## **CURRICULUM VITAE OF MIKAEL KUBISTA**



Name: Address: Born: Marital Status: Children: Residence: Home page: Wikipedia: Mikael Kubista. Heleneviksbacken 19, 431 36 Mölndal, Sweden. August 13, 1961 in Podborany, Czechoslovakia. Married. Robin, Christian, Josefine Resident in Sweden since 1968. Swedish citizen since 1974. Institute of Biotechnology, CAS https://en.wikipedia.org/wiki/Mikael\_Kubista

## Brief history

Kubista has been interested in life sciences his whole life. After bachelor at Gothenburg University, Kubista joined the team at Astra Hässle (today part of AstraZeneca) that developed the K+/H+-ATPase inhibitor omeprazole, which became the then most sold pharmaceutical drug under the trade names of Losec (Prilosec in US) and Nexium to treat ulcer. He obtained his Ph.D. in chemistry at Chalmers University of Technology in Göteborg and did postdocs at La Trobe University, Melbourne, Australia, and Yale University, New Haven, USA. Returning to Gothenburg in 1991 Kubista started his own research group studying DNA-ligand interactions and elucidated some critical aspects of the RecA catalyzed strand exchange process, which led to the establishment of the current model of DNA strand exchange in homologous recombination. Kubista's team discovered a novel mechanism of transcriptional activation of oncogenes, which led to the development of a new class of anticancer drugs that target quadruplex DNA structures. They developed methods for multidimensional data analysis based on which MultiD Analyses AB was founded, and invented the light-up probes for nucleic acid detection in homogeneous solution, which led to the foundation of LightUp Technologies AB as Europe's first company focusing on quantitative real-time PCR (qPCR) based diagnostics. In 2001 Kubista co-founded TATAA Biocenter as center of excellence in qPCR and gene expression analysis. TATAA Biocenter became under their leadership the largest provider of qPCR training globally, and Europe's largest provider of qPCR services. It was first to obtain flexible ISO 17025 accreditation in Europe. In 2013 TATAA was presented the Frost & Sullivan Award for Customer Value Leadership as Best-in-Class Services for Analyzing Genetic Material and in 2019 TATAA was named "Best Nucleic Acid Analysis Service provider - Europe" by Global Health & Pharma. In 2021 TATAA was on Sweden Technology Fast 50 list.

In 2005 Kubista's team pioneered single cell expression profiling and started the academic Gene Core. In 2014 his team introduced non-invasive prenatal testing (NIPT) in Sweden and founded Life Genomics AB. In 2020 Kubista co-founded SimSen Diagnostics to develop unique technology for liquid biopsy analyses. Kubista coauthored the MIQE guidelines for RT-qPCR analysis, which is the most cited paper in molecular diagnostics (3 citations per day), and he is member of the CEN/ISO working group developing guidelines for molecular diagnostics and the AAPS expert group. Most recently Kubista's invented Two-Tailed PCR, which is arguably the most sensitive and specific method for the analysis of short nucleic acids. Kubista is advisor to Unesco since 1999 supporting the establishment of modern molecular diagnostics in developing countries like Libya, Egypt, Iran, Grenada and Ghana. Since 2007 Kubista heads the Department of Gene Expression at the institute of Biotechnology (IBT), BIOCEV, Czech Academy of Sciences and he is among the 2 % most cited researchers in the world. During the pandemic Kubista's team was on February 3, 2020 among the first in Europe to offer covid-19 testing and Life Genomics AB was responsible for the testing at the Swedish international airports. In 2021 TATAA accepted financing from Care Equity to establish GLP/GCP regulated molecular services to the pharmaceutical industry focusing on Cell and Gene Therapies. In 2023 the founders lost the company due to a legal mistake. Kubista joined MultiD as CTO leading the development of GenEx for regulated bioanalysis and to develop low cost, high throughput multimarker profiling in collaboration with researchers at the institute of Biomedicine, Gothenburg University. Kubista's team at IBT focuses on single cell and spatial transcriptomics and offers services through Gene Core.

