Revolutionizing Medicine

Targeted Drug Delivery for

Late-Stage Cancers, Autoimmune and Genetic Diseases

By **Rojo**pitiavana Solofondrazaintsoanirina
Email: **solofo.rojo@gmail.com**

May 30, 2023

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Problem and Solution

What's the unmet need? We are in 2023, and despite important efforts deployed by academia and life science companies, delivering technological marvels such as RNA or CRISPR to specific tissues or sites, such as tumor lesions, is still very challenging. This problem limits their applications for the treatment of medical conditions with great unmet needs, such as cancer, genetic diseases, or autoimmune diseases.

Here's a Washington Post story that outlines the very big problem that plagues drug delivery:

https://www.washingtonpost.com/business/a-refreshing-gamble-on-crispr-delivery/2023/02/22/c1370d08-b2a5-11ed-94a0-512954d75716_story.html

How to address the unmet need? A new approach to delivering drugs to specific tissues or organs of the body is urgently needed. I have developed an invention, **a drug delivery system,** that has highly promising applications for the treatment of advanced cancers (stages III–IV), autoimmune diseases (rheumatoid arthritis, psoriasis, celiac disease), and genetic diseases (cystic fibrosis, sickle cell disease, hemophilia).

The Opportunity

I've invented an improved and versatile delivery system that uses T cells to ferry disease-fighting drugs precisely where they're needed in the body.

I’m seeking partners, backers, or investors to fund this project or collaborate with me to bring this breakthrough technology to market.

The goal is to license the drug delivery system to industry partners (large pharmaceutical and biotechnology companies), but before doing so, we must secure a patent for the invention, and carry out in vitro testing and in vivo validation on laboratory mice.

We will license the delivery system as soon as data obtained from in vivo experiments on mice (preclinical data) is available. These preclinical data will serve as evidence of our technology's effectiveness and will be key in securing licensing agreements.

The delivery system has numerous applications, from treating solid cancers to delivering CRISPR to tissues such as the bone marrow. **I anticipate that licensing opportunities will be vast**.

How we make money ?

This drug delivery system is a form of cell therapy. Its primary purpose is to deliver cancer-killing drug to tumor lesions while minimally impacting healthy tissues. For illustration, let's say that we want to target EGFR-positive (EGFR+) cancers.

We negotiate a collaboration and licensing deal with large biotechnology or pharmaceutical companies interested in developing and bringing to market a treatment for EGFR+ cancers.

Our industry partner will be granted an exclusive right to use our technology to target EGFR+ cancers, which means that we will not develop any other competing treatments targeting EGFR+ cancers during the collaboration period. In exchange for that exclusivity, **our partner must**: (a) pay a licensing fee; (b) cover the full cost of research and development related to the treatment; (c) make development and commercial milestone payments; and (d) pay a royalty (a percentage of the profit) on sales of the treatment when it is commercialized.

Some examples of collaborations and licensing deals that involve preclinical assets are available on **page 16**.

How much are we excepted to make ?

EGFR is an example of abundantly expressed Tumor-Associated Antigens (**TAAs**) that can serve as biomarkers to identify cancer cells. More than 20 clinically explored **TAAs** are known [1], giving us the ability to start at least 20 programs. Our partners will make an upfront payment of $10-100 million per program, giving us **$200-2,000 million** if we launch 20 programs.

Development, regulatory, and commercial milestone payments are estimated to be $300-$1,000 million per program. Clinical trials have a success rate of 10%, that's 2 winning programs out of 20, giving **$600-$2,000 million**. We will also receive a royalty of 5-15% on future sales.

Beside cancer, we will also target other diseases, including: **(a) Autoimmune diseases** (Systemic Lupus Erythematosus (SLE), Psoriasis, Rheumatoid Arthritis, Inflammatory Bowel Diseases, Multiple Sclerosis); and **(b) Genetic diseases** (Muscular dystrophy, Sickle cell disease, Cystic fibrosis, Hemophilia).

