

Honorary
Doctorate ^{dr.}
**Katalin
Karikó**



**RADBOUD
UNIVERSITY
PRESS**

Doctor Honoris Causa Series
Radboud University | Faculty of Science

Honorary Doctorate Dr. Katalin Karikó

Honorary Doctorate **Dr. Katalin Karikó**

20th of October 2022

Radboud Universiteit



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This publication is part of the Radboud University Doctor Honoris Causa Series
Faculty of Science, Radboud University

Published by RADBOUD UNIVERSITY PRESS
Postbus 9100, 6500 HA Nijmegen, the Netherlands
www.radbouduniversitypress.nl | www.ru.nl/radbouduniversitypress
radbouduniversitypress@ru.nl

Editing: Radboud University Press

Design: Textcetera, The Hague

Print: Pumbo.nl

Photography: Dick van Aalst and Katalin Karikó

ISBN: 978-94-9329-600-8

DOI: 10.54195/BNYC2439

Free download at: www.radbouduniversitypress.nl

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FLORIS RUTJES
LAUDATIO





FLORIS RUTJES

LAUDATIO

Dear professor Karikó,

It is a real privilege to have you here on this occasion to receive an Honorary Doctorate at the Dies Natalis of our university. It is a rather special birthday, as today we celebrate the 99th year of existence of Radboud University.

At Radboud University, we aim to perform research of high scientific quality in an environment of integrity and academic freedom. Research performed by academics who follow their own ideas and ambitions, with scientific curiosity being one of the prime drivers. They connect to other researchers, sometimes in other disciplines, to organizations in society, and address scientific questions but also societal needs and challenges. By doing so, Radboud University makes an impact on society, both by educating and training people, from students to professors and by contributing to solving societal challenges.

Your career fits this profile perfectly well. Since the start of your academic career in a modest Hungarian university, you developed your scientific vision, namely that there must be opportunities to develop mRNA into therapeutic applications to prevent or cure disease. Being convinced of your own revolutionary ideas is one thing, but if others, your peers, in fact, are not, this may not be easy. Not being able to convince your colleagues in the field means that grant applications are turned down and that there may be few resources to carry out your plans. It requires perseverance and courage to continue, leaving your home country, in your case, moving with a baby and husband to the USA to further pursue your scientific ideas. Also, there, it required a long road with disappointments at times before you reached a point where you actually produced the scientific evidence that mRNA can be of therapeutic value. The breakthrough was the 2005 paper in *Immunity*, published jointly with your colleague Drew Weissman “Suppression of RNA recognition by Toll-like receptors: the impact of nucleoside modification and the evolutionary origin of RNA”, reporting how an immune response of the body could be circumvented



by changing one component in the transcription reaction (pseudouridine instead of uridine). Eventually, it was that simple, you said.

That simple finding turned out to have an enormous impact, driven by the disruptive Covid-pandemic that started in the spring of 2020 and called for a worldwide vaccination campaign. Herein, the mRNA-based vaccines appeared particularly effective and thereby unequivocally demonstrated your vision of the importance of mRNA for medical use. I anticipate that medical applications will not stop at this point but that many researchers, inspired by this success, are studying new applications for mRNA technology. Your leading role in the therapeutic use of mRNA has been crucial and is one reason for this honor today.

Besides these scientific merits, there is another aspect that is important to us, which is the diversity of the research community, and in particular, the role of women in Science, Technology, Engineering, and Mathematics (STEM) programs. With your career and scientific achievements and the visibility that you now have in the academic community and beyond in society, you are an eminent role model for female researchers and most certainly will inspire many young women to pursue a career in STEM as well.

You have made important scientific discoveries in fundamental research, discoveries that turned out to be key to solving a societal challenge, and you are a prominent role model for women in science. This is what makes that we are pleased to award you this honorary degree of doctorate.



RECTOR ET DECANI RADBODI UNIVERSITATIS NOVIOMAGENSIS
LECTORIBUS SALUTEM!

