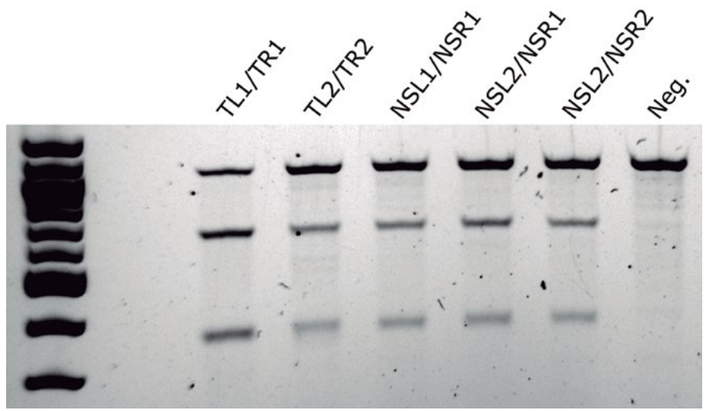


Figure 2. High-efficiency gene editing of the AAVS1 genomic safe harbor locus in human iPS cells.

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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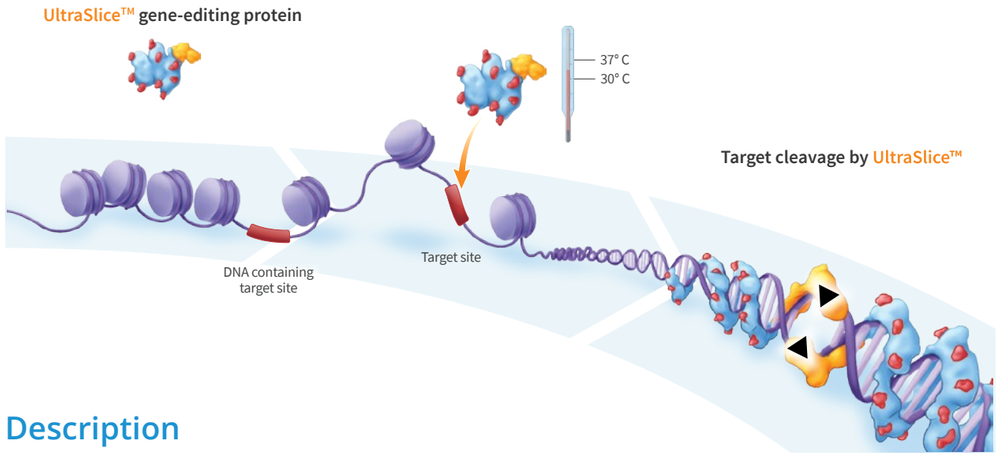
Temperature-Tunable Gene-Editing Endonuclease



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 physiological and 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.

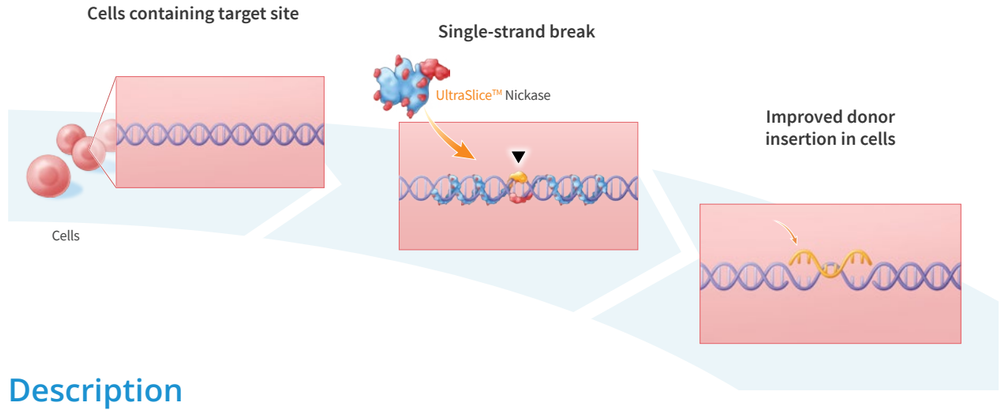
The Temperature-Tunable Gene-Editing Endonuclease is protected by a pending U.S. patent (with additional patents pending in other countries).

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-Editing Endonuclease with Nickase Functionality



Description

Many gene-editing strategies involve the use of nucleases to generate targeted double-strand breaks in genomic DNA, which can cause cytotoxicity and off-target effects, limiting clinical translation.

Our scientists developed a novel high-specificity gene-editing endonuclease with nickase functionality that enables high-efficiency on-target single-strand breaks in genomic DNA and scarless targeted gene insertion in cells[5]. This technology can be used to improve transgene insertion, reduce off-target effects, minimize cellular toxicity, and enable enhanced safety for therapeutic applications.

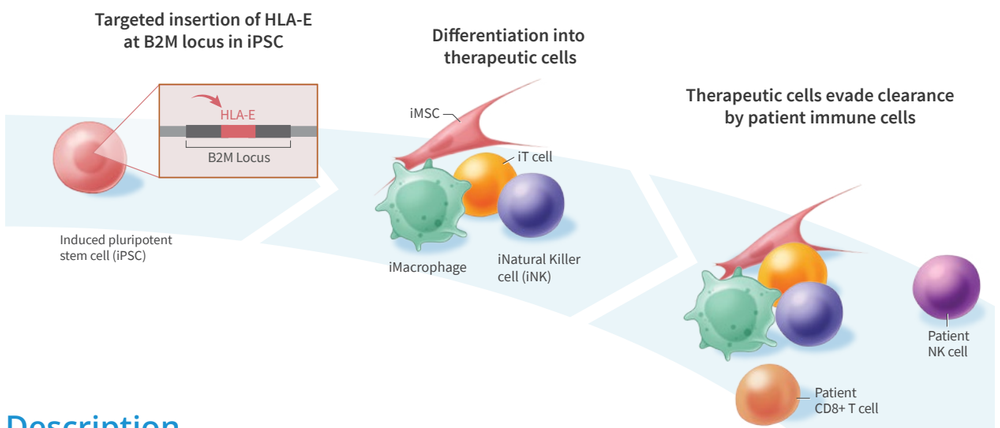
The Gene-Editing Endonuclease with Nickase Functionality is protected by a pending U.S. patent (with additional patents pending in other countries).

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
- Scarless 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

[5]Belcher, E., et al. Mol Ther, Vol 31, No 4S1, 2023.

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[6]. This technology can be used to generate allogeneic cell therapies with high potency and enhanced targeting.

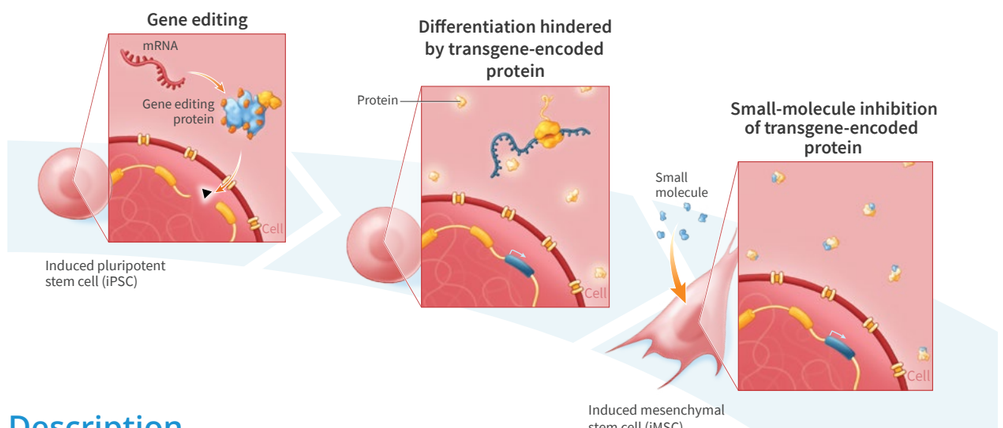
The Gene-Edited Allogeneic Cell Therapies technology is protected by a pending U.S. patent (with additional patents pending in other countries).

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.)

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

Directed Differentiation of Gene-Edited Pluripotent Stem Cells



Description

Pluripotent stem cell-derived therapies can involve directed differentiation of pluripotent stem cells to specific cell lineages. In gene-edited cells, directed differentiation can be hindered by transgene-encoded proteins.

Our scientists developed a technology for differentiating gene-edited pluripotent stem cells comprising a transgene that uses small-molecule inhibitors of the transgene-encoded protein[7].

Directed Differentiation of Gene-Edited Pluripotent Stem Cells is protected by a pending U.S. patent (with additional patents pending in other countries).

Example Applications

- High-efficiency differentiation of gene-edited pluripotent stem cells
- High-purity transgene-expressing pluripotent stem cell-derived cells
- Autologous and allogeneic engineered cell therapies (e.g., CAR-T, CAR-NK, gene-edited 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

[7]Klee, D., et al. Mol Ther, Vol 31, No 4S1, 2023.

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.

Abigail Blatchford, Associate Scientist

"A huge benefit of working at Factor is that everyone is exceptionally receptive to new ideas. If you can make the case for why you should try it, you'll get the support you need."

Finding a Supportive Environment

Abigail began pursuing her career in science at Northeastern University, majoring in bioengineering and minoring in women, gender, and sexuality studies. As an undergraduate, she took advantage of her school's cooperative education ("co-op") program to explore potential career paths. In her first co-op, she worked at a formulation-focused biotech company and quickly discovered that small-molecule drug formulation and polymer engineering were *not* her passions.

In her next co-op, Abigail worked on the scale-up manufacturing of induced pluripotent stem cells using vertical wheel bioreactors. "I realized I was much more interested in working with living things than small molecules." When she graduated in 2021, Abigail knew that she was looking for an opportunity that would allow her to continue to explore her interest in stem cells.

Abigail learned about mRNA cell reprogramming, mRNA gene editing, and Factor Bioscience's work related to stem cells on Factor's website, and decided to apply for a position as Research Associate. Her experience and enthusiasm for scientific research made Abigail an excellent fit.

Abigail's first project at Factor involved optimizing the design of DNA repair templates for inserting transgenes into stem cells. Abigail worked closely with Factor's Co-Founder and Chief Technology Officer, Dr. Christopher Rohde, designing and testing oligonucleotides and discovering that the inclusion of an immunosuppressive motif could improve insertion efficiency. Abigail presented her findings at the annual meeting of the American Society of Gene & Cell Therapy (ASGCT) in 2022.

An Idea Leads to Success

As a result of her accomplishments, Abigail was promoted to Associate Scientist and she began a new project working with pluripotent stem cell-derived myeloid cells. Abigail collaborated closely with fellow Associate Scientist, Mackenzie Parmenter, who had been working with pluripotent stem-cell derived lymphocytes. Leveraging her past experience with bioreactor-based cell culture, Abigail proposed transitioning Factor's existing differentiation protocols to bioreactors. She recalled, "I reached out to my former colleagues to see if a collaboration of some sort would be possible and if any of their clients had done this kind of work. They said they hadn't had clients do this kind of work, but they were very interested in it."

Abigail pitched the idea to Factor's Co-Founder and CEO, Dr. Matt Angel, who approved the project and authorized the purchase of a bioreactor. Abigail's initial testing proved highly successful, and after just a year, she had formalized a process for producing hundreds of millions of immune cells for preclinical testing of candidate therapies to treat cancer.

"A huge benefit of working at Factor is that everyone is exceptionally receptive to new ideas. If you can make the case for why you should try it, you'll get the support you need. That was a very cool experience to be able to pitch something and then to discover that it actually works." Abigail presented the results of her work at the ASGCT annual meeting in 2023.

"Abigail has enormous talent for scientific research and her achievements are far above and beyond what would normally be expected of a Research Associate," said Dr. Angel. "In particular, the initiative that Abigail showed in proposing the development of bioreactor-based cell culture at Factor has transformed the way our company produces cells across multiple project areas. I am incredibly proud of Abigail's success and the environment at Factor that has fostered her ingenuity."

Following Her Passion

Since she decided to major in bioengineering, Abigail had always wanted to combine her degree with her passion for gender equality in health. As she debated whether or not to pursue graduate study, Dr. Angel encouraged Abigail to try to identify a program that would align with her passion. "Dr. Angel provided a reference and was very helpful in obtaining a position for me at my top choice Ph.D. program. He's really supportive of people who want to go to grad school," she said. "He wants to see people grow and evolve as scientists. He helps us discover our passions and definitely facilitates our ability to follow them. I'm so thankful for all of his help." Last fall, Abigail left Factor to pursue her Ph.D. in Women's and Reproductive Health Sciences at the University of Oxford.

Mackenzie Parmenter, Associate Scientist

"I think everything at Factor is driven by what you want to do."

Exploring an Interest in Translational Science

Mackenzie joined one of Factor Bioscience's spinoffs, Novellus Therapeutics, as a Research Associate after graduating with a Bachelor's degree in Biology from Tufts University. She quickly realized that her passion for research was focused on translating scientific discoveries into technologies that can be used to improve peoples' lives.

"I discovered that I really enjoyed working with human cells, and being part of Factor allowed me to work on creating next-generation cell therapies. I find that part of the job very rewarding," she said. Mackenzie began researching the development of novel mRNA constructs encoding gene-editing proteins and protocols for differentiating pluripotent stem cells into cytotoxic lymphocytes for applications in the treatment of cancer. Her work was exceptionally fruitful, and she presented her results at the 2021 annual meeting of the American Society of Gene & Cell Therapy.