## **Professional preparation**

Yale University, New Haven, USA, 1991 (postdoc) La Trobe University, Melbourne, Australia, 1990 (postdoc) Chalmers University of Technology, Ph.D. in chemistry, 1988. Chalmers University of Technology, Licentiate in Physical chemistry, 1986. Göteborg University, B. Sc. with major in chemistry, 1984

## Appointments

2007 -	Head of the department of gene expression profiling at the Biotechnology Institute, Academy of
	Sciences, Czech Republic (50 %)
2024 - 2025	Adjunct professor, department of Biomedicine, Gothenburg University
2023 -	CTO at MultiD Analyses AB (50 %)
2001 - 2023	CEO of TATAA Biocenter AB (part-time)
2015 - 2016	CEO of Life Genomics AB (part time)
2006 - 2007	Visiting Professor, Department of Chemistry, A Coruña University, Spain
2003	Visiting Professor, Department of Chemistry, A Coruña University, Spain
2000 (June)	Visiting professor, University of Maryland, College Park, USA
1997 - 2006	Professor, Department of biochemistry, Chalmers University of Technology.
1993 – 1997	Associate Professor, Department of biochemistry, Chalmers University of Technology.
1991 – 1993	Assistant professor (forskarassistent), Chalmers University of Technology.

## **Commissions of trust**

Advisor in scientific questions to UNESCO

Adjunct board member <u>Life Genomics</u> Chairman of the board of <u>MultiD Analyses AB</u> Board member of <u>Nygen Analytics AB</u> Board member of <u>Aplex Bio</u>

Scientific advisor to Roche Scientific advisor to ThermoFisher Scientific advisor to Qiagen Scientific advisor to Bio-Rad Scientific advisor to <u>RealSeq Biosciences</u>

Member of the Scientific Advisory Council of Genetic Engineering News

Expert advisor for the <u>European Commission Research Directorate General</u> Expert advisor for The European Commission's Health Emergency Preparedness and Response Authority (<u>HERA</u>)

Special consultant in the Life Science area for AFRY.

Advisor for United Nations Educational Scientific and Cultural Organization (<u>UNESCO</u>) and Member of the scientific advisory board for the International Biotechnology Research in Tripoli, Libya (a UNESCO effort)

Editor of Scientific Reports, Nature Publishing group Editor of Molecular Aspects of Medicine Editor of International Journal of Oncology Founding Editor of Biomolecular Detection and Quantification

Member of the <u>American Association of Pharmaceutical Scientists</u> Member of the <u>International Artificial Intelligence Industry Alliance</u> Member of <u>Academia Europaea</u>

## Areas of expertise

Bioinformatics Biotechnology Chemometry Fluorescence spectroscopy Gene expression profiling Molecular Diagnostics Physical chemistry Spectroscopy/optics

Education

Teaching Leadership Entrepreneurship

## **Publications**

<u>Published more than 200 research papers that have been cited 36000 times. h-index: 66</u>. The MIQE guidelines, cited over 15000 times, is the most cited paper in molecular diagnostics. One of the world's 2% most cited scientists.

## Major research accomplishments

Characterized several biologically important chromophores and many of the dyes that are popular labels of biomolecules. These include tryptophan, DAPI, fluorescein, thiazole orange and BEBO. Our papers are key references to nucleic acid staining dyes in the Molecular Probes catalogue.

Elucidated the mechanism of DNA strand exchange in homologous recombination. Our results appear in the popular textbook "Biochemistry" by Mathew, Van Holde and Ahern (3:rd edition, 2000, Benjamin Cummings - ISBN: 0-8053-3066-6).

Identified nucleosome positioning sequences in an experiment referred to in the field as the Widlund experiment. It is detailed in the book "Chromatin" by A. Wolfe (1999, Academic Press - ISBN: 0-12-761914-3).

Discovered a novel mechanism of oncogene activation that involves internal G-quadruplex formation. This work has attracted much attention and has been incorporated in Textbook of Biochemistry with Clinical Correlations 5th ed. by Devlin (2002, John Wiley & Sons Inc – ISBN: 0-471-41136-1) and the Encyclopedia of Molecular Medicine (2002, John Wiley & Sons Inc – ISBN: 0-471-37494-6). This discovery also led to the start of Cylenepharma (www.cylenepharma.com), a San Diego based Biotechnology Company that develops quadruplex interacting agents to block expression of the cmyc oncogene.

Developed powerful experimental designs to study chemical equilibria and chemical reactions by multidimensional spectroscopy.

Developed probes that become luminescent upon binding to target nucleic acid.

Developed a highly sensitive test for Non-Hodgkin lymphoma based on measuring differential expression of target genes by real-time PCR.

Pioneered the field of single cell and subcellular expression profiling

Discovered horizontal transfer of mitochondria in vivo

## **Seminars and courses**

I have extensive experience in teaching and lecturing. I have lectured in essentially all areas in Biosciences, and in 1994 I designed the Molecular Biotechnology course at Chalmers University, which, when I left, was the most popular course in the Chemistry and Biotechnology undergraduate programs at Chalmers University.