INTERIMUS HONORIS CAUSA, Insuper consilio a nostris hunc honorem tibi, si non modo ingenuitate animi, sed etiam scientia, eruditione, dignitateque illis parvis, honorifice potuisse adhibitis, ergo traditione honorifice, verum etiam hominis doctus qui studio erga litteras hunc omnia excellens et ad alta doctorumque sublimanda studio committimus, nullis honoris significatione Universitatis quibus nos decipere possunt.

Quapropter, cum Universitatis nostra communitatem illustrandam

Katalin Karikó

Nomen in archibus obsequitur que vocatur Karikó, doctoris hunc causa et doctoris est.

Dignitas doctoris hunc causa Karikó consistit in ob meritum honoris quo ad hunc, quod modis et honorificis instituit, ut, acceptandis ad hunc partem. Hoc honoris illius, necesse vacuatur congrua dote et pluribus ad certissimum honoris tunc conferentur coram. Karikó Karikó per omnia tempora honorificis et dote, ut dote optime tunc congruatur, ergo in exemplum hunc quo doctoris hunc optime present.

Quapropter hunc honoris doctoris hunc causa Karikó hunc honoris et dignis et quo ad Universitatis nostra ergo hunc doctoris honoris, tunc, quo omnia honorificis ad hunc, necesse hunc et hunc present.

Quapropter Nos pro potestate nobis concessa mandamus

Katalin Karikó
DOCTOREM HONORIS CAUSA

Nullatenus tunc obsequitur tunc tunc et ad certissimum quodlibet tunc et hunc legitime causa doctoris vel lege vel more velis velis.
Causa et quo ad hunc honoris hunc, Diploma hunc causa Radboudi subscriptum et nostra Universitatis sigillo confirmatum et tradendum causa-tunc.
Datum Novomagi, in celebranda hunc Universitatis nostra dies natalis undecimbris, a.d. mil. Kalendas Novembriis MDCCCXXII

Rector

Decanus

Professores J.B.M. van Erckelen

Professores F.P.J. Ruijs

Radboud Universiteit

Radboud Universiteit
SINCE 1223



HONORARY DOCTORATE CERTIFICATE





HONORARY DOCTORATE CERTIFICATE

**GREETINGS TO THE READER
FROM THE RECTOR AND DEANS OF
Radboud University Nijmegen**

By virtue of the authority of our predecessors, an academic degree may be conferred upon individuals who have distinguished themselves in their academic and scientific pursuits and successfully completed the academic requirements. Universities may also choose to confer such an academic distinction upon individuals who have excelled in the arts and sciences and who have made a significant contribution to the promotion thereof.

For this reason, our university has decided to confer an honorary doctorate upon the illustrious

**Karikó, Katalin
born in Szolnok (Hungary)**

This honorary doctorate is awarded for uncovering fundamental insights that make mRNA suitable for medical applications and the development of a scientific basis for a new generation of vaccines. This work makes a significant contribution to the eradication of viral diseases.

Katalin Karikó has shown proof of courage and perseverance in pursuing her scientific vision. She is a role model for female scientists.

By consensus of all learned people, she is deserving of the highest praise and is therefore being awarded with the most honourable of academic distinctions.

For this reason, and by virtue of the authority vested in us, we hereby present the degree holder with this honorary doctorate and confer upon him all associated honours and rights accorded by law and custom.

This certificate, signed by the Rector Magnificus and authenticated by the university seal, has been presented to the degree holder as permanent and valid proof of their achievements.

Issued in Nijmegen on October 20, 2022 on the occasion of our university's 99th anniversary.

Professor J.H.J.M. van Krieken
Rector Magnificus

Professor F.P.J.T. Rutjes
Promotor



RECTOR ET DECANI RADBODI UNIVERSITATIS NOVIOMAGENSIS LECTORIBUS SALUTEM!