Rising to Meet a Complex Challenge

In early 2021, Factor was approached by a company interested in developing both a gene-edited pluripotent stem cell line and a process for differentiating the cells into cancer-killing lymphocytes. To support this project, Factor would be required to rapidly design and test novel gene-editing constructs, use these constructs to develop and characterize the gene-edited cell line, and develop, from scratch, a scalable process to differentiate the cells into well-defined functional lymphocyte populations.

This project was easily the most complex that Factor had ever undertaken, and required not only knowledge of genetics, immunology, and stem cell biology, but also great skill in the application of this knowledge to the molecular and cell biology processes required to generate and test the resulting cells. The experience that Mackenzie had gained in her first year at Factor made her an excellent fit for the project team, and she was selected to lead the development of the gene-edited pluripotent stem cell line and the differentiation and characterization of the resulting lymphocytes. Mackenzie's work on this project resulted in a multimillion-dollar contract for the development of novel treatments for hematologic and solid malignancies, and she presented her results at the ASGCT annual meeting in 2022.

"Mackenzie has demonstrated the highest level of skill in challenging areas of molecular and cell biology, and she has brought immense value to our company and has advanced the field of cell engineering," said Dr. Matt Angel, Co-Founder and CEO of Factor. "She is a very talented scientist, but more than that, she has the tenacity and resilience needed to design and carry out complex experiments that often require weeks and sometimes months before yielding a result."

As a result of her achievements, and in recognition of her demonstrated ability to carry out independent research, Mackenzie was promoted to Associate Scientist.

Mackenzie credits Dr. Angel for recognizing her motivation and allowing her to help drive company innovation in cancer-fighting therapy research. She noted, "Dr. Angel always likes people to have a plan. He's always asking, 'What's the next step?' I think everything at Factor is driven by what you want to do."

Launching a Career in Science

Mackenzie's work with pluripotent stem cells and directed differentiation has helped her develop questions that she hopes to study during her graduate research, including how self-renewing hematopoietic stem cells behave *in vitro* and, more broadly, how cell fate is determined in certain lineages. "This has been an incredible opportunity for me. I've been able to grow into myself as a scientist. I'm so glad to have gotten the practical experience at Factor that has helped me solidify my future."

Last fall, Mackenzie left Factor to pursue her Ph.D. in the Developmental and Stem Cell Biology program at Duke University.

I. Caglar Tanrikulu, Ph.D., Principal Scientist

"I couldn't have had a better first step into industry, or found a better match."

Making a Connection

Caglar Tanrikulu developed an early interest in chemistry and biology at the Robert College of Istanbul. He received a full scholarship to Ohio Wesleyan University and graduated with a degree in Biochemistry before going on to complete a Ph.D. in Biochemistry and Molecular Biophysics at the California Institute of Technology in computational enzyme design. As a Postdoctoral Research Associate at the University of Wisconsin-Madison, Caglar studied collagen-like peptides that could self-assemble into biomaterials. He continued this work at the Massachusetts Institute of Technology as a full-time Research Scientist, developing synthetic-collagen hydrogels.

Caglar first met Factor Bioscience's Co-Founder and CEO, Dr. Matt Angel at MIT's 2018 Fall Career Fair. "Factor's work seemed quite interesting, especially their use of novel gene-editing endonucleases, but I had no gene-editing experience," said Caglar. "I was open to exploring new research and had some cell-culture experience at the time, but gene-editing definitely wasn't my strong suit." The next time the two met was at the 2019 career fair, where Dr. Angel was accompanied by five employees. "I think I talked with everyone," recalled Caglar, "I was really impressed by their curiosity and enthusiasm." It was there that Dr. Angel asked for Caglar's resume.

A few days later, Caglar received an invitation to speak at Factor. "I was looking at my slide deck and couldn't find anything that seemed relevant for this audience." Upon asking Dr. Angel for guidance, Caglar was very surprised to hear that they were interested in his current research on biomaterials. "Dr. Angel told me that their primary interest was how I conducted my research. They simply want people who can do exceptional science". Caglar was not opposed to switching research areas. "Science is science, after all," he said, "but prioritizing candidates' intellectual abilities over their technical skills is quite uncommon in industry."

Taking a Chance on a New Direction

Caglar was offered a position as Senior Scientist at one of Factor's spinoffs, Novellus Therapeutics, and quickly accepted. "The research was definitely interesting, and after seeing Dr. Angel's vision, I wanted to give it a try." That wasn't the only thing that influenced his decision, however. "It simply felt good to be here. It is important to me to be in a place where people get along and communicate freely. Yes, this definitely makes daily life easier, but it also lets you better focus on the science."

Caglar worked closely with his colleagues at Novellus, and their hard work and success led to Novellus' acquisition two years later. "I couldn't have had a better first step into industry, or found a better match. Dr. Angel is always available to help direct our research efforts, and Dr. Rohde (Dr. Christopher Rohde, Co-Founder and CTO of Factor) is an inspiration—he will come up with novel ideas and turn them into reality at a record pace. Intellectually, you will never be bored here. Factor provides its employees with as much opportunity and responsibility as they can handle. The environment here has helped numerous entry-level employees join excellent graduate programs at world-renowned universities. I know Dr. Angel takes a lot of pride in helping his employees build their careers. That's just wonderful."

"Caglar is an excellent researcher who has done exemplary work throughout his career. We are very fortunate to have him as a team member and a mentor to our other employees," said Dr. Angel.

The Work Environment Makes All the Difference

According to Caglar, one of his favorite things about working at Factor is the open exchange of ideas. He explained that people in meetings will chime in on many specialized topics. No one gets shut down when asking a question, even if it's outside of their background and experience. "Everyone can tolerate the occasional, incredibly naive question," he joked, "but that does show you how the team lifts everybody up." "The most fun part of my work is somebody putting data in front of me and asking, 'What do you think?' And being a small company, you can get everybody's feedback on a new idea really fast, including Dr. Rohde's and Dr. Angel's. I love this place for that."

"I believe that science never operates linearly," said Caglar. "The world is continuously changing, and we'll never run out of problems to solve. The finish line will keep moving, but so will technology, and it's incredible to be part of this journey with Factor."

Nucleic Acid Delivery

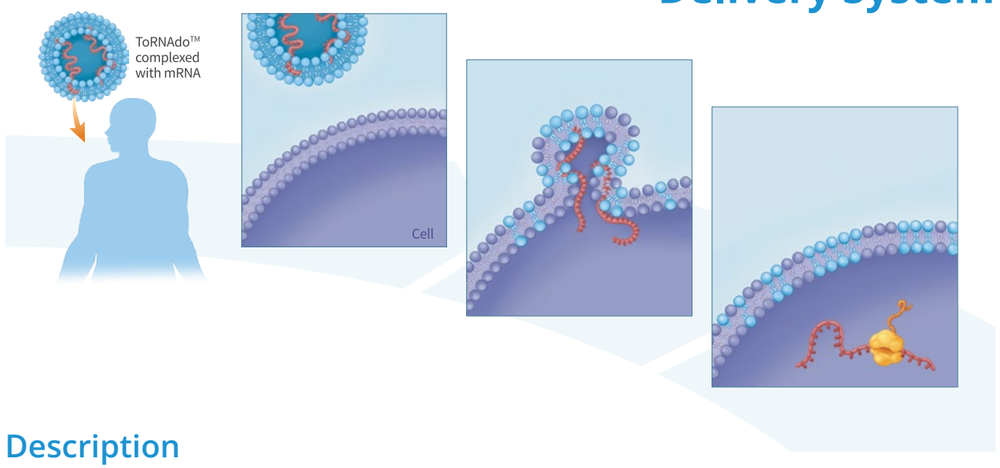
Nucleic acids, such as mRNA, can be used to induce cells to express proteins, including proteins that are capable of re-writing genetic and epigenetic cellular programs. However, nucleic acids are susceptible to degradation by intracellular and extracellular nucleases and can trigger immune responses that can block protein translation and cause cell death. The plasma membrane also 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 DNA sequences into defined genomic loci, and efficient in vivo delivery of mRNA to the brain, eye, skin, and lung.

Human skin containing cells expressing red fluorescent protein after in vivo 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[8].

The ToRNAdo™ Nucleic Acid Delivery System 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 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
- 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

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

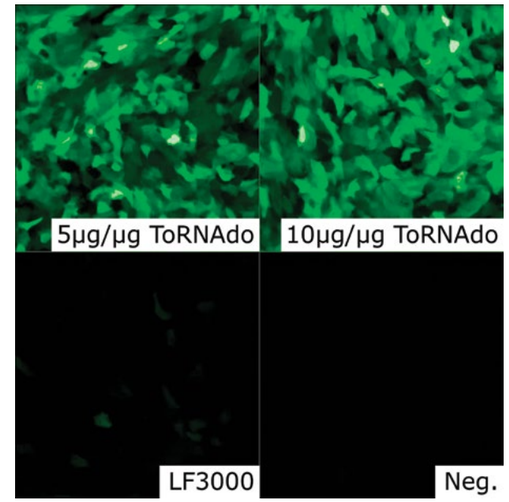


Figure 1. ToRNAdo™ delivery of GFP mRNA to human epidermal keratinocytes in vitro.

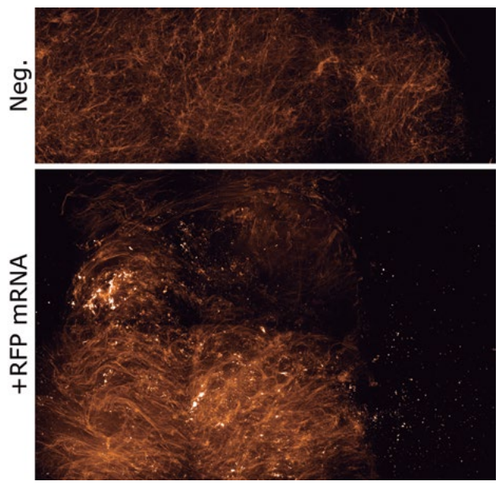
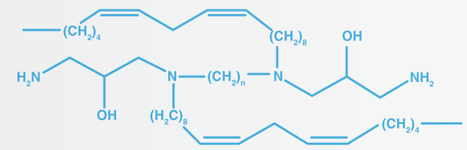


Figure 2. ToRNAdo™ delivery of RFP mRNA to human skin in vivo.

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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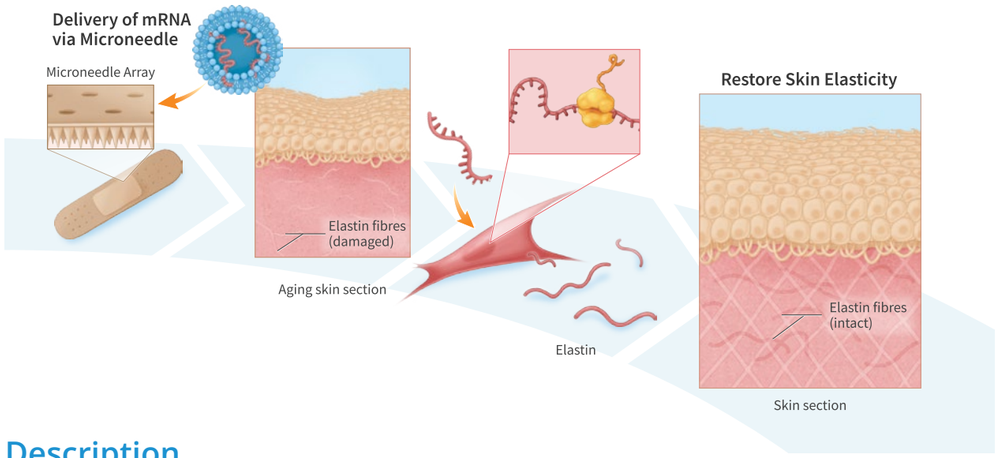
mRNA Delivery to Skin



Description

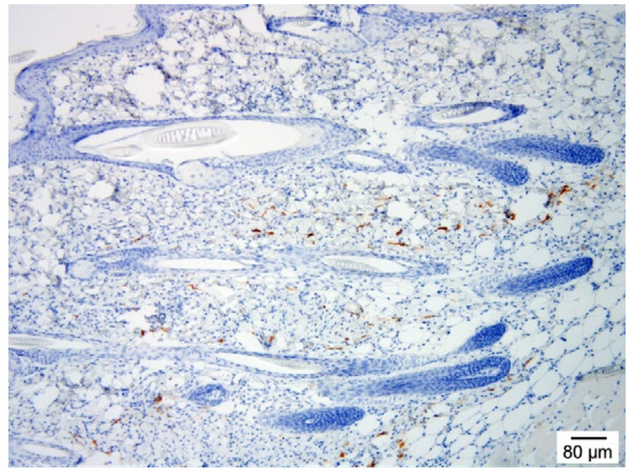
In addition to being the largest and most accessible organ of the body, the skin contains large numbers of highly active cells that have a high capacity for protein synthesis. These characteristics make the skin an ideal platform for expressing therapeutic proteins, both locally, for the treatment of 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 U.S. Patent Number 11,241,505 (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, target sequence, type of gene-editing protein, method of transfection, mRNA sequence or chemistry, or formulation.