I was the initiator, and during 1991-1994, the organizer of a seminar series for graduate students and scientists in Chemistry at Chalmers and Gothenburg universities. The seminar series has become integrated in the graduate educational program in chemistry and are still today very popular.

In 1992 I founded the 'Arne Brändström lectures in biophysical chemistry' held annually by renowned scientists in honor of Dr. Arne Brändström, who was a leading scientist behind the development of Omeprazole at Astra. The lectures were heavily sponsored by AstraZeneca. During 1992-1996 four Nobel laureates visited Gothenburg to deliver the lecture, and the day culminated with a large party for university and AstraZeneca scientists.

During 1996-1998 I organized courses about legal protection of Biotechnology innovations for the Industry in partnership with among others AstraZeneca, PharmaciaUpjohn, the Swedish patent and trademark office (PRV) and Ström & Gulliksson patent bureau.

In 2000 I assisted Conferator AB in organizing 'Bioteknikdagarna' for investors in Life Sciences, and arranged a round-table discussion how to avoid the 'Biotechnology bubble'. Those who listened saved money.

In 2001 I founded TATAA Biocenter in Gothenburg, as a Swedish center of excellence in real-time PCR. Today TATAA Biocenters are being planned at several locations in Europe, and have become the leading real-time PCR training provider globally.

Since 2003 I am arranging Unesco training in real-time PCR for scientists from developing countries

Since 2004 I am in the organizing committee of EMBO training courses in real-time PCR. Annually we arrange a real-time PCR course for scientists from all over the world.

Since 2004 I am giving the real-time PCR course at Pittcon, US, Annually I give a real-time PCR course for scientists in US.

For several years I was in the organizing committee of FEBS organizing training courses in real-time PCR for scientists from all over the world.

#### **Entrepreneurial achievements**

The following companies were founded by Mikael Kubista

#### LIGHTUP TECHNOLOGIES AB

Founded in 1998. <u>LightUp Technologies AB</u> develops real-time PCR tests for human infectious diseases based on proprietary technology. LightUp was the Connect company of the year in 1999 and in 2003 it was the first company to receive CE certification for the European market for its CMV real-time PCR test. The company is located in the Stockholm area.

#### MULTID ANALYSIS AB

Founded in 2001. <u>MultiD Analyses AB</u> develops GenEx software for gene expression data analysis. MultiD received the VinnNu award in 2002.

#### TATAA BIOCENTER AB

Founded in 2001. <u>TATAA Biocenter AB</u> provides training in real-time PCR, offers contract research in real-time PCR, and develops real-time PCR assays for the research market. The company is located in Göteborg.

#### LIFE GENOMICS AB

Founded in 2014. <u>Life Genomics</u> AB offer genetic testing to the consumer market. Among company products is <u>Non-Invasive Prenatal Testing</u>.

#### GENDOKTORN MEDICINSK SERVICE I GÖTEBORG AB

Founded in 2018. Gendoktorn offers clinical genetic testing and consulting.

#### LIFE TEST s.r.o.

Founded in 2019. Life Test offers sports and nutrigenetic testing and life style advise.

#### SimSen Diagnostics AB

Founded in 2020 jointly with the SimSen Seq inventors Anders Ståhlberg and Tone Godfrey, and Gothenburg University holding <u>SimSen Diagnostics</u> develops ultrasensitive diagnostics for cancer.

## Patents taken by Mikael Kubista

#### PROBE FOR ANALYSIS OF TARGET NUCLEIC ACIDS

Inventors: Mikael Kubista, Nicke Svanvik Patents: US6329144, AU3112997, BR9709495, CN1226928, EP0918852, JP2000511057T, NZ333473, PL330201, SE506700, <u>SE9602183</u>, WO9745539 Exploited by: <u>LightUp Technologies AB</u>

#### METHOD FOR THE PREPARATION OF A PROBE FOR NUCLEIC ACID HYBRIDIZATION

Inventors: Mikael Kubista, Gunnar Westman, Nicke Svanvik Patents: US6461871, AU9100598, DE19882655T, GB2344823, JP2001515923T, SE9703251, WO9913105 Exploited by: LightUp Technologies AB

#### METHOD FOR CHARACTERIZING SAMPLES

Inventor: Mikael Kubista Patents: AU8754998, US6876954, WO9957543 Exploited by: <u>MultiD Analyses AB</u>

#### METHOD TO MEASURE GENE EXPRESSION RATIO OF KEY GENES

Inventors: Mikael Kubista, Pierre Åman, Anders Stålberg Patents: SE 0103991, WO02099135 Exploited by: <u>CanAg Diagnostics AB</u>