IN CHRISTI NOMINE. AMEN. Sapienter consilio a maioribus nostris institutum est, ut non modo ingenuarum artium studiosi, academicis disquisitionibus rite peractis, honorificum peterent industriae atque eruditionis testimonium, verum etiam homines doctos qui studiis atque litteris inter omnes excellentes et ad artes doctrinasque adiuandas maxime contulissent, eadem honoris significatione Universitates sponte sua decorare possent,

Quamobrem, cum Universitas nostra commemoravisset illustrissimam

Katalin Karikó

Natam in civitate Hungariae quae vocatur Szolnok, doctoratus honoris causa ei decretus est.

Dignitas doctoratus honoris causa Katalin Karikó concessa est ob inventionem fundamenti quo mRNA, quod acidum ribonucleicum nuntians est, accuratioribus adaptari potest. Hac inventionem initium novae vaccinatorum categoriae dedit et plurimum ad curationem morborum viro contractorum contulit. Katalin Karikó per omnia animum fortitudinemque exhibuit, ut doctas opiniones suas comprobaret, eoque se exemplum feminis quae doctrinas colunt egregissimum praestat.

Quippe quae hominum doctorum omnium consensu eximias laudes meruerit et digna sit quae ab Universitate nostra insigni laurea decore augetur, Nobis, quo causam honestissimam adiuveremus, summos honores ei tribuere placuit.

Quapropter Nos pro potestate nobis concessa eandem

Katalin Karikó

DOCTOREM HONORIS CAUSA

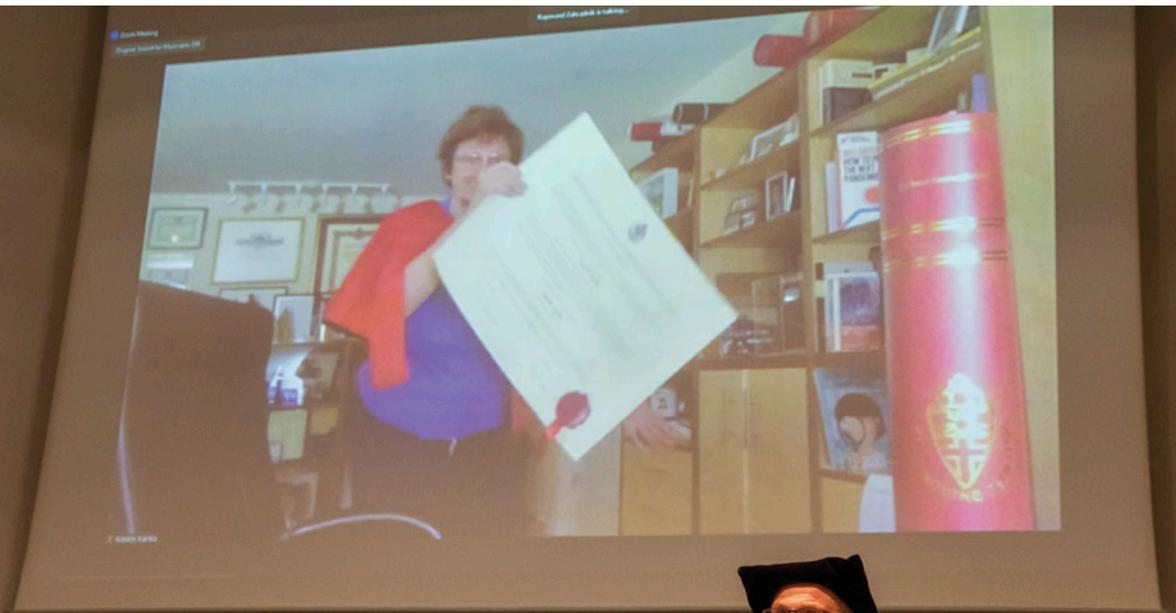
sollemni modo ritumque creavimus et renuntiavimus et ei concessimus quicquid iuris et honoris legitime creato doctori vel lege vel more tribui solet.

Cuius rei quo sit firma testataque fides, Diploma hoc manu Rectoris subscriptum et maiore Universitatis sigillo confirmatum ei tradendum curavimus.