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



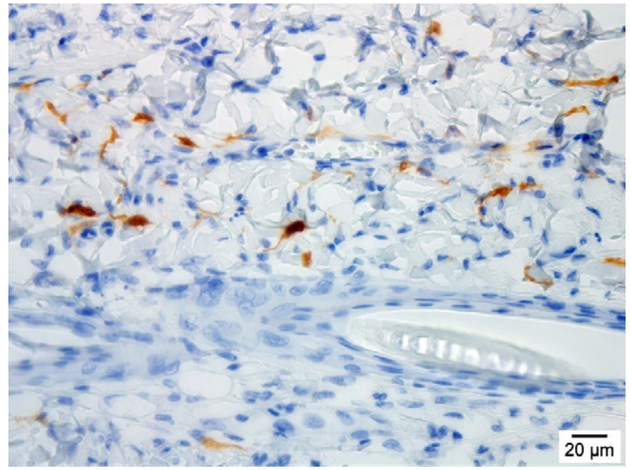


Figure 1. Rat skin containing cells expressing a reporter protein following mRNA delivery.

Representative Claim

U.S. Pat. No. 11,241,505

A method for gene-editing a cell in the skin of a human subject, comprising inducing a single-strand or double-strand break in the DNA of the cell, comprising:

administering intradermally to the human subject a composition comprising an effective dose of about 300 ng of an RNA encoding a protein of interest to result in the cell expressing the protein of interest,

wherein the protein of interest is a gene-editing protein, and

wherein the effective dose of about 300 ng of the RNA encoding the protein of interest provides greater expression of the protein of interest than a dose of 1200 ng of RNA encoding the protein of interest during the second to fifth day after administering the RNA.

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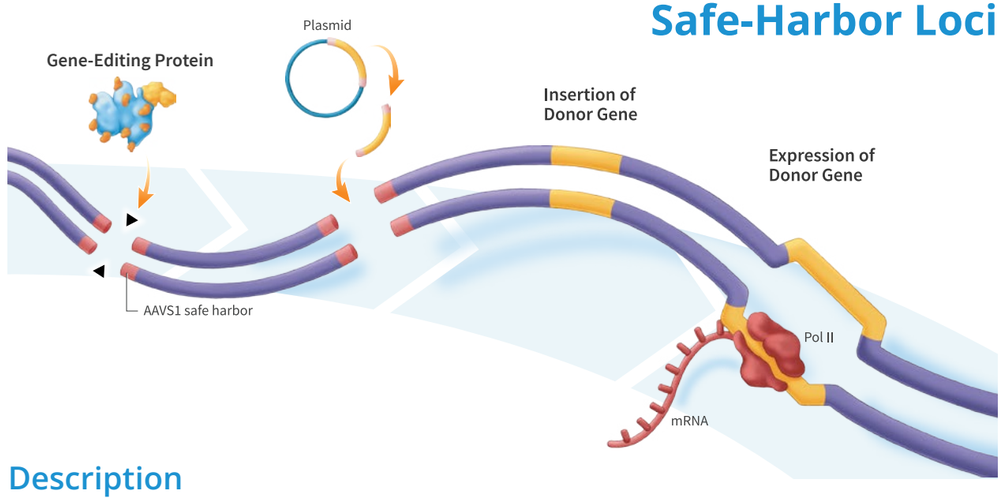
Insertion of Sequences into Safe-Harbor Loci



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 two U.S. patents, as well as patents in Canada, Korea, 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 type of nucleic acid, or formulation.

Example Applications

- High-efficiency insertion into the AAVS1 safe-harbor locus
- Achieve insertion of longer sequences than are possible with AAV donor vectors
- 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
- Combine with Factor's Chromatin Context-Sensitive Gene-Editing Endonuclease for high-specificity ex vivo or in vivo gene editing

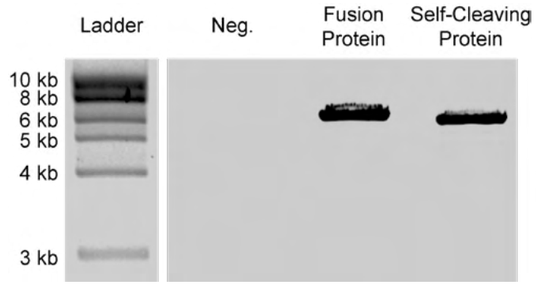


Figure 1. Biallelic insertion of a fusion protein and a self-cleaving protein into the AAVS1 safe-harbor locus of iPS cells.

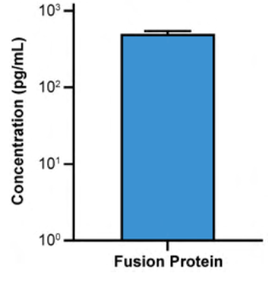


Figure 2. Expression of an inserted fusion-protein sequence.

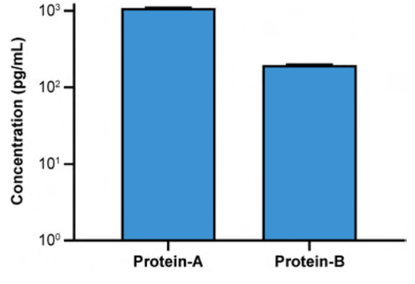


Figure 3. Expression of proteins encoded by an inserted self-cleaving protein sequence.

Representative Claim

U.S. Pat. No.11,332,758

An in vitro method for inserting a nucleic-acid sequence into a safe-harbor location of a genome of a cell comprising transfecting in vitro a cell comprising a safe-harbor location with

(i) a first nucleic acid comprising a nucleic-acid sequence for insertion and

(ii) a second nucleic acid comprising a synthetic ribonucleic acid (RNA) molecule encoding an artificial transcription activator-like (TAL) effector targeting the safe-harbor location, the artificial TAL effector comprising:

(a) a DNA-binding domain and

(b) a nuclease domain,

wherein the DNA-binding domain comprises a repeat domain consisting of a plurality of TAL effector repeat sequences and at least one of the TAL effector repeat sequences consists of the 36-amino-acid sequence LTPvQVVAIAwxyzGHGG (SEQ ID NO: 74), wherein:

"v" is Q, D or E,

"w" is S or N,

"x" is N, H or I,

"y" is any amino acid, and

"z" is GGKQALETVQRLLPVLCQD (SEQ ID NO: 670) or GGKQALETVQRLLPVLCQA (SEQ ID NO: 671); and

wherein the cell is a human cell and the safe-harbor location is the AAVS1 locus, to result in insertion of the nucleic-acid sequence into the safe-harbor location.

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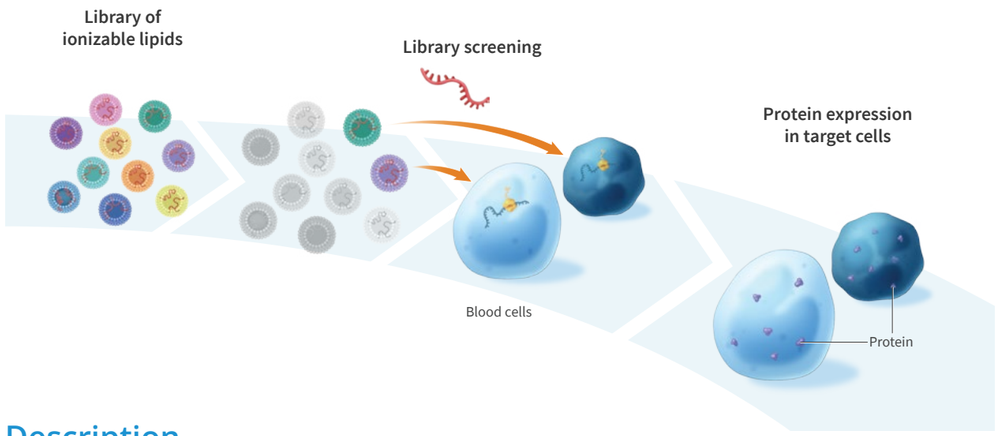
Polyvalent Ionizable Lipid Library



Description

Lipid delivery systems containing ionizable lipids have entered broad clinical use with the introduction of the COVID-19 mRNA vaccines and are now generally considered the gold standard for in vivo mRNA delivery.

Our scientists developed a technology that enables rapid screening of a library of polyvalent ionizable lipids to select for potent application-specific lipid formulations[9].

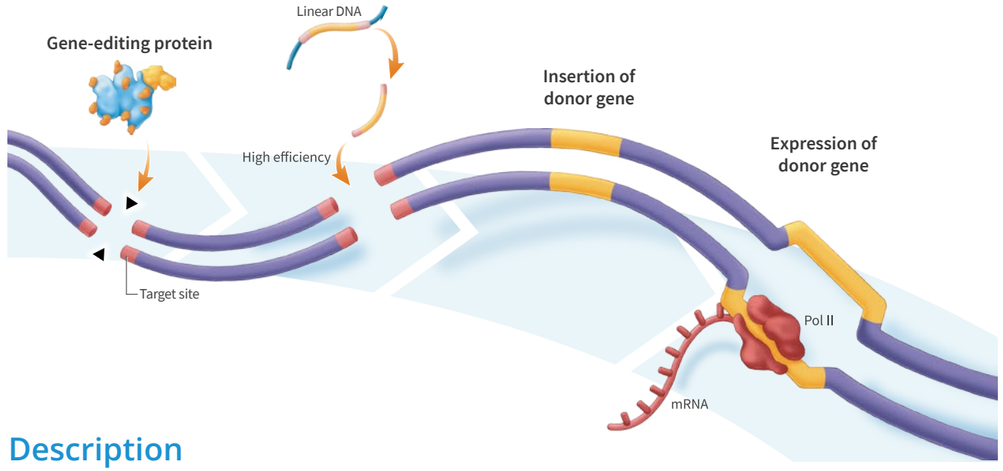
The Polyvalent Ionizable Lipid Library is protected by a pending U.S. patent (with additional patents pending in other countries).

Example Applications

- Application-specific library screening
- Screening for delivery to target cells and/or tissues
- Combine with Factor's Chromatin Context-Sensitive Gene-Editing Endonuclease for high-specificity ex vivo or in vivo gene editing
- Protection of nucleic acids from degradation pathways
- Efficient delivery of RNA and/or DNA to a variety of cell types
- Deliver nucleic acids, including mRNA, in vivo
- Combine with Factor's Engineered Protein-Encoding RNA to streamline manufacturing of nucleic acid therapies

[9]Belcher, E., et al. Mol Ther, Vol 31, No 4S1, 2023.

Engineered 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 engineered linear DNA donors to enable high-specificity on-target insertion[10]. This technology can be used, for example, to generate allogeneic CAR-T therapies for the treatment of cancer in which an engineered 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 engineered 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."

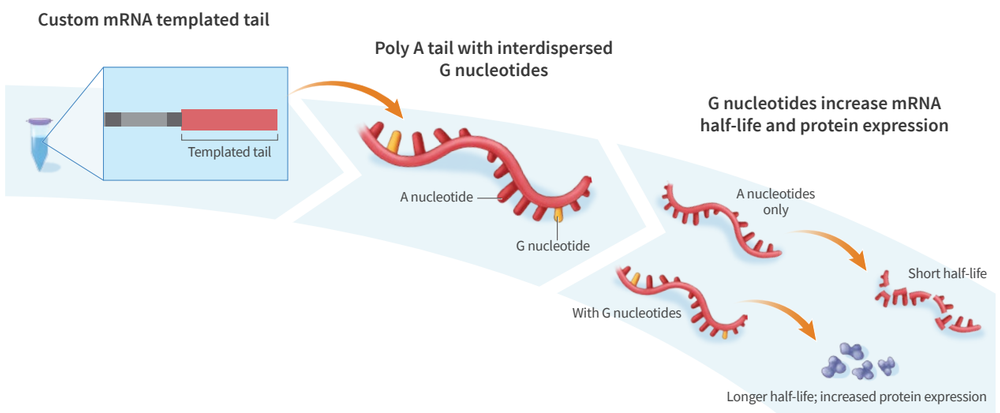
The Engineered Linear DNA Donors technology is protected by a pending U.S. patent (with additional patents pending in other countries).

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

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

Engineered Protein-Encoding RNA



Description

Cells use messenger RNA to carry genetic information encoded in genomic DNA to the cytoplasm for translation into proteins.

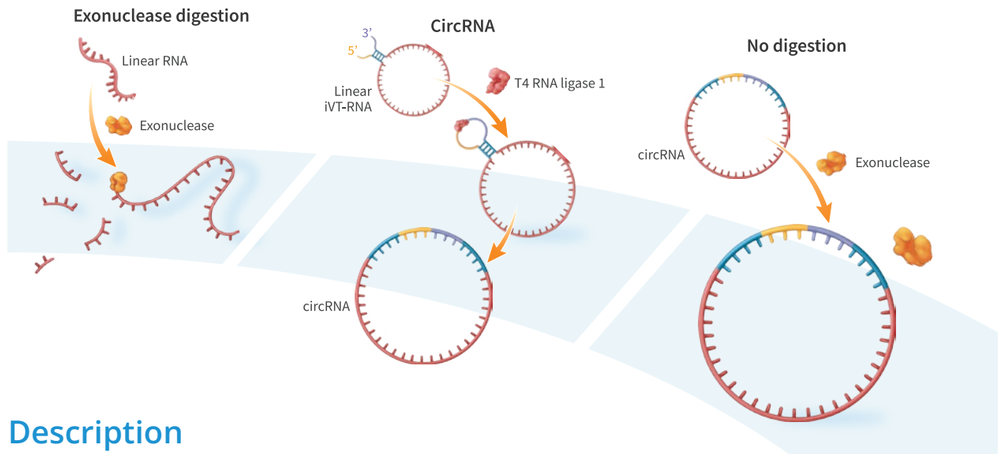
Our scientists developed a technology for inducing cells to translate defined proteins using protein-encoding RNA engineered to enable long-lasting expression of desired proteins.