#### METHOD TO CHARACTERIZE SAMPLES BY FLUORESCENCE MICROSCOPY

Inventor: Mikael Kubista, Björn Sjögreen and Amin Forootan Patents: Swedish patent application Exploited by: MultiD Analyses AB

#### SYNTHESIS AND EVALUATION OF NEW CYANINE DYES AS MINOR GROOVE OR POLY(dAdT)<sub>2</sub> BINDERS

Inventors: Gunnar Westman, Jonas Karlsson, Mikael Kubista (contribution to US patent) Patents: US2004132046, WO02090443, EP1390433. CA2446982, EP1390433 Exploited by: <u>TATAA Biocenter</u> and <u>LightUp Technologies AB</u>

# USE OF PANEL OF PAIRS OF PRIMERS COMPLEMENTARY TO REPORTER GENES OF CELL DIFFERENTIATION

Inventors: Peter Sartipy, Karin Noaksson, Johan Hyllner, Neven Zoric, Mikael Kubista Patents: WO2006094798, EP1859055, US20080280295 A1 Exploited by: <u>Takara & TATAA Biocenter</u>

#### SINGLE-CELL mRNA QUANTIFICATION WITH REAL-TIME RT-PCR Inventors: Mikael Kubista, Martin Bengtsson, Anders Ståhlberg, Linda Strömbom and Neven Zoric Patents: <u>EP 2147119</u>

Exploited by: Roche & TATAA Biocenter

## IMPROVED LYSIS AND REVERSE TRANSCRIPTION FOR mRNA QUANTIFICATION Inventors: Mikael Kubista, Linda Strömbom and Neven Zoric Patents: <u>US 9714448</u> Exploited by: <u>Roche & TATAA Biocenter</u>

METHODS FOR DETERIMINING THE EXPRESSION LEVEL OF A GENE OF INTEREST INCLUDING CORRECTION OF RT-QPCR DATA FOR GENOMIC DNA-DERIVED SIGNALS Inventors: Mikael Kubista, Henrik Laurell, Jason Iacovoni

Inventors: Mikael Kubista, Henrik Laurell, Jason Iacovo Patents: <u>WO2012171997</u> Exploited by: <u>TATAA Biocenter</u>

#### METHODS FOR ASSESSING RNA QUALITY

Inventors: Mikael Kubista, Jens Björkman

Patents: <u>US9932633B2</u> Exploited by: <u>Roche & TATAA Biocenter</u>

#### METHODS AND COMPOSITIONS FOR NUCLEIC ACIDS DETECTION

Inventor: Mikael Kubista, Robert Sjöback Patents: <u>WO 2016027162, EP3183054A2, USPTO 20170233801</u> Exploited by: <u>Roche & Biovendor</u>

## Awards

Winner of the 1996 Innovation Cup in western Sweden for the LightUp probes.

Awarded the SKAPA price in 2002 for the most promising Swedish innovation.

Pioneer of the year in western Sweden in 2012

In 2013 Frost & Sullivan Award for Customer Value Leadership as Best-in-Class Services for Analyzing Genetic Material (to TATAA Biocenter)

In 2019 named "Best Nucleic Acid Analysis Service Provider - Europe" by Global Health & Pharma

In 2021 the standards and innovation award to SPIDIA by CEN ELEC.

## **External funding and major grants**

Kubista has always been very successful raising grants and support from both the public sector and Industry. Some important international grants I have received are:

- H2020-FETPROACT-2020-2 "Combining optoacoustic imaging phenotypes and multi-omics to advance diabetes healthcare" <u>OPTOMICS</u>
- H2020-SC1-BHC-2018-2020 "Molecular Mechanisms Associating Chronic Pain with Fatigue, Affective Disorders, Cardiovascular Disease and Total Comorbidity" <u>PAINFACT</u>
- H2020- SC1-PHECORONAVIRUS-2020: "Three Rapid Diagnostic tests (Point-of-Care) for COVID-19 Coronavirus, improving epidemic preparedness, public health and socio-economic benefit" CORONADX
- H2020-MSCA-ITN-2017 "European Liquid Biopsy Academy" ELBA
- Medtech4Health "Ultrasensitive detection of fusion oncogenes in liquid biopsies of pediatric cancer"
- Vinnova Challenge-driven innovation "Ultra sensitive analyses for improved health and forensics" <u>ULTRA-UDI</u>
- SWElife <u>"Ultra-sensitive test for Epstein-Barr virus to monitor patients after organ transplantation to prevent</u> rejection"
- H2020-NMBP-2016-2017 (H2020-NMBP-X-KET-2017) "Point-of-Care implementation of TB testing with ultrafast Local Heating PCR" <u>PITBUL</u>
- H2020-SC1-HCO-02-2016. "Standardisation of pre-analytical and analytical procedures for in vitro diagnostics in personalised medicine" <u>SPIDIA4P</u>
- H2020-EU.2.1.1. "Next generation sepsis diagnosis" <u>SMARTDIAGNOS</u>
- IMI call 11 "Blood-based biomarker assays for personalised tumour therapy: value of latest circulating biomarkers". <u>CANCER-ID</u>.
- ERASysAPP call 1 "Systems Biology of acidophile biofilms for efficient metal extraction" SysMeTex.
- EU Framework VII FP7-HEALTH Specific Programme "Cooperation": Health "Heart OMics in AGEing"
  <u>HOMAGE</u>
- EU Marie Curie Initial Training Networks FP7-PEOPLE-2012-ITN: EpiTrain.
- EU Framework VII FP7-HEALTH-2012-INNOVATION-1: <u>www.homage-hf.eu</u>
- EU Framework VII HEALTH.2011.2.2.2: "European ResearcH on devElopmentAL, BirTH and Genetic Determinants of Ageing". <u>EurHealthAging</u>

- EU Marie Curie Initial Training Networks FP7-PEOPLE-ITN-2008: "Innovative Techniques and Models to Study Glia-Neuron Interactions". <u>EduGlia</u>
- EU Framework VII Health-2007-1.2-5: "Standardisation and improvement of generic pre-analytical tools and procedures for in vitro diagnostics". <u>SPIDIA</u>
- EU Framework VII FP7-2007-ICT-1-216031: "Coeliac Disease Management Monitoring and Diagnosis using Biosensors and an Integrated Chip System". <u>CD-MEDICS</u>
- EU Framework VII FP7-2007-ICT-2: "Laboratory Skin Patches and SmartCards based on foils and compatible with a smartphone". LABONFOIL
- EU Framework VI LSHE-CT-2006-037957: "Fully automated and integrated Microfluidic Platform for Realtime Molecular Diagnosis of Methicillin-resistant Staphylococcus Aureus". <u>MagRSA</u>
- EU Framework VI LSHB-CT-2006-037575: "Comet assay and cell array for fast and efficient genotoxicity testing. <u>COMICS</u>
- EU Framework VI FP6-2004-IST-NMP-2: "Smart Integrated Biodiagnostic Systems for Healthcare". <u>SmartHEALTH</u>
- EU Biomed II grant to develop PNA based biosensors. The grant contributed to the development of the LightUp probes behind LightUp Technologies.
- 2004 -2014 Vinnova grant of 20 million Euro for Biomedical research in Western Sweden. Together with Arthur D. Little we gathered decision makers in western Sweden, had them to agree on a vision how to develop biomedical research in the region, and wrote the application on behalf of Business Region Gothenburg.

## Laboratories setup

Set up the biotechnology laboratory at Chalmers University in 1991around which the department of Molecular Biotechnology eventually was founded. Headed the laboratory between 1991 and 2003 and recruited several of the staff members and young researchers

Since 2001 Member of the Unesco scientific advisory board overseeing and coordinating the Biotechnology Research Center in Tripoli, Libya. Responsibility included planning and executing research strategy, purchasing and installing equipment, interviewing and selecting students and young researchers, arranging training for the researchers, and evaluating proposals. Today my role is less active, but I am still member of the Scientific Advisory Board of the institute and we have annual meetings planning strategy and helping setting up international collaborations.

Recruited in 2007 as one out of five founding group leaders to set up the Biotechnology Research Institute of the Czech Academy of Sciences (<u>www.ibt.cas.cz/en</u>). This was the first institute setup in Czech Republic in over 40 years. Responsibilities include heading a laboratory and recruiting students, postdocs and young researchers, developing research strategy for the laboratory, setting up support and collaborative agreements with industry, applying for grants, and equipping the laboratory. I still hold a part-time position at the institute.

Founded in 2001 the TATAA Biocenters with laboratories in Gothenburg, Sweden, and in Prague, Czech Republic. Recruited the Scientific Advisory Board, all personnel, set up research program and industrial collaboration, and equipped the laboratory. Under Kubista's leadership TATAA became the best equipped laboratory in Europe for qPCR and dPCR molecular analysis and was in 2021 listed as one of <u>Sweden's Technology Fast 50 companies by Deloitte</u>.

## **Faculty opponent**

PhD thesis evaluator/opponent in Norway, United Kingdom, Australia and Spain.