References

1. CAR Based Immunotherapy of Solid Tumours-A Clinically Based Review of Target Antigens, http://www.ncbi.nlm.nih.gov/pmc/articles/pmc9953298

The Business Model, illustrated

We secure license and collaboration deals with industry partners (biotech & pharma companies)

OUR COMPANY

1 UPFRONT PAYMENTS

Our partners pay licensing fees and cover the cost of research and preclinical development **($10 - $100 million)**.

$300 - 1,000 million

We receive **royalties (5-15%) + commercial milestone payments** on the sales of all marketed products.

Additional payments are made by our partners when pre-established development milestones are reached.

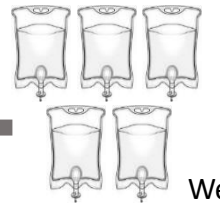
The product is now regulatory approved and marketed.

Phase I Clinical trial

Phase II Clinical trial

Phase III Clinical trial

5 Our partners are in charge of clinical trials.



4 We (or a Contract Manufacturing Organization, CMO) will be in charge of producing **cGMP-grade therapeutic candidates** for the clinical trials

3 Best candidate

2 We generate multiple candidate drugs by leveraging our proprietary technology.

3

We carry out the preclinical testing of all therapeutic candidates.
We select the best candidate that will undergo clinical trials.

Starting a company

We will license our technology through a newly created limited liability company (LLC). The cost of incorporation is $140; registered agent service is $50–300/year; and trademarking a business name will cost $250–750. The company will also need a US bank account. As we expand, we can convert the LLC into a C corporation, which is more attractive to investors.

To secure exclusivity, we must patent the invention. We will present the invention to a patent attorney, and he or she will decide on the best strategy to protect it. A patent has a validity period of 20 years. It will grant us the right to exclude others from making, selling, or using a patented invention. It will also increase our company's value.

We will need to conduct in vitro testing and experiments on laboratory mice to generate preclinical data that will provide evidence of the efficacy of our delivery system.

We will earn revenue through licensing fees each time we secure a collaboration and licensing deal with industry partners. They will reimburse the costs of research and development and make milestone payments when the treatments that we develop achieve certain milestones.

Roadmap, illustrated

		Duration
1	**We start a new company (LLC or C corp.)** ➢ Investors will transfer their investment funds to the company's US bank account. ➢ Inventor(s) must assign patents' ownership rights to the company.	< 1 month
2	**We draft and file US provisional patent applications** ➢ Counsel by a patent agent/attorney is highly recommended. ➢ The goal is to secure an early filing date for the patent.	4-6 months
3	**We carry out a proof-of-concept (PoC) study** ➢ The goal is to demonstrate that the delivery system works as intended, ➢ Experiments will be performed in a laboratory setting.	9-20 months
4	**We license the delivery system to industry partners** ➢ Proof-of-concept data will be used to convince partners and secure collaboration deals. To secure our intellectual assets, partners will be required to sign a Non-disclosure agreement. Our technology will be kept as **a trade secret** up until patents are granted.	Can be initiated as soon as supporting data are available
5	**We draft and file PCT applications** ➢ Applications will be filed in the USPTO. After filing, we have 18 months to decide where we desire to seek patent protection (USA, China, Japan, Korea, European Union, Canada, etc.)	Must be done within 12 months of the earliest provisional application filing date

What I’m Working On ?