Engineered Protein-Encoding RNA is protected by a pending U.S. patent (with additional patents pending in other countries).

Example Applications

- High-level expression of defined proteins ex vivo and in vivo
- Ultra-high efficiency editing of primary cells and pluripotent stem cells
- 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 – proven delivery to human skin in vivo
- Combine with Factor's Polyvalent Ionizable Lipid Library for in vivo application-specific delivery

Splint & 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[11]. 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 & 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

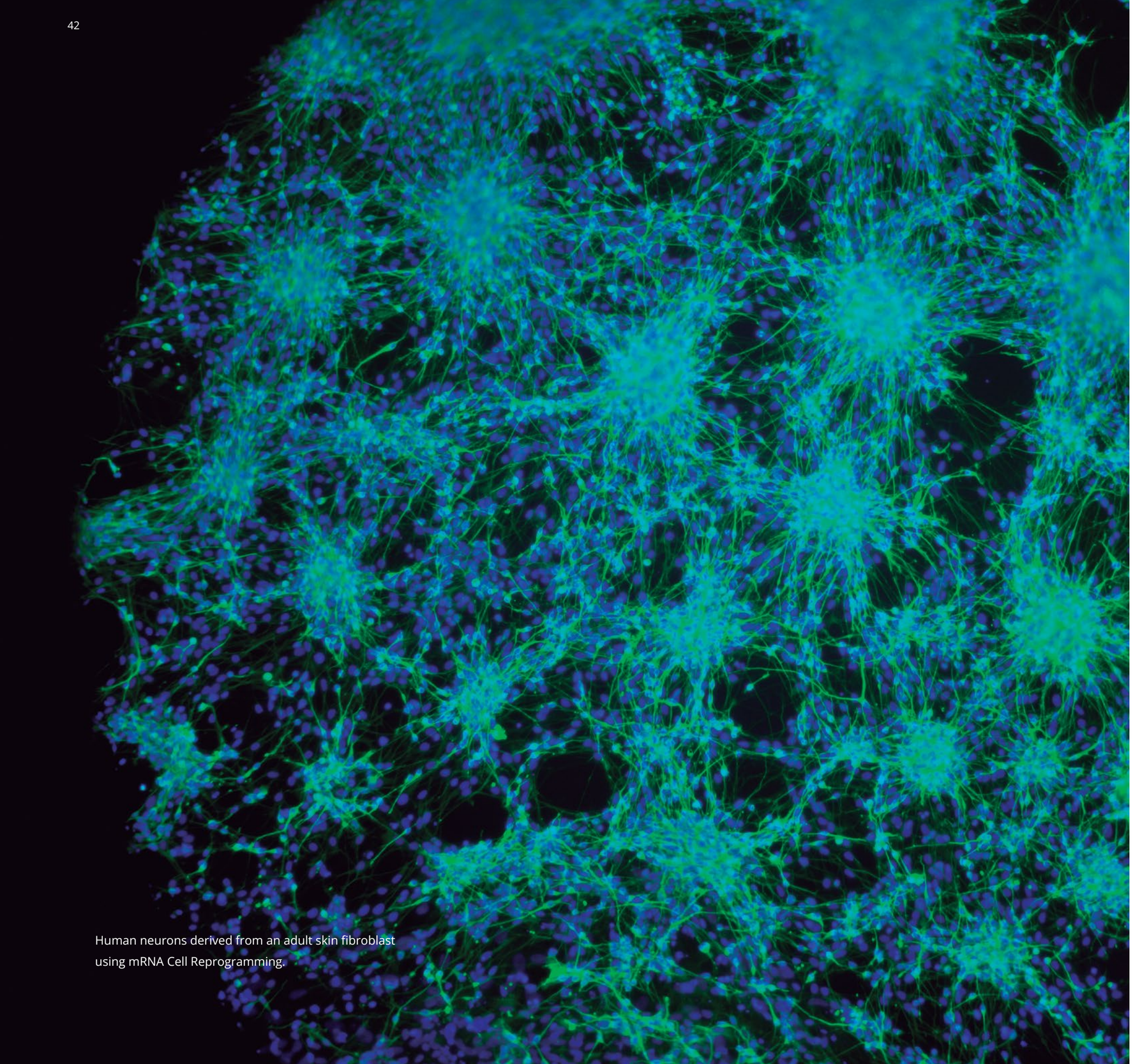
[11]Svihla, A., et al. Mol Ther, Vol 29, No 4S1, 2021.

ISO Class 7 Cleanroom Facility

We use our ISO Class 7 cleanroom facility, located at our headquarters in Cambridge, Massachusetts, to produce cutting-edge mRNA and cellular medicines for clinical testing.

In this facility, we are producing cells that have been reprogrammed and gene-edited using mRNA for anti-inflammatory, anti-cancer, and regenerative-medicine applications. These cells are planned for eventual testing in human subjects in support of our pipeline of therapeutic programs.

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.



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

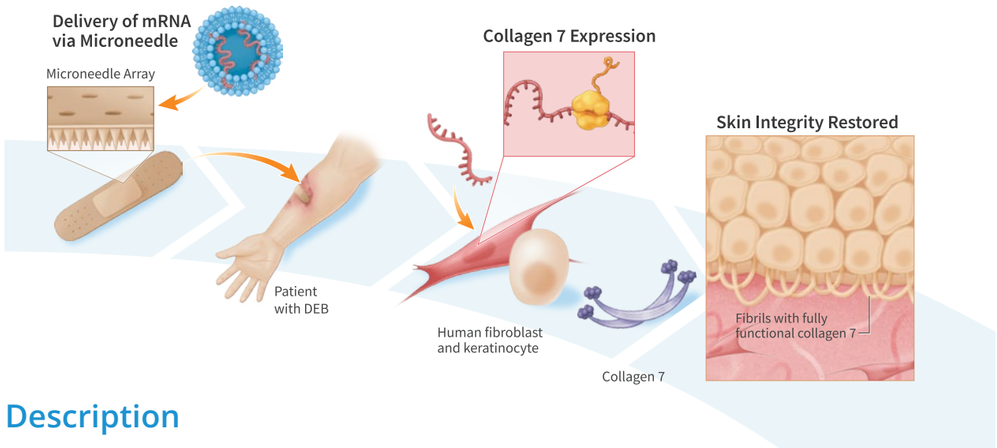
Disease-Focused Technologies

Human disease is caused by cellular dysfunction. Genetic diseases and cancer result from errors in a cell's genetic program (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 can 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.

mRNA Therapies for the Treatment of 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.

mRNA Therapies for the Treatment of Dystrophic Epidermolysis Bullosa (DEB) is protected by U.S. Patent Number 9,770,489 (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 target sequence, mRNA sequence or chemistry, type of gene-editing protein, 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

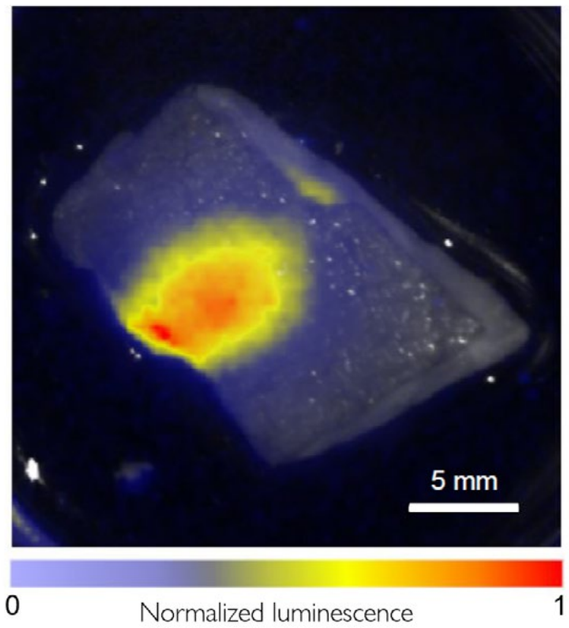


Figure 1. Human skin explant expressing a reporter protein following ToRNAdo™-mediated injection.

Representative Claim

U.S. Pat. No. 9,770,489

An in vivo method for treating dystrophic epidermolysis bullosa, comprising

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

delivering a COL7 repair template to the patient,

thereby editing the COL7 gene, wherein:

the synthetic RNA and repair template are 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 and causes a double-strand break in the COL7 gene of the patient's keratinocytes.

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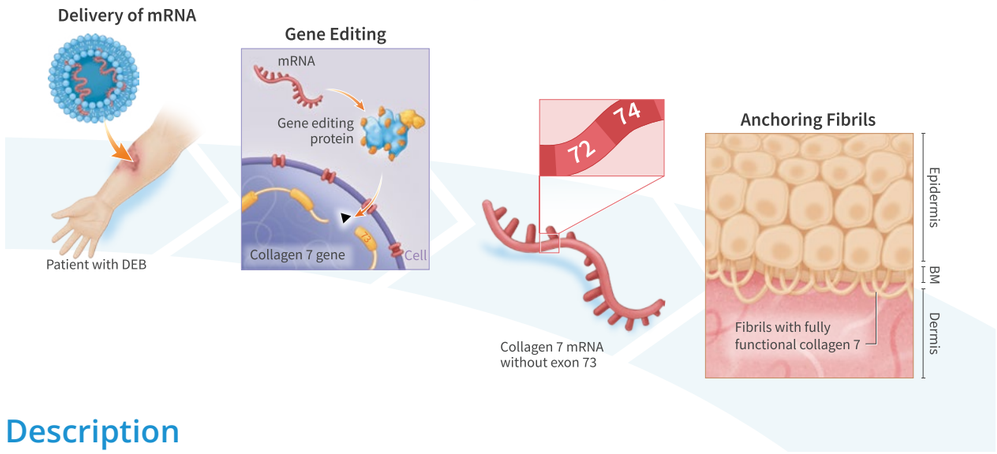
Gene-Editing Therapies for the Treatment of Epidermolysis Bullosa (EB)



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 the Treatment of Epidermolysis Bullosa (EB) is protected by two U.S. patents, as well as patents in Europe, Australia, Korea, Russia, 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 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[12]
- 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

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

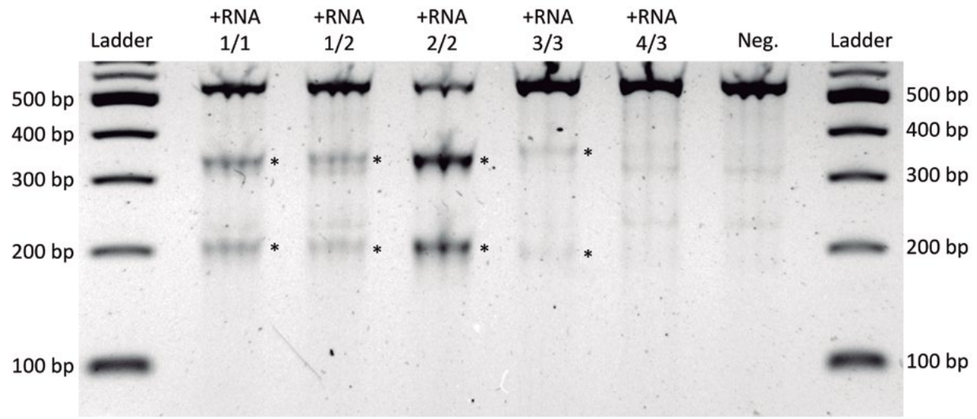


Figure 1. Gene editing of the COL7A1 gene in primary human cells using mRNA encoding gene-editing proteins.

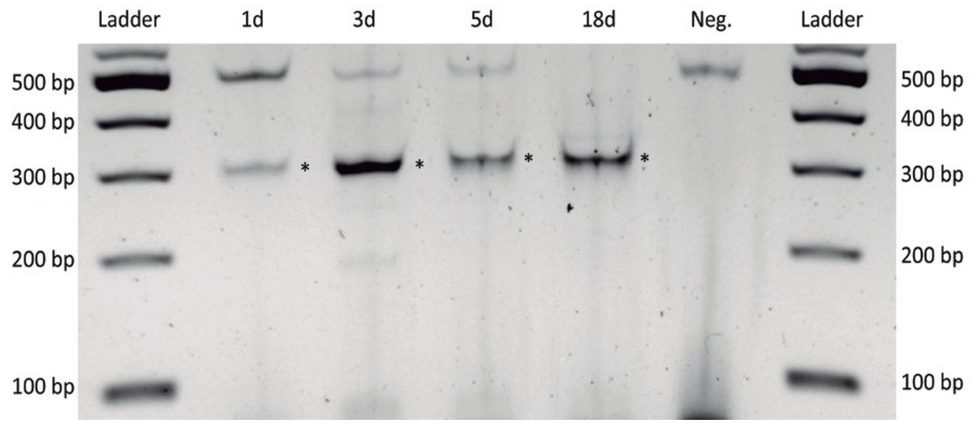


Figure 2. Durable exclusion of exon 73 in collagen 7 mRNA of treated cells.