Datum Noviomagi, in celebranda festivitate Universitatis nostrae diei natalis undecentesimi, a.d. xiii Kalendas Novembres MMXXII

Rector

Promotor



KATALIN KARIKÓ

ACCEPTANCE SPEECH





KATALIN KARIKÓ

ACCEPTANCE SPEECH

Dear Professors, students, fellow researchers, distinguished guests,
dear ladies and gentlemen,

I am very grateful to the nominating committee of Radboud University for selecting me to receive an honorary doctorate degree. It is a wonderful feeling to be recognized for my work. I am humbled and excited and have a deep sense of appreciation.

I have not been in the spotlight; my life has not been like that. For four decades, I worked quietly in the laboratory performing the experiments myself, writing the lab notes and the papers. I knew what I was doing was important and didn't expect anybody to tap my shoulder to praise me for my work. The only award ceremonies I attended were when my daughter won gold medals in rowing in the women 8 at the Olympic Games in Beijing and London, where the Dutch women's team was also very successful.



Katalin (Kati) and her sister with Kati's daughter Susan Francia at the Olympic Games in Beijing in 2008, where Susan won a gold medal in rowing.



Kati with her husband and daughter at the Olympic Games in London in 2012, where Susan became a gold medalist rower again.

I grew up in a small Hungarian town with a population of ten thousand. My mother was a bookkeeper, my father a butcher, and I learned from them that hard work is part of our life, and of course, I learned how to make sausage.



Kati with her parents and older sister in 1957.



Kati with her older sister in their yard in Hungary in 1957.

We had a big garden and animals in the yard. As a little girl, I watched the chickens hatching from the eggs and the plants growing out of the small seeds we put into the soil. I was curious. I had great teachers, and they encouraged me to keep learning. So, that was my humble beginning, and there was a long winding road on which I arrived here.

My greatest joys in science have been the small and large victories at the bench in the lab. Many times, when I got disappointed that my experiment didn't work, a quote from Leonardo da Vinci written on the wall in the lab cheered me up. It said "Experiments never err, only your expectations do", so there is no failure, we just need to think critically.

We spent years working on technologies that seemed unconventional and almost science fiction to some, but we shared an immense belief that if the

result of our work could improve the life of at least one person, then we have succeeded. It is such a relief to know that by now, the mRNA vaccine has successfully protected millions of people from the serious effects of COVID-19.



Kati receiving a dose of the COVID-19 vaccine
(Credit: Penn Medicine).

I learned so much during these 40 years, so I thought I share some of my experiences with you.

1. It is important to love your work.

We spend most of our life working, so it is important to enjoy it. And if you like your work, you will be good at it and enjoy it even more.

2. You need to learn how to handle stress.

Hans Selye coined the word stress in the 1930s. He said that stress can kill you depending on how you react to it, but without stress, life is boring. You need stress, but learn that by “adopting the right attitude, you can convert a negative stress into a positive one”. You need positive stress, expectation, and excitement. I wouldn’t be here today if I had not been terminated from my position several times. I couldn’t change that decision, but it was up to me what I did next.

3. You can upload a lot of stress if you **focus on what you can do, and what you can change.**

People get burned out in their work because they compare themselves with others, those who might work less, but achieve more, are paid more and are promoted. You can't change that, so do not pay attention; it is a distraction. Instead, spend your energy improving yourself, working harder, being more creative, and performing better.

4. You have to **believe in yourself.**

The environment can be intimidating. As a small-town girl from Hungary to an American Ivy League school, I asked myself if I could think of something that all those very smart scientists working in that famous university couldn't. I had to answer YES, why not. "Believing in yourselves is an endless destination, believing you will fail is the end of your journey."



"Please be nice to your fellow students, and follow their professional work." Kati and fellow students at her home in 1977.

5. Please **be nice to your fellow students, and follow their professional work.**

When I needed advice to perform my experiments, I called upon my former classmate, who at that time worked at the University of Toulouse or another one in Germany, so that I could make the best mRNA. Your classmates will be experts one day, and you may need their help.

