



# THE MESSENGER RNA REVOLUTIONS

**A DOCUMENTARY**

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# SUMMARY

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mRNA opens the door to a new era in medicine. But what has made it possible to move quickly in the development of vaccines against Covid-19 is all the very small steps taken by researchers since the discovery of mRNA sixty years ago. A path strewn with pitfalls, mistakes, disappointments but also hope and tenacity.

Telling the story of the messenger RNA revolutions is therefore telling the story of a science being made before our eyes by a constellation of extraordinary scientists, devoted to their mission. A deeply human story made of unexpected encounters at the photocopier that count as much as the carefully calibrated experiments in the laboratories...

The acceleration we have experienced in mankind's perpetual battle with diseases has made our new enemy – the coronavirus – our best ally to start an unprecedented medical and scientific revolution.





# A CAST THAT WILL **MAKE HISTORY!**

We have access to all the historical and key players in RNA research.

These characters of the “mRNA revolution” are portrayed in their laboratories but also in more intimate and daily surroundings. This is of key importance to create a greater empathy for the researchers whose journey has often been difficult. It features science through scientists and illustrates scientific values such as perseverance and collaboration so to inspire younger generations and the audience at large. Without emphasis, they appear like common people whose main superpower is to continue their efforts. Their extraordinary story is above all a human story.



A man with a backpack is running up a steep, rocky mountain slope. The background shows a vast valley with green fields and distant mountains under a cloudy sky.

# THE STORY STYLE AND STRUCTURE

## THE DIFFICULT PATH OF SCIENCE

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The image of a difficult path is present from the very beginning of the film with Steve Pascolo's ascent to the surrounding heights of Zurich. The metaphor is then spun through the narration and the visual situations. Our characters are in action : they bike, they play the guitar, they run... They personify the "science in motion".

The mRNA vaccine story plunges us into the classic canons of the "hero's journey", an epic tale with many twists and turns. The mRNA vaccine is the object of the scientists / heroes' quest: the elixir. The «call of adventure», the «road of trials», the «meeting of the allies and enemies», the «return with elixir»: all these steps give this epic documentary the strength of a real scientific saga!



# VISUAL STYLE AND ANIMATIONS

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**LINK TO MOODBOARD :** <https://xd.adobe.com/view/72aa4a21-277f-45b3-81ac-027f6ec8dd7e-27f9/>

The visual setting is designed to bring out the strong narrative dimension and the cinematography of this story. Our palette is based on the saturated and slightly faded colors of the personal photos of our protagonists. This light saturation of colors (Polaroid style) evokes the spirit of the 1980s-2000s present in the archives and the graphic universe of the historical evocations and animations.

It allows us to play on subtle transitions (see moodboard). We will rely on the cinematography to switch to the animated evocations: an object, a personal souvenir, a silhouette filmed is transmuted into a drawing. There is a unified underlying aesthetic: we will also install a graphic and narrative continuity between the historical evocations and the scientific animations.

The joy of storytelling and the joy of science are both there. The knowledge contained in the scientific animations is gradually distilled: having seen the first one allows the viewer to understand the second one, etc. They will also be assembled to form an independent animated film that will have its own life on social networks so to reach a younger audience.