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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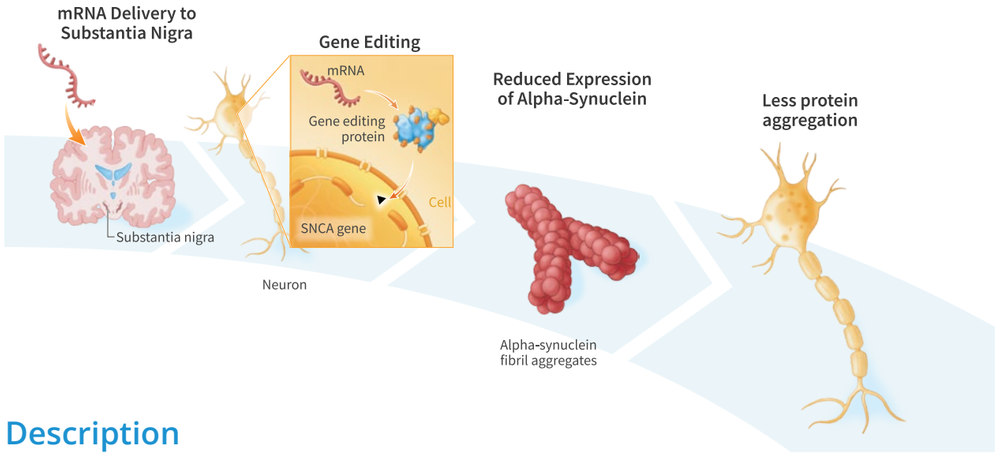
Gene-Editing Therapies for the Treatment of Parkinson's Disease



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 the Treatment of Parkinson's Disease is protected by two U.S. patents, as well as patents in Canada 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 specific target sequence, type of nucleic acid, formulation, or method of transfection.

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

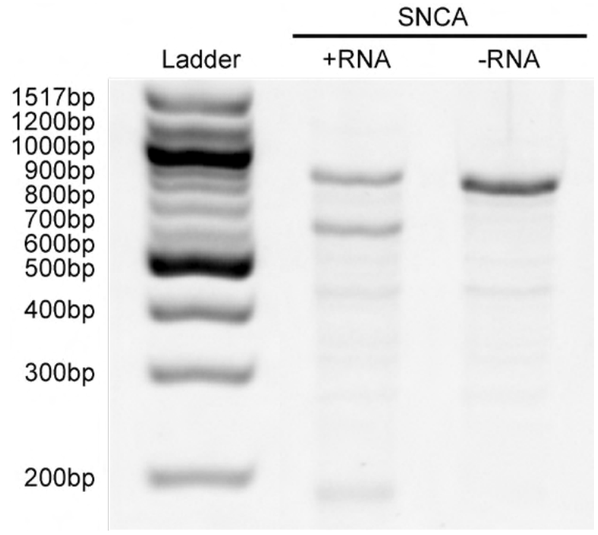


Figure 1. Gene editing of the SNCA gene in human iPS cells.

Representative Claim

U.S. Pat. No. 10,752,919

An in vitro method for producing a gene-edited cell comprising transfecting in vitro a cell comprising an α-synuclein (SNCA) gene with a nucleic acid encoding a gene-editing protein, wherein the gene-editing protein comprises: (a) a DNA-binding domain and (b) a nuclease domain and is capable of binding to a nucleotide sequence that encodes a protein comprising the amino acid sequence of SEQ ID NO: 51, 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 or H,

"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, to result in a gene-edited cell.

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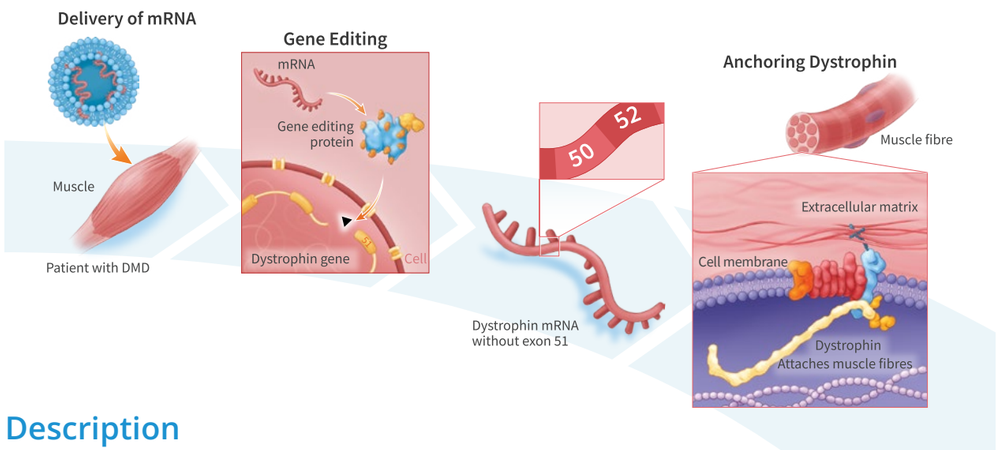
Gene-Editing Therapies for the Treatment of Duchenne Muscular Dystrophy (DMD)



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 the Treatment of Duchenne Muscular Dystrophy (DMD) is protected by three U.S. patents, as well as patents in Canada, Australia, 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 specific target sequence, mRNA sequence or chemistry, cell type, or method of transfection.

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

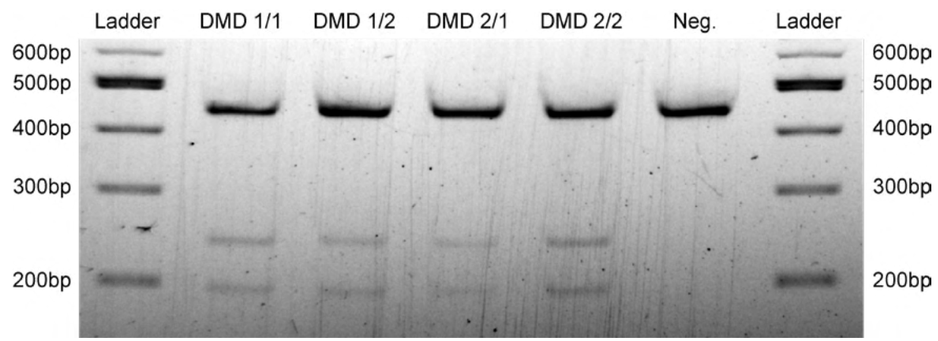


Figure 1. Gene editing of the DMD gene in primary human epidermal keratinocytes.

Representative Claim

U.S. Pat. No. 10,752,918

An in vitro method for producing a gene-edited cell comprising transfecting in vitro a cell comprising a Duchenne muscular dystrophy (DMD) gene with a nucleic acid encoding a gene-editing protein, wherein the gene-editing protein comprises: (a) a DNA-binding domain and (b) a nuclease domain and is capable of binding to the DMD gene, 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: LTPvQWAlAwxyzGHGG (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 or H,

"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, to result in a gene-edited cell.

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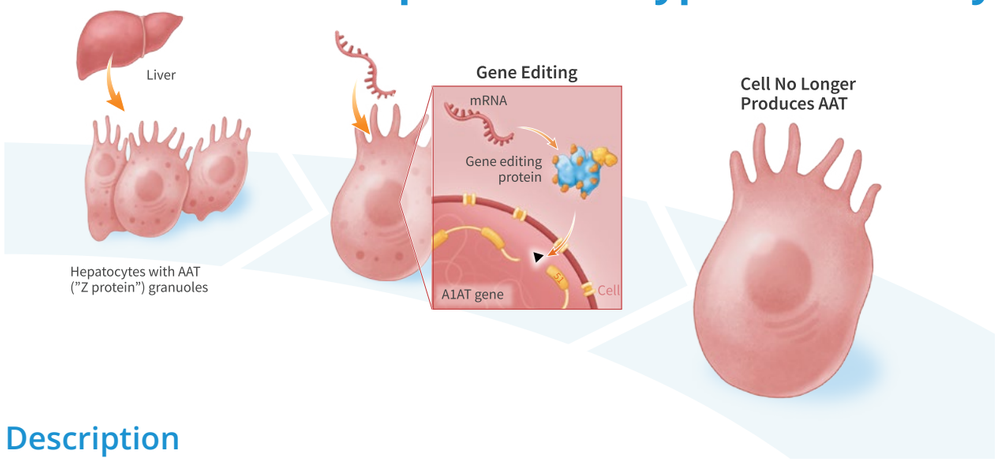
Gene-Editing Therapies for the Treatment of Alpha-1-Antitrypsin Deficiency



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 the Treatment of Alpha-1-Antitrypsin Deficiency is protected by U.S. Patent Number 10,576,167, as well as a patent in Israel (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, 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

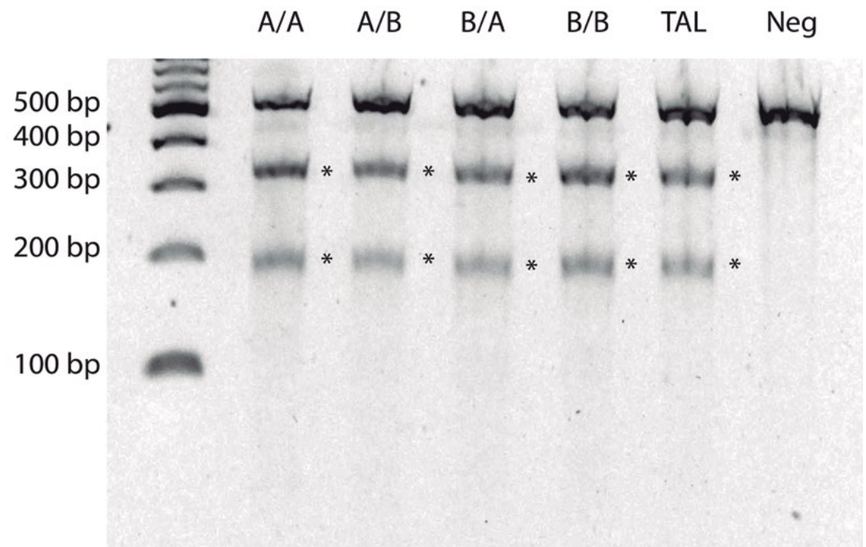


Figure 1. Gene editing of the A1AT gene in primary human cells using mRNA encoding gene-editing proteins.

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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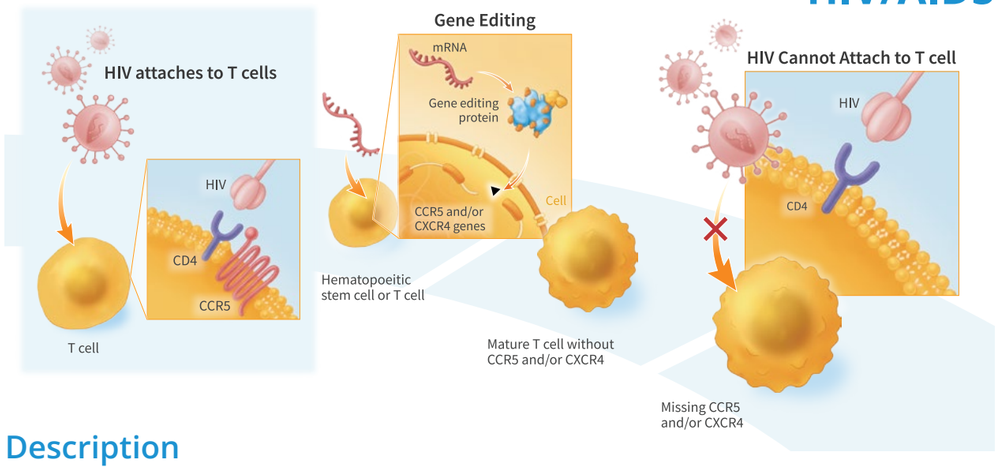
Gene-Editing Therapies for the Treatment of HIV/AIDS



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 the Treatment of HIV/AIDS is protected by three U.S. patents, as well as patents in Japan, Australia, 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 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

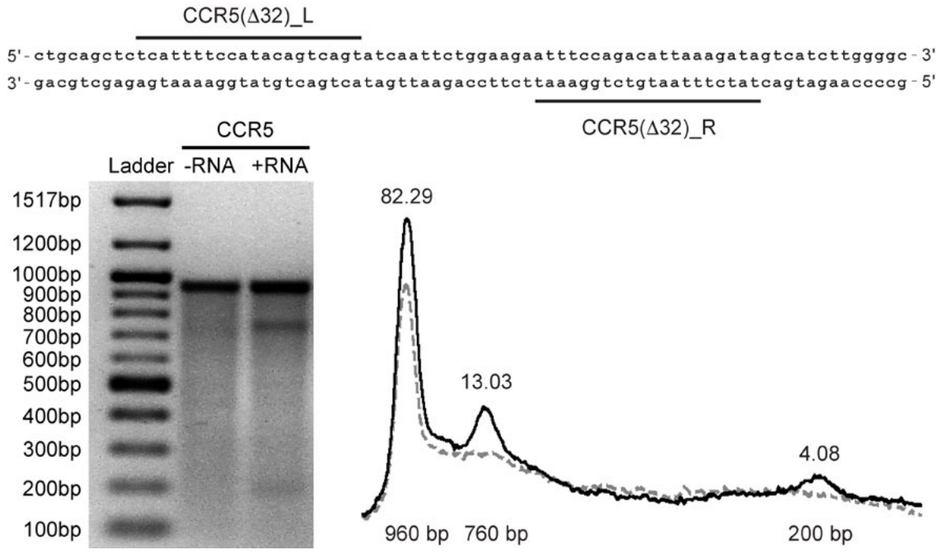


Figure 1. Gene editing of the CCR5 gene in human iPS cells.

Representative Claim

U.S. Pat. No. 9,605,278

A therapeutic composition, comprising a gene-edited hematopoietic cell, wherein:

the gene-edited hematopoietic cell comprises:

an in vitro transcribed synthetic RNA molecule encoding a gene-editing protein, the gene-editing protein comprising a DNA-binding domain and a nuclease catalytic domain that causes a double-strand break in the DNA of the hematopoietic cell; and

a double-strand break in its DNA, the double-strand break being caused by the gene-editing protein and reducing the function of one or more of CCR5 and CXCR4.