6. Find the right partner for life.

I met my husband while we were students. He has supported my decision every step of the way, moved to a foreign country with me when we had hardly any money in our pockets and our 2-year-old child by our side... all so that I could continue my research. He knew how important science was to me. My daughter Susan Francia grew up to appreciate my lifelong commitment to my science and has always encouraged me.



Kati and her husband Béla Francia in 1980.



In August 1985, Kati arrived in the USA with her husband Béla and daughter Susan.

Girls, my advice is that you do not need to choose between your career and having a child. Find the right partner who cares about your dreams and supports your decisions.

And finally, let me tell you a story about my daughter. She was seven years old, just finished 2nd grade, and when she got home started writing a letter right away. I asked her, “Who are you writing to?” and she said, “To my teacher, Misses Wilson. I am thanking her for the wonderful year; we learned so much.” I was 35 years old and realized I had not sent a letter to my teachers, but then it all changed. Now I visit them, call them, send letters and express my appreciation.

So, the conclusion: Do not hesitate to learn from anybody; even a 7-year-old can teach you something, and from time to time, tell those who helped you on your journey how much you value what they have done for you.



Kati with her family on 1 January 1987.

CURRICULUM VITAE

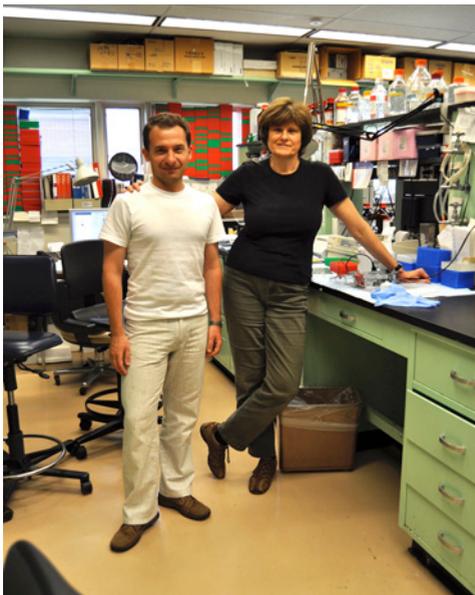




CURRICULUM VITAE

Katalin Karikó is a professor at the University of Szeged and adjunct professor of neurosurgery at the Perelman School of Medicine, University of Pennsylvania, where she worked for 24 years. She is the former senior vice president at BioNTech SE, Mainz, Germany, where she worked between 2013-2022.

For four decades, her research has focused on RNA-mediated mechanisms with the ultimate goal of developing *in vitro*-transcribed mRNA for protein therapy. She investigated RNA-mediated immune activation and, together with Dr. Drew Weissman, discovered that nucleoside modifications suppress the immunogenicity of RNA. This groundbreaking work unlocked the opportunity for the therapeutic use of mRNA. The nucleoside-modified mRNA-lipid nanoparticle vaccine platform developed by Drs. Weissman, Pardi, and Karikó was used to create the FDA-approved anti-SARS-CoV-2 mRNA vaccines by BioNTech/Pfizer and Moderna/NIH that is crucial to fight the pandemic.



Kati with Dr. Norbert Pardi in 2012.

Kati with Dr. Drew Weissman in 2015.

Milestones of mRNA development for therapy.

- | | |
|-----------|--|
| • 1961 | Discovering mRNA |
| • 1978 | Isolated mRNA delivery into mammalian cells |
| • 1984 | Synthesizing mRNA in vitro |
| • 1990s - | Optimizing performance of the mRNA |
| • 2010s - | Optimizing formulation for mRNA delivery |
| • 2021 | FDA approval of COVID-19 LNP-mRNA vaccine |



She received her Ph.D. in biochemistry from the University of Szeged, Hungary, in 1982. Her thesis work involved the synthesis and antiviral evaluation of 2'-5'-linked oligoadenylates, called 2-5A, responsible for the interferon-induced antiviral mechanism. She performed her research at the Biological Research Center, focusing on 2-5A generated with nucleoside analog, cordycepin. She delivered liposome-formulated cordycepin analogs of 2-5A into cells and measured their antiviral effect.