Here’s a paper that describes my invention: https://doi.org/10.5281/zenodo.7985550

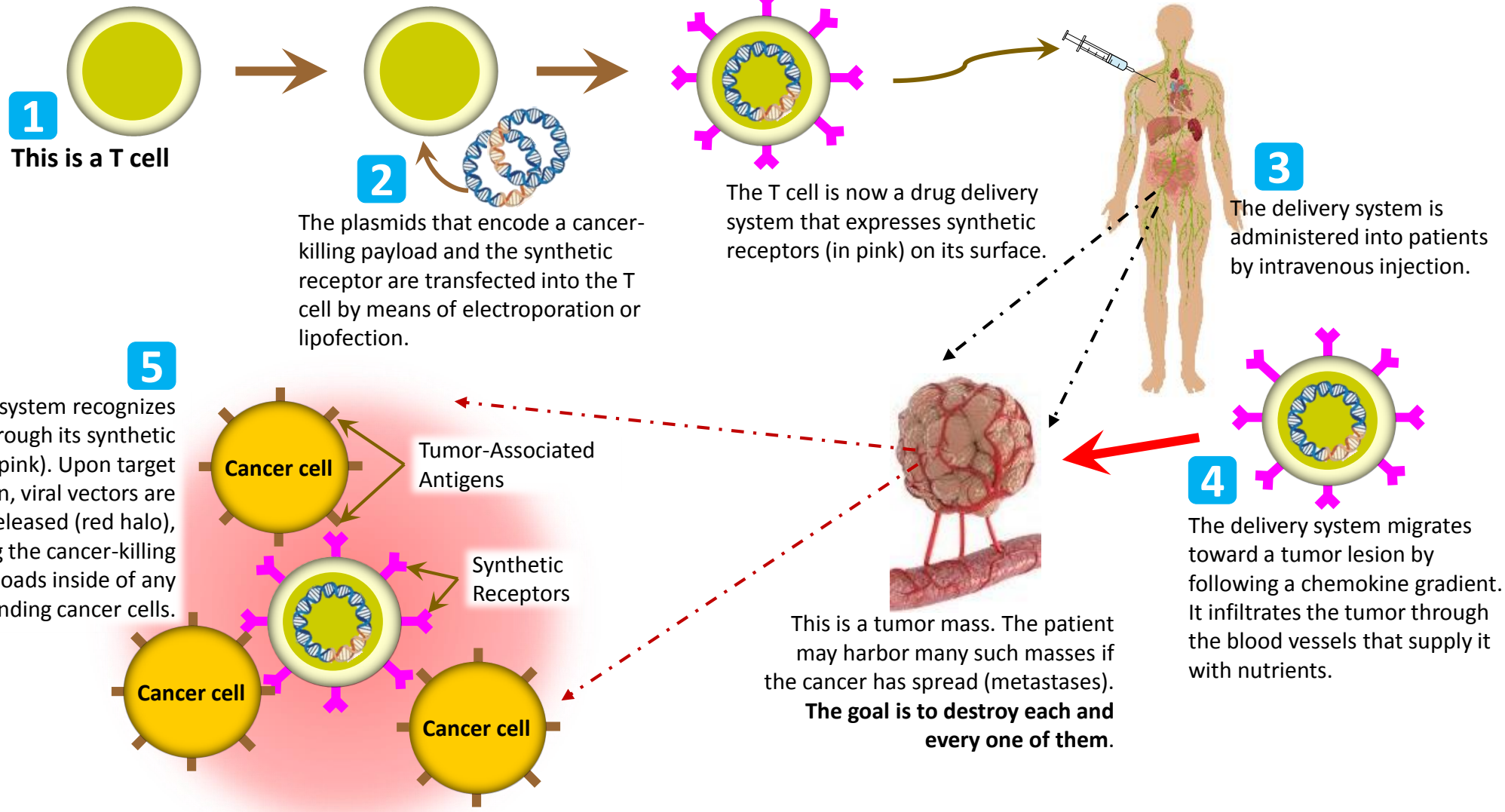
How to deliver payloads such as CRISPR, RNAs, or DNAs to cancer cells ? First of all, we need a vehicle. T cells circulate in the lymphatic and blood systems, and they can infiltrate tumor lesions, making them the perfect drug delivery system for this job.

How is the payload transferred from the vehicle (T cells) to the target (cancer cells) ? The best approach is to use viral vectors that will efficiently introduce the payload into the target.