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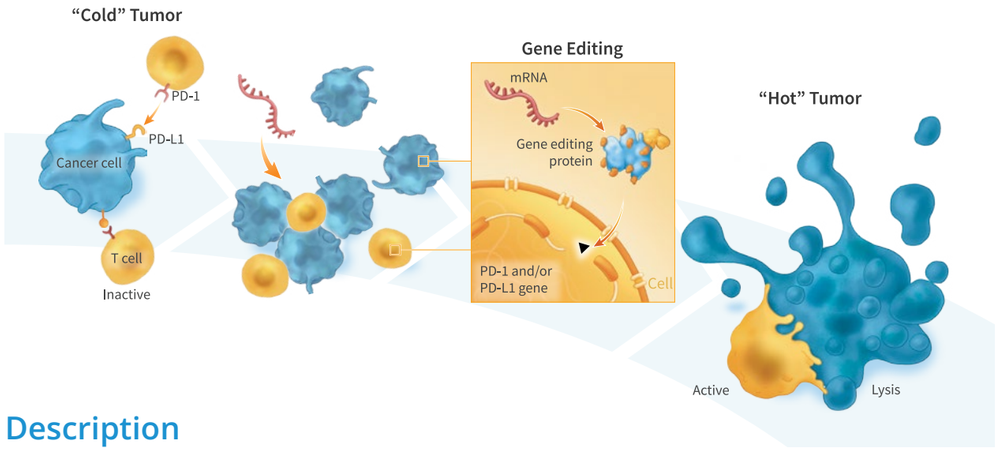
Gene-Editing Checkpoint Molecule Genes for the Treatment of Cancer



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 seven U.S. patents, as well as patents in China and Australia (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

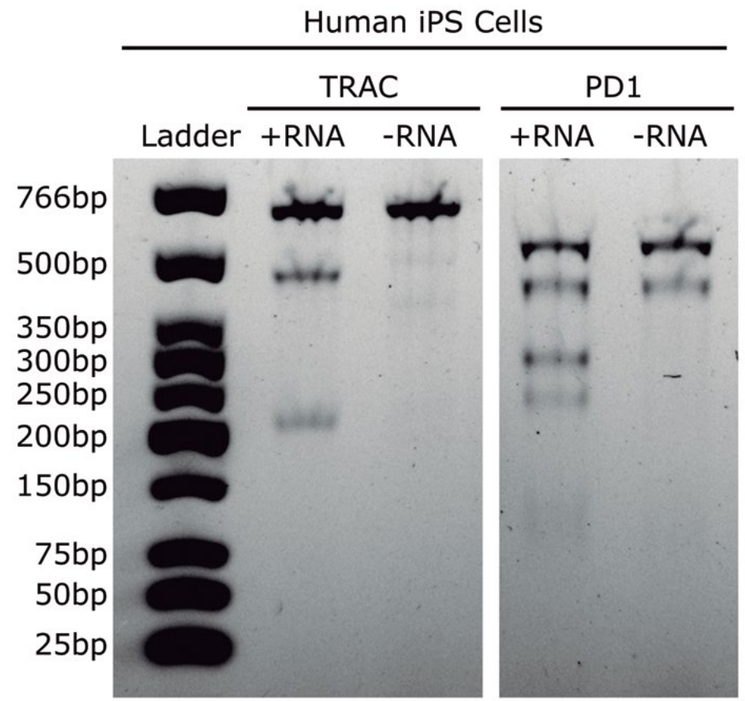


Figure 1. Gene editing the TRAC gene and the checkpoint molecule gene PD1 in human iPS cells.

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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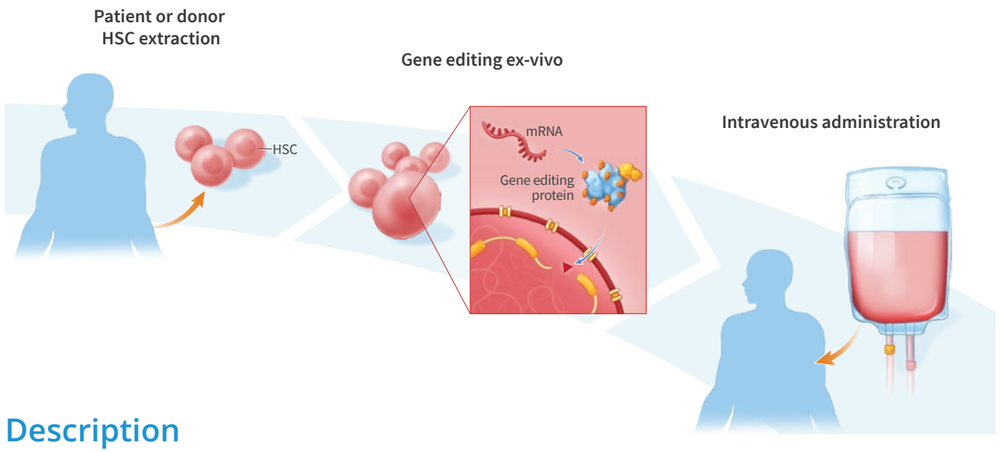
Gene-Editing Therapies for the Treatment of Sickle Cell Disease



Description

Sickle cell disease is caused by a mutation in the HBB gene that results in a lack of functional hemoglobin and sickle-shaped red blood cells that can accumulate in blood vessels and lead to vaso-occlusive crises.

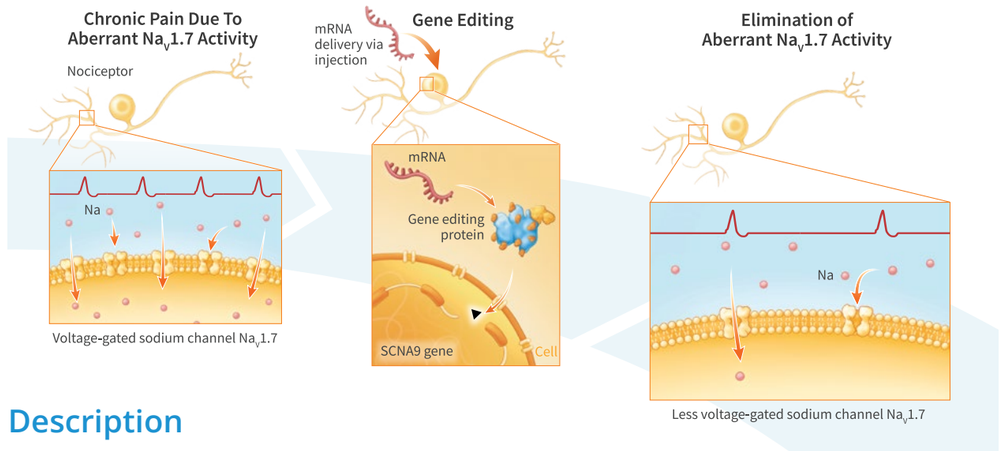
Our scientists developed a method for treating sickle cell disease by using mRNA encoding gene-editing proteins in donor or patient hematopoietic cells to promote the expression of functional hemoglobin.

Gene Editing Therapies for the Treatment of Sickle Cell Disease is protected by a pending U.S. patent (with additional patents pending in other countries).

Example Applications

- Replicate natural expression of functional hemoglobin 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
- Administer a cell replacement therapy following an immune cell depletion treatment
- Develop a single product that can treat sickle cell disease with a single administration
- Achieve complete replacement of functional HSCs and a persistent therapeutic benefit
- Gene edit somatic cells to avoid the risk of germline transmission
- Combine with Factor's Engineered Protein-Encoding RNA to streamline manufacturing of sickle cell therapies
- Combine with Factor's Chromatin Context-Sensitive Gene-Editing Endonuclease for high-specificity ex vivo or in vivo gene editing

Gene-Editing Therapies for the Treatment of Chronic Pain



Description

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

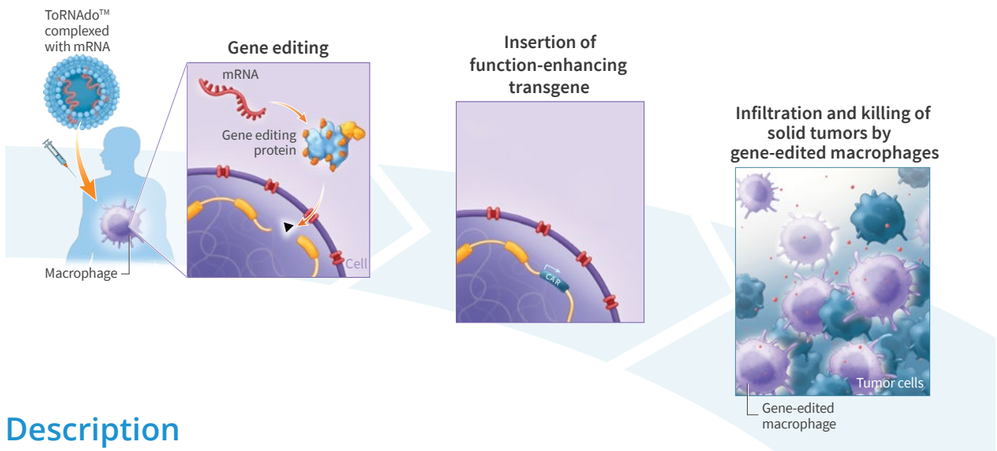
Our scientists developed a method for treating chronic pain by editing genes encoding voltage-gated sodium channels in cells of the central nervous system or peripheral nervous system.

Gene-Editing Therapies for the Treatment of Chronic Pain is protected by a pending U.S. patent (with additional patents pending 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

Rapid Prototyping of Gene-Editing Strategies for the Treatment of Cancer



Description

Cancer is a heterogeneous set of diseases that are characterized by diverse cellular phenotypes. This heterogeneity can lead to patient populations responding differently to different therapies.

Our scientists developed a method for screening cancer therapies by rapidly prototyping gene-editing strategies using engineered protein-encoding RNA[13].

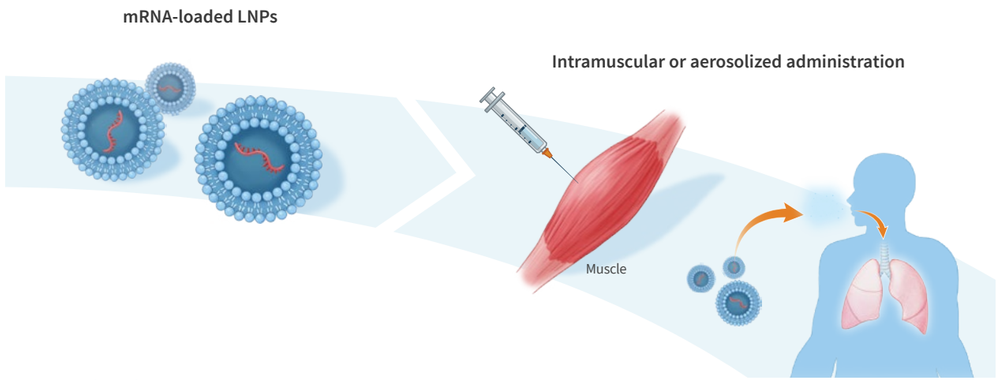
Rapid Prototyping of Gene-Editing Strategies for the Treatment of Cancer is protected by a pending U.S. patent (with additional patents pending in other countries).

Example Applications

- Indication-specific therapy screening
- Rapidly characterize novel CAR constructs in vitro
- Combine with Factor's Engineered Protein-Encoding RNA to characterize cells while they transiently express proteins of interest
- Combine with Factor's Chromatin Context-Sensitive Gene-Editing Endonuclease for high-specificity ex vivo gene editing
- Combine with Factor's ToRNAdo™ Nucleic Acid Delivery System for high efficiency nucleic acid delivery

[13]Hay, I., et al, Mol Ther, Vol 31, No 4S1, 2023.

RNA Vaccines for the Prevention & Treatment of Infectious Diseases & Cancer



Description

mRNA vaccines can be useful for the prevention of certain diseases. However, the design and formulation of the RNA in these vaccines can limit the diseases that they can be used to prevent or treat.

Our scientists developed a method for preventing and treating infectious diseases and cancer using RNA vaccines[14].

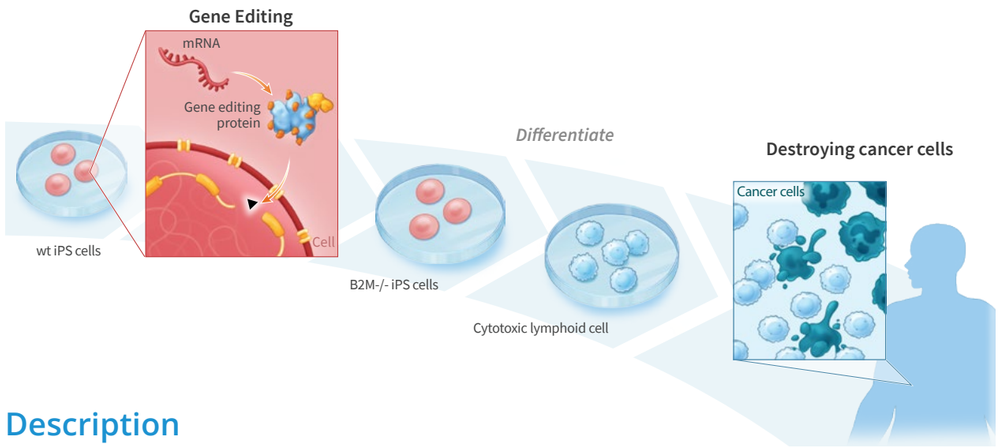
RNA Vaccines for the Prevention & Treatment of Infectious Diseases & Cancer is protected by a pending U.S. patent (with additional patents pending in other countries).