Kati receiving her diploma of her Ph.D. degree in biochemistry from the University of Szeged, Hungary, in 1983.



Kati at the Biological Research Center in 1980.

In 1985, after moving to the Temple University, Philadelphia, she expanded her research on 2-5A molecules modified at their nucleosides and internucleotide linkages. In 1986, she helped to perform a clinical trial run at Hahnemann University, where HIV-infected patients were treated with mismatched double-stranded RNA to induce their antiviral systems. She invented an assay that helped identify an RNaseL inhibitor in the PBMCs of the infected patients.

After moving to Bethesda in 1988, she studied the anticancer effect of interferon at USUHS using the most advanced molecular biology techniques. In 1989 she started to work as a Research Assistant Professor at the Medical School of the University of Pennsylvania. There, she used in vitro-transcribed (IVT) mRNA to overexpress selected proteins in cultured cells.



Kati in the lab at Temple University, Philadelphia, 1985.



Kati at the Medical School of the University of Pennsylvania, 2005.

Her first success was when she demonstrated that functional, highly processed proteins were generated from in vitro-transcribed (IVT) mRNA transfected into cultured mammalian cells, suggesting that mRNA-encoding therapeutic proteins have the potential to treat various diseases. However, she and Dr. Drew Weissman demonstrated that IVT mRNA is immunogenic and thus unfit for therapeutic use. They identified uridine as being responsible for this activation. After searching for years, they discovered that by incorporating naturally-occurring modified nucleosides, such as pseudouridine, into the mRNA, the newly created mRNA was highly translatable and avoided activation of TLR7 and TLR8 in human immune cells. They also invented a purification procedure that further increased the translational capacity of the mRNA. As the result of this work, together with her colleagues, she demonstrated the practical use of nucleoside-modified mRNA encoding antibodies targeting cancer and infectious diseases. In animal models of multiple sclerosis, they used



Kati's lab at the University of Pennsylvania in 2013.

autoantigen-encoding mRNA. They proved that this novel mRNA technology can induce tolerization, thus opening the possibility of treating autoimmune diseases. She also initiated a clinical study in which patients' tumors were injected with modified mRNAs encoding cytokines, thus promoting potent antitumor immunity and tumor eradication at local and remote sites.

She is a co-inventor on ten patents granted by the US related to the application of non-immunogenic, nucleoside-modified RNA. She and Dr. Weissman founded RNARx, a company dedicated to developing nucleoside-modified mRNA for therapy. She served as CEO of RNARx from 2006 till 2013. She is a founding member of the scientific planning committee for the International mRNA Health Conference, an annual non-profit meeting for advancements in mRNA technology, inaugurated in 2013. She served as a guest editor of the *Molecular Therapy* special issue on mRNA therapy in 2019.



Katalin Karikó in 2020.

On 20 October 2022, the day that Radboud University celebrated its 99th anniversary, Dr. Katalin Karikó received a Radboud honorary doctorate in recognition of her scientific contributions to developing mRNA-based vaccines. This edition includes the laudatio of the honorary supervisor and the speech of the honorary doctor.

Karikó spent years researching medical applications of mRNA. Her dream was to develop synthetic mRNA and use this to cure cancer, strokes, and influenza. Eventually, after years of toil, rejection, and criticism from colleagues, she and fellow researcher Drew Weissman demonstrated that it is possible to trigger an immune response in the body with mRNA without the body turning against the mRNA itself. With this breakthrough, a new revolutionary technique was born.

Thanks to Karikó's scientific work, BioNTech/Pfizer and Moderna were able to develop the current mRNA vaccines against COVID-19. This is a prime example of the beneficial impact that fundamental research can eventually have on society.

Honorary supervisor Floris Rutjes, Professor in Organic Synthesis: "With courage and determination, she pursued her scientific vision for a very long time, and by doing so, she has ultimately made a significant contribution to the fight against viral diseases."

ISBN 978-94-9329-600-8



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