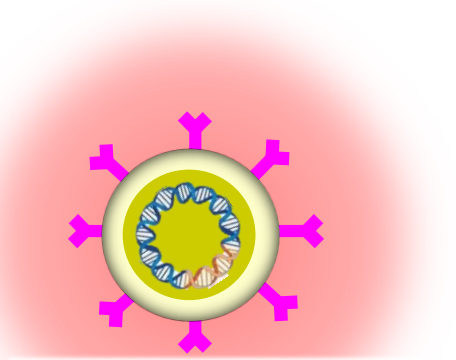
My invention is **a set of plasmids that transform T cells into vehicles that produce and release viral vectors inside tumor lesions**. Viral vectors’ production is triggered when specific antigens that are abundantly expressed on the surface of target cancer cells bind to synthetic receptors expressed on the surface of the delivery system.

My work focuses on designing the plasmids, which are crucial to the success of this drug delivery system. T cells transformed with the plasmids can ferry all sorts of therapeutics (CRISPR, shRNA, mRNA, DNA, etc.) to not only cancerous lesions but also to specific tissues or organs of the body, enabling the treatment of a broad range of diseases.

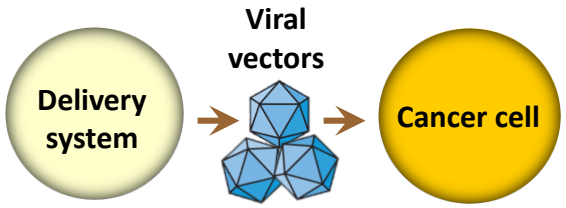
The science of my Drug Delivery System



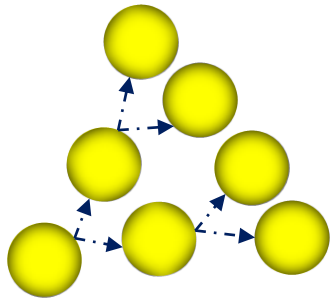
Characteristics of the delivery system



Producing and releasing viral vectors at the diseased site maximizes target reach while reducing side effects through a more localized delivery of payloads.

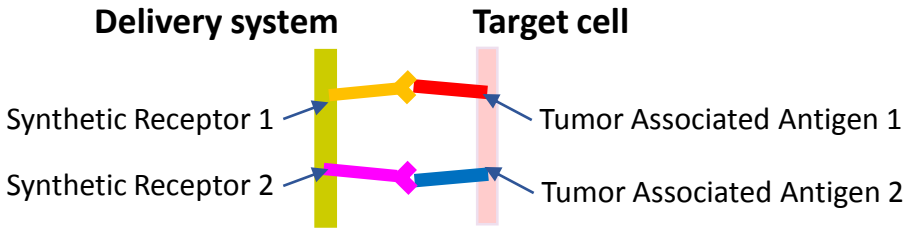


Viral vectors allow the efficient transfer of the payload from the delivery system to the target cells. The payload is translocated into the nucleus, where its expression is driven by a constitutive or tissue-specific promoter.

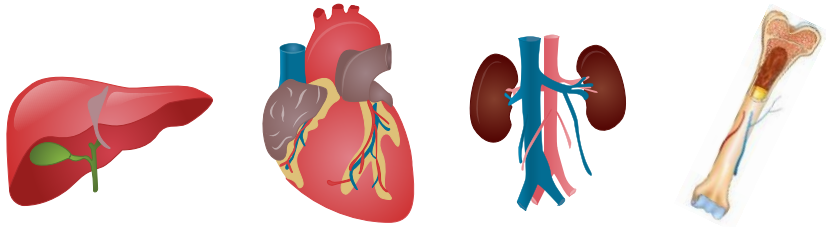


After interacting with target cells, the delivery system undergoes clonal expansion at the diseased site, resulting in a massive production of viral vectors.

Multiple safety systems ensure that the delivery system will be destroyed when it's no longer required or behave unexpectedly.