THE STORY  
1961

# THE DISCOVERY OF RNA

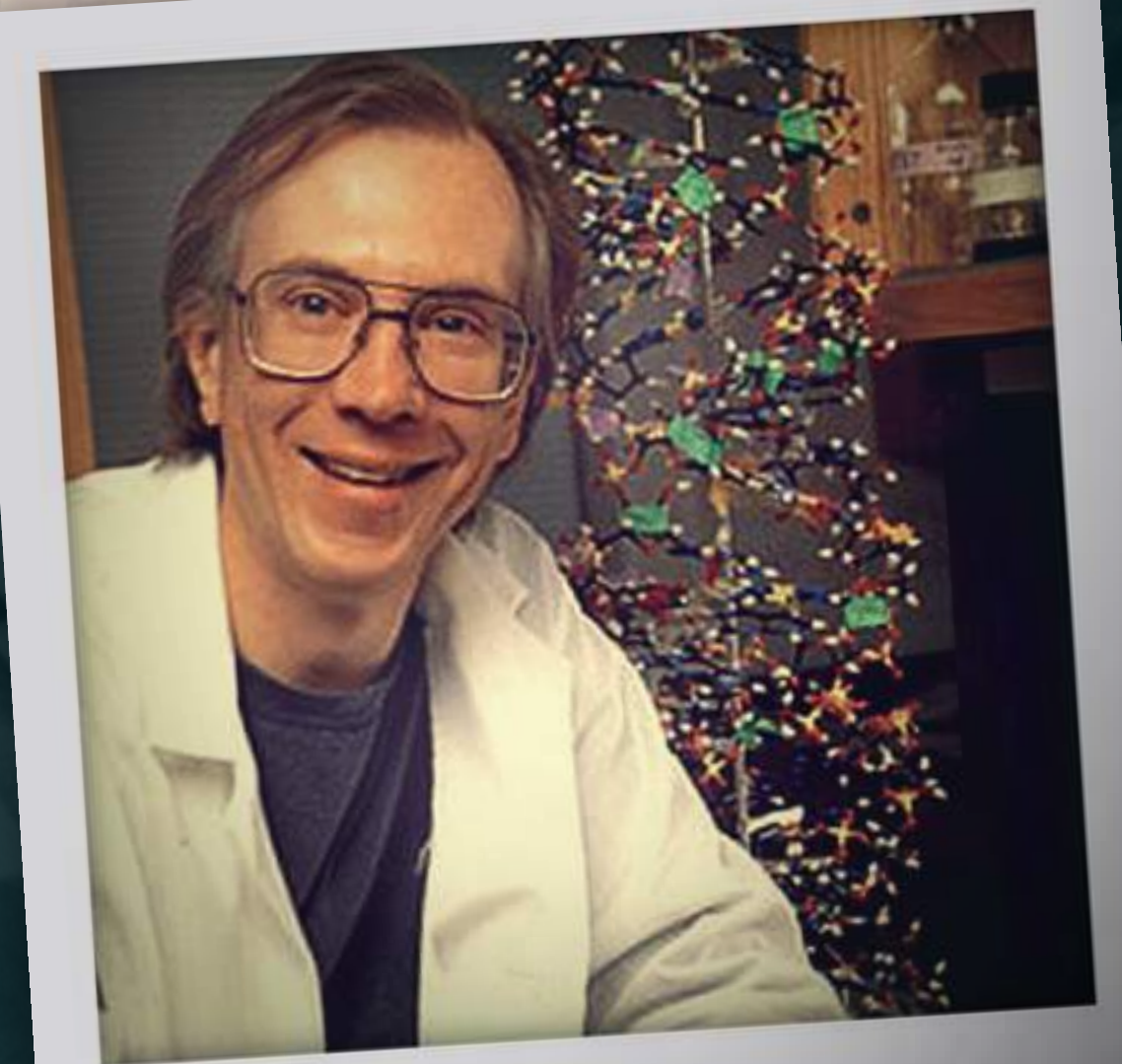
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In the 1960s, three good fairies leaned over the cradle of mRNA: Jacob, Lwoff and Monod from the Pasteur Institute. They managed to prove that DNA uses messenger RNA to make proteins. When the body needs to lower the blood sugar level, then its DNA sends a messenger RNA into the cells to command them to make insulin proteins. It's the same thing for a blood cell to make hemoglobin or a neuron to make serotonin.

The 3 researchers received the Nobel Prize for this discovery and became worldwide famous: archives from that time show the ebullient scientists and celebrate their prowess.

In the 70s and 80s, Tom Cech extended the research of Jacob, Lwoff and Monod. This work earned him, in turn, a Nobel Prize in 1989. mRNA was becoming better known, but the idea of using it to cure was not yet a reality. All eyes were turned towards DNA and gene therapies that repair or replace damaged DNA in patients.

For Tom Cech, *"those who, like me, were working on mRNA felt like we were missing the boat. The industry was investing billions on DNA! mRNA remained a subject of fundamental research, with very little financial means"*.





# THE VICTORY OF THE RNA

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The race for the vaccine is a tribute to BioNtech and Moderna, but more importantly to mRNA technology and the persistence of researchers who have been pushing it for decades. For Drew Weissman: *"Without Covid 19, the mRNA technology would have eventually taken hold I think, but when? It would have taken many more years."*

*"Warp Speed was able to leverage the network of clinical trials that had been established for AIDS across the country."* Graham said. That's how tens of thousands of volunteers were recruited in a matter of weeks.

At the end of 2020, the miracle of mRNA made the front pages of the world press and scientific prizes rained down on the protagonists of the RNA story, like Kati Kariko who speaks of it with emotion: *"Frankly, after so many years of hardship, it is an immense satisfaction to see RNA recognized."*

Frédéric Martinon does not have any regrets: *"It's science. I am proud to have made my contribution to this story."* Steve Pascolo is as enthusiastic as ever: *"For mRNA, there will be a before and after Covid, that's a certainty!"*

With the Covid episode, biotech companies have pocketed billions. So what will they do with it? What are the consequences for medicine? What will the messenger revolution look like for patients?