Example Applications

- Low dose RNA vaccines
- Initiation of targeted immune responses
- Combine with Factor's Engineered Protein-Encoding RNA and Polyvalent Ionizable Lipid Library for enhanced application-specific delivery
- Combine with Factor's Rapid Prototyping of Gene-Editing Strategies for the Treatment of Cancer Technology to streamline the development of personalized medicines

[14]McCarthy, S., et al. Nucleic Acid Ther, Vol 33, No 2, 2023.

Pluripotent Stem Cell-Derived Therapies for the Treatment of Hematological Cancers



Description

Engineered cell therapies can effectively treat certain hematological cancers. However, conventional approaches using viruses to express targeting molecules on autologously derived cells can result in high manufacturing complexity and limited cancer targeting.

Our scientists developed a method for treating hematological cancers using engineered pluripotent stem cells[15].

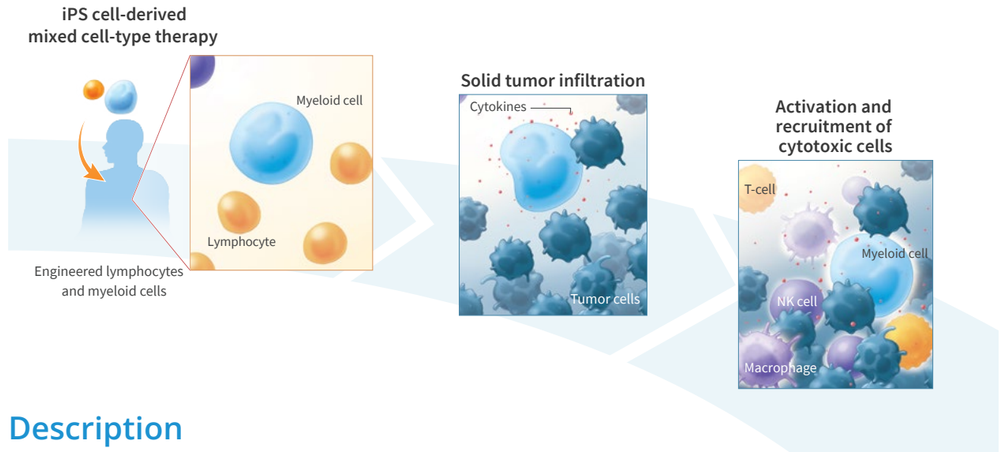
Pluripotent Stem Cell-Derived Therapies for the Treatment of Hematological Cancers is protected by a pending U.S. patent (with additional patents pending in other countries).

Example Applications

- Target hematological cancer using pluripotent stem cell-derived cytotoxic lymphocytes
- Combine with Factor's Combined mRNA Cell Reprogramming & Gene Editing for streamlined manufacturing
- Combine with Factor's Rapid Prototyping of Gene-Editing Strategies for the Treatment of Cancer Technology to streamline the development of personalized medicines
- Combine with Factor's Gene-Edited Allogeneic Cell Therapies Technology to create "off-the-shelf" therapies

[15]Parmenter, M., et al. Mol Ther, Vol 30, No 4S1, 2022

Pluripotent Stem Cell-Derived Therapies for the Treatment of Solid Tumors



Description

Solid tumors can be refractory to many cytotoxic T cell therapies, such as CAR-T therapy, which can have difficulty infiltrating the tumor microenvironment to exert their cancer-killing function.

Our scientists developed a method for treating solid tumors by engineering pluripotent stem cells to create cell therapies that can promote tumor infiltration of cancer-killing immune cells[16].

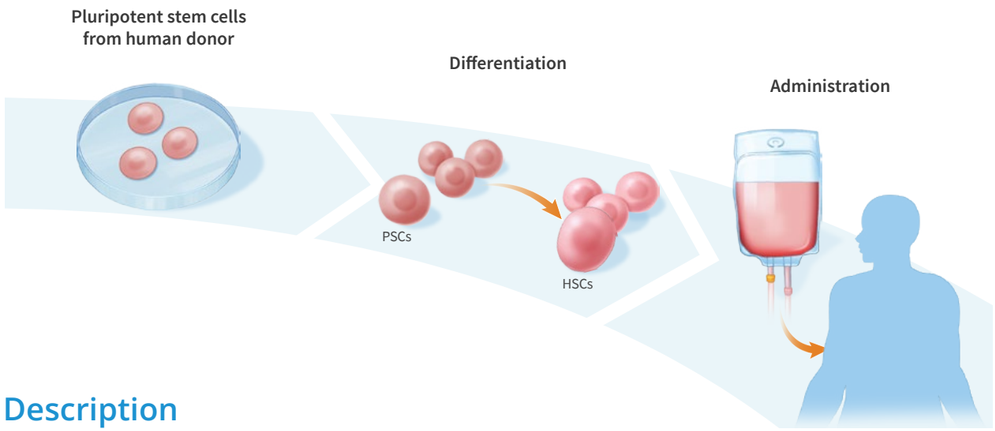
Pluripotent Stem Cell-Derived Therapies for the Treatment of Solid Tumors is protected by a pending U.S. patent (with additional patents pending in other countries).

Example Applications

- Target solid tumors using pluripotent stem cell-derived myeloid cells
- Administer pluripotent stem cell-derived therapies: intratumorally, intraperitoneally, intravenously, or via nebulizer-mediated inhalation
- Combine with Factor's Combined mRNA Cell Reprogramming & Gene Editing for streamlined manufacturing
- Combine with Factor's Gene-Edited Allogeneic Cell Therapies Technology to create "off-the-shelf" therapies

[16]Blatchford, A., et al. Mol Ther, Vol 31, No 4S1, 2023

Pluripotent Stem Cell-Derived Therapies for the Treatment of Genetic Blood Disorders



Description

Genetic blood disorders can be caused by mutations in genes that are important for normal blood cell function.

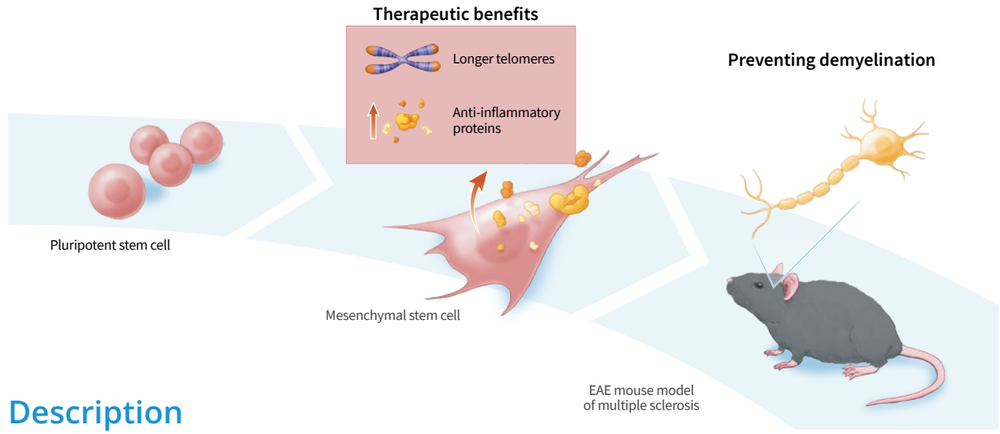
Our scientists developed a method for treating genetic blood disorders by engineering pluripotent stem cells to create cell therapies that can restore the function of the hematopoietic system.

Pluripotent Stem Cell-Derived Therapies for the Treatment of Genetic Blood Disorders is protected by a pending U.S. patent (with additional patents pending in other countries).

Example Applications

- Replace lost or damaged cells following immune cell depletion treatment
- Develop a single product that can treat genetic blood diseases with a single administration and independent of specific disease-causing mutations
- Gene edit somatic cells to avoid the risk of germline transmission
- Combine with Factor's Combined mRNA Cell Reprogramming & Gene Editing for streamlined manufacturing
- Combine with Factor's Gene-Edited Allogeneic Cell Therapies Technology to create "off-the-shelf" therapies

Pluripotent Stem Cell-Derived Therapies for the Treatment of Autoimmune Diseases



Description

Autoimmune diseases involve dysregulation of one or more aspects of a patient's immune system, often leading to inflammation that can ultimately result in irreversible tissue and organ damage.

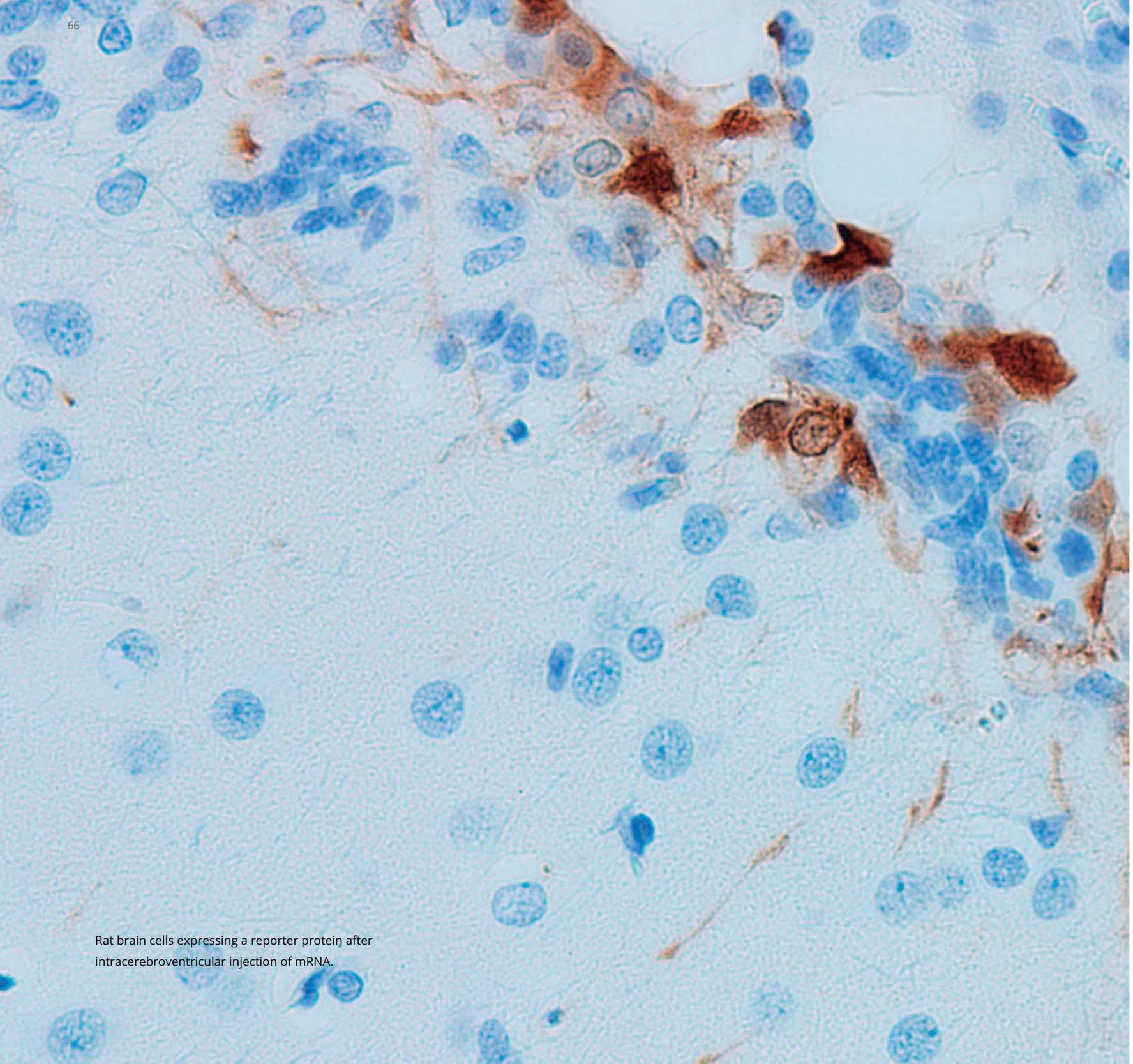
Our scientists developed a method for treating autoimmune and inflammatory diseases by engineering pluripotent stem cells to create cell therapies that can restore the function of the immune system[17].

Pluripotent Stem Cell-Derived Therapies for the Treatment of Autoimmune Diseases is protected by a pending U.S. patent (with additional patents pending in other countries).

Example Applications

- Target neurodegenerative and inflammatory diseases using immunomodulatory pluripotent stem cell-derived therapies
- Combine with Factor's Combined mRNA Cell Reprogramming & Gene Editing for streamlined manufacturing
- Combine with Factor's Gene-Edited Allogeneic Cell Therapies Technology to create "off-the-shelf" therapies

[17]Hashimoto, K., et al. Cytotherapy, 23(5), S33, 2021.



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

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 at licensing@factorbio.com to explore licensing opportunities for your application(s).