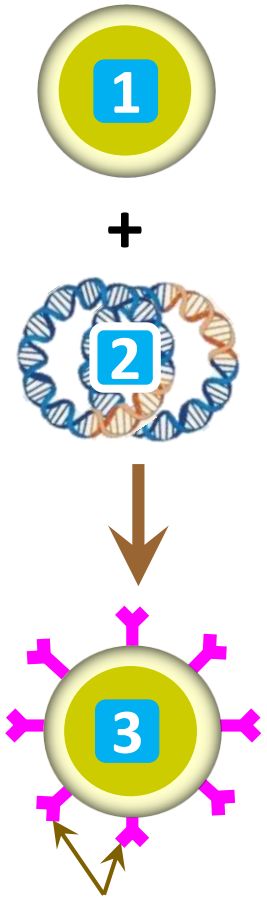


Two or more synthetic receptors can be used to recognize and discriminate the target. Viral vector production is only initiated when all receptors bind to their respective tumor associated antigens, thus minimizing the risk of off-target effects.



Payloads can be delivered beyond the liver. The delivery system can actively infiltrate other tissues or organs of the body, where it initiates viral vector production after interacting with target cells that express tissue-specific antigens on their surfaces.

Applications and Possibilities

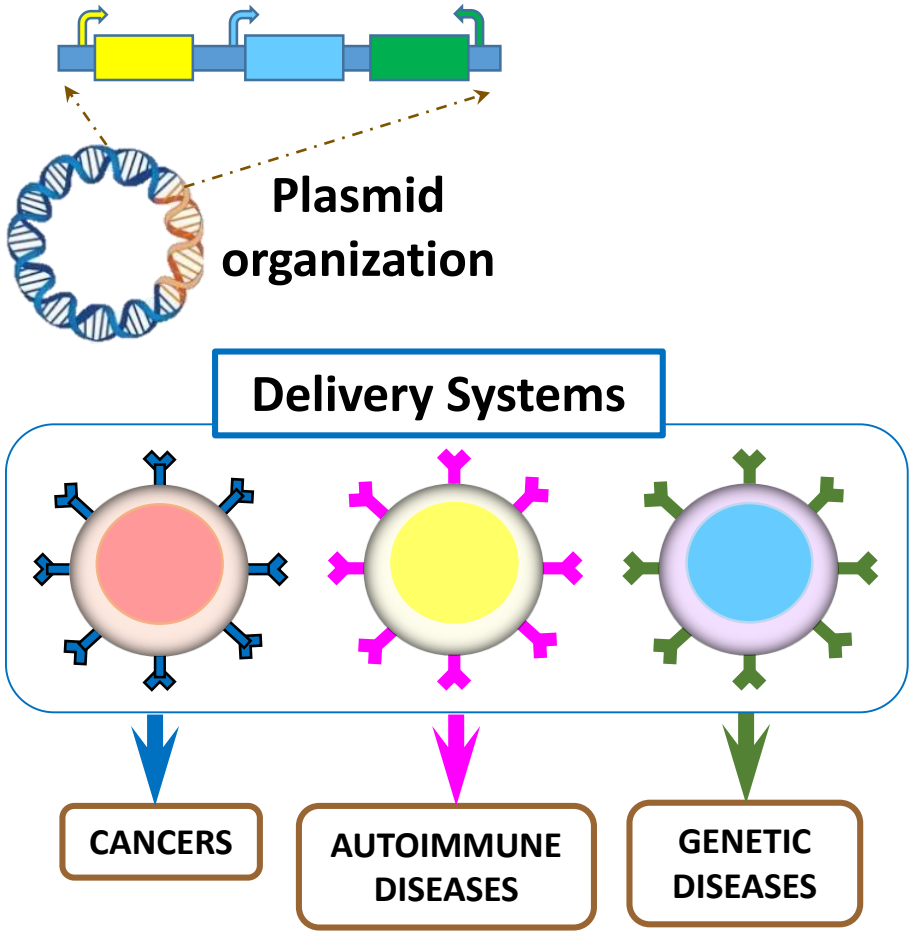


A given delivery system 3 is obtained by transfecting the plasmids 2 into a T cell 1.