# THE REVOLUTIONS TO COME

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## PERSONALIZED RNA TREATMENT FOR CANCER

Steve Pascolo now works in the Department of Oncology at the University Hospital of Zurich. After co-founding Curevac in 2000, the world's first RNA biotech, and testing a prototype vaccine on himself, he is organizing clinical trials with anti-tumor messenger RNA. With this technique, the treatment is manufactured by the patient's own body, which means that production costs are much lower than for conventional immunotherapies.

Technology also allows for more effective treatments by personalizing therapy. Each cancer is different. mRNA makes it possible to provide a specific and adapted response.

This custom manufacturing is a far cry from the current industrial model. Usually, Big Pharma produces the same drug for everyone in large factories. To personalize treatments, will mini-messenger RNA factories soon be set up in hospitals, close to patients?

## NUTCRACKER, A DRUG PRODUCTION ON DEMAND

New industrial processes are already in the pipeline. Founded in 2018, Nutcracker Therapeutics is developing micro platforms for messenger RNA production. Benjamin Eldridge is the company's CTO and gives the tour, *"No warehousing with us, we produce on demand there and when there is a need."* The fully automated device has the dimensions of a refrigerator, which he reveals to us: *"The four elementary bricks of RNA arrive through these four pipes in the chemical reactor. Two hours later, we get ready-to-use doses of mRNA, 99.99% pure."*

These "RNA printers" threaten the manufacturing and distribution channels of conventional big pharma. So, to position themselves, they are multiplying the number of big catches in the sector.

Like Translate-bio, which has developed a messenger RNA-based therapy for cystic fibrosis and which Sanofi recently acquired for \$3.2 billion!



# THE REVOLUTIONS TO COME

## LIPOSOMES OF THE FUTURE

But to fulfill the new promise of messenger RNA, R&D offices still need to work on packaging techniques. Better targeting of RNA delivery to the body is the industry's priority.

In his Vancouver lab, Pieter Cullis is working to solve this problem: when a drug is swallowed, only a tiny fraction of the dose reaches the target organ.

His team is therefore developing a new generation of liposomes designed to deliver RNA only where it is needed. How do they do this? By shining a laser on the target organ. The light-sensitive liposomes release their cargo only at the illuminated site. Is it just a gadget or will it be a must-have invention in 10 years? Impossible to say, it is research. But the patent is already registered.

## UNIVERSAL FLU VACCINE AND FINALLY AN AIDS VACCINE

In a long corridor, we find Drew Weissman walking with a colleague, Norbert Pardi "Kati Kariko's heir". Hungarian like her, he is proud to show the photo of their respective fathers who worked in the same butcher shop in the small town of Kisjszalls. It was Kati who, returning every summer to their hometown, gave him a taste for science and the opportunity to work at the University of Pennsylvania.

Following in the footsteps of his elder brother and in close collaboration with Drew Weissman, Norbert Pardi is using RNA to improve the effectiveness of the flu vaccine. The latest results suggest that soon a single injection will be enough to protect against the virus for 10 years.

When Covid 19 arrived, the AIDS epidemic was entering its 40th year. Could it be that the messenger is also blowing the whistle on the most elusive of viruses? According to Drew Weissman, RNA is reshuffling the deck and an HIV vaccine is finally within reach. Results from the first clinical trial, launched by Moderna in 2021, are expected in 2024.



# CONCLUSION

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AIDS, cancer, influenza, malaria, genetic or cardiac diseases, diabetes, Alzheimer... After being ignored for years, messenger RNA is now appearing in all major medical research programs. But will it really deliver on all these promises?

As a wise scientist, Thomas Cech recognizes the medical potential of RNA but puts its scope into perspective: “The list of diseases that RNA will effectively treat is not written down anywhere. For some of them, the answer may be DNA rather than RNA or another technique. It is impossible to say. In the field of medical research, we must remain humble”.

A humility shared by Barney Graham: “Despite how far we have come, we still understand only a tiny part of life. To overcome a virus as twisted as AIDS, we will need to make other fundamental discoveries like that of messenger RNA in the 1960s”.

And Thomas Cech draws lessons from history: “Messenger RNA technology is a summary of what science really is: a collective adventure never written in advance. To get to this point, hundreds of researchers have tried, failed for some and fortunately persevered for others”.

The gigantic race for applications triggered by the success of mRNA against Covid, and the enormous profits that are expected, should not make us forget what made them possible: the fundamental research that was considered at the time to be unusable or useless and that was above all financed by public money.



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