Case	Country	Application	Patent	Status
FAB-001C1	USA	14/296,220 Jun-04-2014	9,422,577 Aug-23-2016	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-001C8	USA	16/567,059 Sep-11-2019	11,466,293 Oct-11-2022	PATENTED
FAB-001C9	USA	16/776,765 Jan-30-2020	10,662,410 May-26-2020	PATENTED
FAB-001C10	USA	16/857,894 Apr-24-2020	10,829,738 Nov-10-2020	PATENTED
FAB-001C11	USA	16/869,232 May-07-2020	10,982,229 Apr-20-2021	PATENTED
FAB-001C12	USA	16/913,306 Jun-26-2020	11,692,203 Jul-04-2023	PATENTED
FAB-001C13	USA	16/913,315 Jun-26-2020	11,708,586 Jul-25-2023	PATENTED
FAB-001EP	Europe	12813595.1 Dec-05-2012	2788033 May-31-2017	PATENTED
FAB-001EPD1	Europe	17170810.0 Dec-05-2012	3260140 Feb-03-2021	PATENTED
FAB-001DE	Germany	12813595.1 Dec-05-2012	602012033063.5 May-31-2017	PATENTED
FAB-001DED1	Germany	17170810.0 Dec-05-2012	3260140 Feb-03-2021	PATENTED
FAB-001FR	France	12813595.1 Dec-05-2012	2788033 May-31-2017	PATENTED
FAB-001FRD1	France	17170810.0 Dec-05-2012	3260140 Feb-03-2021	PATENTED
FAB-001GB	United Kingdom	12813595.1 Dec-05-2012	2788033 May-31-2017	PATENTED
FAB-001GBD1	United Kingdom	17170810.0 Dec-05-2012	3260140 Feb-03-2021	PATENTED
FAB-001BED1	Belgium	17170810.0 Dec-05-2012	3260140 Feb-03-2021	PATENTED
FAB-001CH	Switzerland	12813595.1 Dec-05-2012	2788033 May-31-2017	PATENTED
FAB-001CHD1	Switzerland	17170810.0 Dec-05-2012	3260140 Feb-03-2021	PATENTED
FAB-001DKD1	Denmark	17170810.0 Dec-05-2012	3260140 Feb-03-2021	PATENTED
FAB-001IE	Ireland	12813595.1 Dec-05-2012	2788033 May-31-2017	PATENTED
FAB-001IED1	Ireland	17170810.0 Dec-05-2012	3260140 Feb-03-2021	PATENTED
FAB-001NLD1	Netherlands	17170810.0 Dec-05-2012	3260140 Feb-03-2021	PATENTED
FAB-001AU	Australia	2012347919 Dec-05-2012	2012347919 Feb-18-2017	PATENTED

Case	Country	Application	Patent	Status
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 Dec-05-2012	2019203662 May-14-2020	PATENTED
FAB-001AUD4	Australia	2020202780 Dec-05-2012	2020202780 Jul-28-2022	PATENTED
FAB-001AUD5	Australia	2022204659 Dec-05-2012	2022204659 Jan-05-2023	PATENTED
FAB-001BRD3	Brazil	1220230041860 Dec-05-2012	N/A	ALLOWED
FAB-001CA	Canada	2858148 Dec-05-2012	2858148 Mar-14-2023	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 Mar-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 Jul-31-2020	PATENTED
FAB-001JP	Japan	2014-546024 Dec-05-2012	6073916 Jan-13-2017	PATENTED
FAB-001JPD1	Japan	2016-213019 Dec-05-2012	6294944 Feb-23-2018	PATENTED
FAB-001KR	South Korea	10-2014-7018569 Dec-05-2012	10-2196339 Dec-22-2020	PATENTED
FAB-001KRD1	South Korea	10-2020-7036814 Dec-05-2012	10-2320571 Oct-27-2021	PATENTED
FAB-001MX	Mexico	MX/a/2014/006663 Dec-05-2012	354995 Mar-27-2018	PATENTED
FAB-001MXD1	Mexico	MX/a/2018/003987 Dec-05-2012	382822 Jun-18-2021	PATENTED
FAB-001RU	Russia	2014127505 Dec-05-2012	2624139 Jun-30-2017	PATENTED
FAB-001RUD1	Russia	2017118312 Dec-05-2012	2691027 Jun-07-2019	PATENTED
FAB-001HK	Hong Kong	15103141.5 Dec-05-2012	1202443 Mar-23-2018	PATENTED
FAB-001HKD1	Hong Kong	16108558.9 Dec-05-2012	1220490 Feb-23-2018	PATENTED
FAB-001HKD2	Hong Kong	16110473.7 Dec-05-2012	1222203 Sep-11-2020	PATENTED
FAB-001HKD3	Hong Kong	16110474.6 Dec-05-2012	1222204 Mar-19-2021	PATENTED
FAB-001HKD4	Hong Kong	18101023.9 Dec-05-2012	1241704 Aug-13-2021	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

Case	Country	Application	Patent	Status
FAB-003C2	USA	14/810,123 Jul-27-2015	9,399,761 Jul-26-2016	PATENTED
FAB-003C3	USA	15/178,190 Jun-09-2016	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-003C10	USA	16/562,497 Sep-06-2019	11,492,600 Nov-08-2022	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-005C8	USA	16/654,532 Oct-16-2019	11,339,409 May-24-2022	PATENTED
FAB-005C9	USA	16/654,536 Oct-16-2019	10,752,917 Aug-25-2020	PATENTED
FAB-005C10	USA	16/654,726 Oct-16-2019	11,339,410 May-24-2022	PATENTED
FAB-005C11	USA	16/655,744 Oct-17-2019	10,724,053 Jul-28-2020	PATENTED
FAB-005C12	USA	16/655,760 Oct-17-2019	11,332,758 May-17-2022	PATENTED
FAB-005C13	USA	16/655,766 Oct-17-2019	10,767,195 Sep-08-2020	PATENTED
FAB-005C14	USA	16/657,318 Oct-18-2019	11,332,759 May-17-2022	PATENTED
FAB-005C15	USA	16/657,321 Oct-18-2019	10,752,918 Aug-25-2020	PATENTED
FAB-005C16	USA	16/657,325 Oct-18-2019	10,752,919 Aug-25-2020	PATENTED

Case	Country	Application	Patent	Status
FAB-005C17	USA	16/912,321 Jun-25-2020	N/A	ALLOWED
FAB-005EP	Europe	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-005CH	Switzerland	13850281.0 Nov-01-2013	2914728 Jul-08-2020	PATENTED
FAB-005IE	Ireland	13850281.0 Nov-01-2013	2914728 Jul-08-2020	PATENTED
FAB-005AU	Australia	2013337651 Nov-01-2013	2013337651 Mar-28-2019	PATENTED
FAB-005AUD1	Australia	2018264115 Nov-01-2013	2018264115 Nov-25-2021	PATENTED
FAB-005BR	Brazil	1120150098045 Nov-01-2013	N/A	ALLOWED
FAB-005BRD1	Brazil	BR122019025678-0 Nov-01-2013	BR122019025678-0 Apr-18-2023	PATENTED
FAB-005BRD2	Brazil	BR122019025681-0 Nov-01-2013	BR122019025681-0 Apr-18-2023	PATENTED
FAB-005BRD3	Brazil	1220190256837 Nov-01-2013	N/A	ALLOWED
FAB-005CA	Canada	2890110 Nov-01-2013	2890110 May-02-2023	PATENTED
FAB-005JP	Japan	2015-540833 Nov-01-2013	6510416 Apr-12-2019	PATENTED
FAB-005JPD1	Japan	2018-073676 Nov-01-2013	6890565 May-27-2021	PATENTED
FAB-005JPD2	Japan	2018-073677 Nov-01-2013	6793146 Nov-11-2020	PATENTED
FAB-005JPD3	Japan	2021-027831 Nov-01-2013	7436406 Feb-13-2024	PATENTED
FAB-005KR	South Korea	10-2015-7013918 Nov-01-2013	10-2121086 Jun-03-2020	PATENTED
FAB-005KRD1	South Korea	10-2020-7015879 Nov-01-2013	10-2315098 Oct-14-2021	PATENTED
FAB-005KRD2	South Korea	10-2021-7033133 Nov-01-2013	10-2596302 Oct-26-2023	PATENTED
FAB-005MX	Mexico	MX/a/2015/005346 Nov-01-2013	363017 Mar-04-2019	PATENTED
FAB-005MXD1	Mexico	MX/a/2019/002498 Nov-01-2013	410292 Feb-06-2024	PATENTED
FAB-005RU	Russia	2015120524 Nov-01-2013	2711249 Jan-15-2020	PATENTED
FAB-005HK	Hong Kong	16102376.2 Nov-01-2013	1214304 Apr-23-2021	PATENTED
FAB-008	USA	14/761,461 Jul-16-2015	9,770,489 Sep-26-2017	PATENTED

Case	Country	Application	Patent	Status
FAB-008C1	USA	15/678,491 Aug-16-2017	10,124,042 Nov-13-2018	PATENTED
FAB-008EP	Europe	15743915.9 Jan-30-2015	3099801 Mar-18-2020	PATENTED
FAB-008EPD1	Europe	20161924.4 Jan-30-2015	3690056 Dec-28-2022	PATENTED
FAB-008DE	Germany	15743915.9 Jan-30-2015	3099801 Mar-18-2020	PATENTED
FAB-008DED1	Germany	20161924.4 Jan-30-2015	602015082143.2 Dec-28-2022	PATENTED
FAB-008FR	France	15743915.9 Jan-30-2015	3099801 Mar-18-2020	PATENTED
FAB-008FRD2	France	20161924.4 Jan-30-2015	3690056 Dec-28-2022	PATENTED
FAB-008GB	United Kingdom	15743915.9 Jan-30-2015	3099801 Mar-18-2020	PATENTED
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FAB-008BED1	Belgium	20161924.4 Jan-30-2015	3690056 Dec-28-2022	PATENTED
FAB-008CH	Switzerland	15743915.9 Jan-30-2015	3099801 Mar-18-2020	PATENTED
FAB-008CHD1	Switzerland	20161924.4 Jan-30-2015	3690056 Dec-28-2022	PATENTED
FAB-008DKD1	Denmark	20161924.4 Jan-30-2015	3690056 Dec-28-2022	PATENTED
FAB-008ES	Spain	15743915.9 Jan-30-2015	3099801 Mar-18-2020	PATENTED
FAB-008ESD1	Spain	20161924.4 Jan-30-2015	E20161924 Dec-28-2022	PATENTED
FAB-008FID1	Finland	20161924.4 Jan-30-2015	3690056 Dec-28-2022	PATENTED
FAB-008IE	Ireland	15743915.9 Jan-30-2015	3099801 Mar-18-2020	PATENTED
FAB-008IED1	Ireland	20161924.4 Jan-30-2015	3690056 Dec-28-2022	PATENTED
FAB-008NLD1	Netherlands	20161924.4 Jan-30-2015	3690056 Dec-28-2022	PATENTED
FAB-008SED1	Sweden	20161924.4 Jan-30-2015	3690056 Dec-28-2022	PATENTED
FAB-008AU	Australia	2015210769 Jan-30-2015	2015210769 May-23-2019	PATENTED
FAB-008JPD1	Japan	2020-128881 Jan-30-2015	7235702 Feb-28-2023	PATENTED
FAB-008KR	South Korea	10-2016-7019564 Jan-30-2015	10-2415811 Jun-28-2022	PATENTED
FAB-008MX	Mexico	MX/a/2016/009771 Jan-30-2015	372651 Jun-16-2020	PATENTED
FAB-008HK	Hong Kong	17105411.1 Jan-30-2015	1231917 Feb-11-2021	PATENTED
FAB-008NOD1	Norway	20161924.4 Jan-30-2015	3690056 Dec-28-2022	PATENTED

Case	Country	Application	Patent	Status
FAB-009	USA	15/550,280 Aug-10-2017	11,241,505 Feb-08-2022	PATENTED
FAB-009AU	Australia	2016218977 Feb-16-2016	2016218977 Nov-03-2022	PATENTED
FAB-009JP	Japan	2017-542098 Feb-16-2016	7199809 Dec-23-2022	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-010C6	USA	17/018,728 Sep-11-2020	11,904,023 Feb-20-2024	PATENTED
FAB-010AU	Australia	2017312113 Aug-17-2017	2017312113 May-25-2023	PATENTED
FAB-010CN	China	201780059632.7 Aug-17-2017	ZL201780059632.7 Mar-17-2023	PATENTED
FAB-012A	USA	16/526,621 Jul-30-2019	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
FAB-012AC4	USA	16/930,901 Jul-16-2020	11,242,311 Feb-08-2022	PATENTED
FAB-012AC5	USA	17/553,564 Dec-16-2021	11,814,333 Nov-14-2023	PATENTED

Patented Technologies Available for Licensing

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

Patent Pending Technologies Available for Licensing

- Temperature-Tunable Gene-Editing Endonuclease
- Gene-Editing Endonuclease with Nickase Functionality
- Gene-Edited Allogeneic Cell Therapies
- Directed Differentiation of Gene-Edited Pluripotent Stem Cells
- Polyvalent Ionizable Lipid Library
- Engineered Linear DNA Donors
- Engineered Protein-Encoding RNA
- Splint & Ribozyme-Independent Circular RNA Synthesis
- Gene-Editing Therapies for Sickle Cell Disease & Chronic Pain
- Rapid Prototyping of Gene-Editing Strategies for the Treatment of Cancer
- RNA Vaccines for the Prevention & Treatment of Infectious Diseases & Cancer
- Pluripotent Stem Cell-Derived Therapies for Genetic Blood Disorders & Cancer
- Pluripotent Stem Cell-Derived Therapies for Autoimmune Diseases

Contact us at licensing@factorbio.com to explore licensing opportunities for your application(s).

Notes

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