The synthetic receptors endow the delivery system the capacity to recognize the site where viral vectors should be produced and released.

- To kill **cancer cells**, we can use the following payloads: **(a)** prodrug-activating enzymes (they convert an inert drug into a very toxic drug); **(b)** therapeutic antibodies (anti-PD1); **(c)** RNA interferences (miRNA, shRNA).
- **Genetic diseases** are treated using payloads such as: **(a)** CRISPR-Cas; **(b)** plasmids (a stretch of DNA that encodes a healthy version of a faulty gene that we seek to repair).
- **Autoimmune Diseases** are treated with payloads such as: **(a)** TGF-β; **(b)** TNF-α antagonists.
- **Viral infections** can be treated with : **(a)** RNA interferences (miRNA, shRNA); **(b)** virus-neutralizing antibodies.

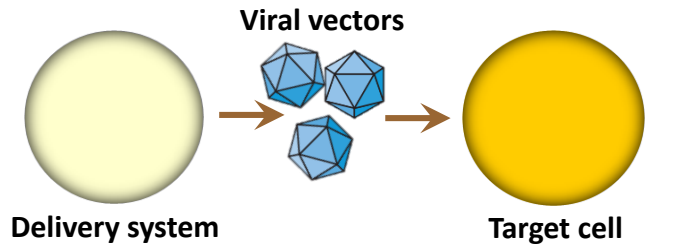
What are we going to patent ?

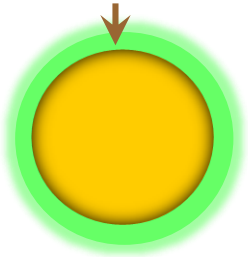


We will patent the plasmids' organization, how the delivery system operates, the method of viral vector production and release upon antigen stimulation, the method of growing the delivery system (to increase its number), and its uses for the treatment of a particular medical condition (cancer, genetic diseases, and autoimmune diseases).

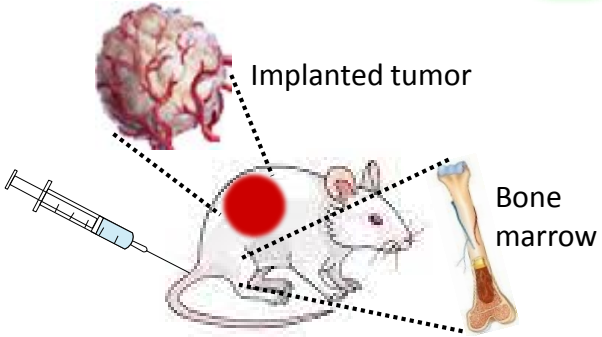
We will also patent every Delivery System (DS) that we generate during a collaboration. Why ? Each DS is unique and comprises a personalized therapeutic payload, and a set of synthetic receptors that specify where the payload will be delivered. Industry partners will be granted exclusive licenses for the patented delivery systems.

Proof-Of-Concept Study





A fluorescing target cell indicates a successful delivery of the payload.



The delivery system should produce and release viral vectors at specific target sites such as the bone marrow, the lung, or into implanted tumor lesions.

Before we could license the delivery system to an industry partner, we must demonstrate that it works. The payload that we are going to use is a piece of DNA that encodes a fluorescent protein and a therapeutic (shRNA, CRISPR-Cas + guide RNA, etc.).

During in vitro testing, we will show that the delivery system produces and releases viral vectors when co-cultured with cells that express target antigens on their surface. The viral vectors introduce the payload into the target cells, which will fluoresce as evidence of a successful payload's delivery.

If in vitro tests are satisfactory, we will test the delivery system on lab mice. After intravenous injection, the delivery system should reach different tissues through the blood and lymphatic circulation. Viral vector production and release should only occur when the delivery system interacts with cells that express the targeted antigen on their surfaces. The payload will be delivered into transplanted tumor lesions or into tissues such as the bone marrow.

Examples of collaboration and licensing deals

Seagen and **Lava therapeutics** announce exclusive worldwide license agreement to advance **LAVA-1223**, a **preclinical** gamma delta bispecific T-cell engager for **EGFR-expressing solid tumors** [1]. LAVA will receive an upfront payment of $50 Million, with potential for milestones of up to $650 million, and royalties ranging from the single digits to the mid-teens on future sales.

Merck and **Kelun-Biotech** announce exclusive license and collaboration agreement for **Seven Investigational preclinical** Antibody-drug Conjugate Candidates for the **Treatment of Cancer** [2]. Kelun-Biotech will receive an upfront payment of $175 million from Merck. Kelun-Biotech is also eligible to receive future development, regulatory and sales milestone payments totaling up to $9.3 billion.

Gilead and **Dragonfly** announce strategic research collaboration to develop **5T4-targeting investigational immunotherapy program, DF7001** [3]. Gilead will make a $300 million upfront payment. In addition, Dragonfly is eligible to receive potential opt-in payments and performance-based development, regulatory and commercial milestone payments, and royalties of up to 20% on worldwide net sales.

Bayer and **Atara Biotherapeutics** enter strategic collaboration for next generation, **mesothelin-targeted** CAR-T cell therapies for **solid tumors** [4]. Atara will receive an upfront payment of $60 million and is eligible to receive payments from Bayer upon achievement of certain milestones totaling $610 million, as well as tiered royalties up to low double-digit percentage of net sales.

AstraZeneca has completed an exclusive global license agreement with **KYM Biosciences Inc.** for **CMG901**, an antibody drug conjugate (ADC) **targeting Claudin 18.2**, a promising therapeutic target in **multiple cancers** [5]. KYM will receive an upfront payment of $63 million, with potential development and sales-related milestone payments of up to $1.1 billion and tiered royalties up to low double digits.

Immatics and **Bristol Myers Squibb** Enter Into Global Exclusive License for Immatics' TCR Bispecific Program **IMA401 targeting MAGEA4/8-positive tumors** [6]. Immatics will receive an upfront payment of $150 million as well as up to $770 million in development, regulatory and commercial milestone payments, in addition to tiered double-digit royalty payments on net sales of IMA401.

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About Me

Name: Solofondrazaintsoanirina **Rojo**pitiavana (Rojo)

Age: 31 yo

Gender: Male

Citizen: Malagasy, Country Madagascar

Diploma: License (2012) and Master's degree (2014) in Biotechnology, Institut Supérieur Polytechnique de Madagascar (ISPM)

Current location: Madagascar, Antananarivo, Ampanotokana

Home address: Lot II E 46 Ter BB Ampanotokana, Antananarivo, Madagascar

Feel free to contact me at: solofo.rojo@gmail.com

Please call me Rojo. My project is aimed at **addressing the drug delivery problem**. This problem has prevented technologies such as siRNA, mRNA, and CRISPR from effectively treating diseases such as cystic fibrosis, sickle cell disease, and cancer. After years of research, I invented a cell-based drug delivery vehicle that delivers drugs to specific sites in the body (more detail here: https://doi.org/10.5281/zenodo.7985550). I also invented a new gene-editing system, which can be found at https://doi.org/10.5281/zenodo.7627924. I'm self-taught and stay up-to-date by reading scientific literature published in high-ranking journals such as Nature, Science, Cell, and Frontier. **I'm fully dedicated to this project**, solving each and every problem that I have encountered thanks to the devotion of thousands of scientists whose research results have helped me a lot. This project is based on their work, and that's why I'm so confident it will be successful. I am now in search of collaborators, backers, or investors who would join me in translating my invention into a revolutionary product that will **change the world and improve the lives of millions of patients suffering from disabling and incurable diseases such as cancer**.