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CV

Michael Molls was born on December 15, 1944, and grew up in the Black Forest (Schwarzwald), Germany, with one sister and two brothers. His father was a general practitioner serving the workforce of a small town with industries as well as the rural population. Due to the Second World War, his mother did not finish her studies in medicine. She took care of the family and supported the work in the medical practice.

In 1970, Michael Molls married Dipl. Ing. Jasmina Hadzibascausevic, who is an architect. Jasmina was born in Sarajevo and grew up in Zagreb. They have two children and three granddaughters.

1963 - 1964

University entrance diploma (Abitur) and military service

1965 - 1974

Michael Molls studied medicine at the University of Freiburg, Germany. After registration as a medical doctor (approbation) he worked for nearly two years for the Federal Labor Office of Germany, practicing occupational medicine in the former Yugoslavia and in Istanbul, Turkey.

1974 - 1976

Michael Molls was resident at the Institute of Pharmacology of the University of Freiburg. The subject of his experimental M.D. thesis was "Protracted anaphylactic shock of guinea pigs and pharmacological interventions."

1976 - 1992

As postdoctoral researcher, Michael Molls headed a laboratory at the Institute of Radiation Biology and Physics of the University Hospital Essen, Germany. In 1977, he was successful in establishing the *in vitro* cultivation of mouse preimplantation embryos (stem cells). In initial studies, early embryonic development was compared under *in vitro* and *in vivo* conditions. Extensive radiation and cell biology experiments were performed under *in vitro* conditions. The embryos were exposed to X-rays, neutrons, and tritium (tritiated water, tritiated thymidine) as well as to combinations of radiation with pollutants (e.g., lead, cadmium) or cytostatic drugs (cyclophosphamide, cis-platinum). In summary, the investigations enabled important findings concerning early embryonic development, cytogenetic damage, altered cell proliferation, mechanisms of cell death, and cellular repair. Teratogenic effects were studied after *in vitro* irradiation of two cell embryos in the G2 phase of the cell cycle. Microsurgical implantation of the irradiated embryos into the uteruses of mice surrogate mothers made it possible to observe further development up to the time of delivery.

Michael Molls also specialized in radiation oncology at the Clinic for Radiation Treatment at the University Hospital Essen. Key areas of his clinical research were the inflammatory pulmonary side-effects of total body irradiation before bone marrow transplantation in leukemia patients, the combination of radiation treatment with hyperthermia, and the pathophysiology of tumors, especially tumor oxygenation in head and neck cancers, and blood perfusion in rectal and other malignancies (dynamic CT and MRI correlated with temperature gradients under hyperthermic treatment). These investigations in patients contributed to improved and less harmful techniques for total body irradiation, as well as deeper insights into tumor temperature distributions in clinical hyperthermia treatments and the biological heterogeneity of malignant tumors. It was found that there exist different patterns of blood perfusion and oxygenation within subregions of a single tumor and between individual tumors of patients suffering from the same tumor disease.

The experimental and clinical research of Michael Molls led to professorial teaching qualifications, initially in embryology and radiation biology, and later on in radiation oncology (habilitation, *venia legendi*).

1992 - 2014

From 1992 to 2014, Michael Molls was Professor and Director of the Clinic for Radiotherapy and Radiation Oncology at the Rechts der Isar Hospital of the Technical University of Munich (TUM). His clinic was committed to the curative or palliative care of cancer patients, to basic as well as clinical research, and to teaching. The Molls group comprised more than 20 physicians, one psycho-oncologist, about 20 physicists and biologists, doctoral students, technicians, nurses, and colleagues responsible for organization and administration.

Michael Molls served as a member of the Board of Management and the Supervisory Board at the Rechts der Isar University Hospital (TUM), and as head of the Munich Tumor Center of both Ludwig-Maximilians-University (LMU) and TUM. His particular interest was to ensure the highest quality in the oncology health care structures in the region of Munich and Upper Bavaria (doctors' practices, institutes, hospitals, etc.) as well as in the processes and results of interdisciplinary oncology (surgery, radiation oncology, medical oncology).

Michael Molls was President of the German Society of Radiation Oncology and head of its academy. He established a curriculum for specialization in radiation treatment according to European standards. In cooperation with the German Cancer Society, he introduced interdisciplinary guidelines for the treatment of cancer patients.

Concerning research related to cancer treatment, the Molls group evaluated imaging techniques under the aspect of personalized therapy planning in high-precision radiotherapy (image guidance, stereotactic and intensity-modulated radiotherapy). The group earned a high international reputation by publishing very early on stereotactic radiation treatment based on biological imaging with PET, CT, and MRI in patients suffering from brain tumors (glioblastomas), primary lung carcinomas, or liver metastases. Molls and colleagues were the first in Europe to show, in a larger group of patients with early stages of lung cancers (using PET, CT staging, and

histology), that a few high single doses of stereotactic radiotherapy resulted in long-lasting tumor control.

A further field of scientific interest was the post-radiotherapy quality of life with breast and prostate cancer. The results of these investigations were published in the most highly ranked international journals of radiation oncology.

The group also initiated multicentric therapy studies funded by the German Research Foundation (DFG) and the German Federal Ministry for Education and Research (BMBF). Unfortunately, these trials could not be completed as initially planned.

The tumor pathophysiology studies in patients that had started in Essen (see above) were continued in Munich. In summary, the Molls group's research on tumor blood perfusion and tumor hypoxia delivered data on intra- and interindividual biological tumor heterogeneity and on alterations of tumor oxygenation status under radiochemotherapy. It was important to generate this new clinical knowledge because oxygen concentration and blood perfusion significantly impact the sensitivity of malignant tumors to radiation and treatments with cytostatic – as well as immunological – medications. In this sense Molls and coworkers contributed to paving the way for the improvement of clinical cancer treatments. In one pioneering publication, the group was able to show that hypoxia imaging with PET enables individualization of radiotherapy in patients with head and neck cancers by “dose painting.” Dose painting means directing an extra high radiation dose to radioresistant hypoxic tumor subvolumes by means of intensity-modulated radiotherapy (IMRT).

As co-spokesperson, Michael Molls has been responsible for the biomedical research area of the Munich Center for Advanced Photonics (MAP), a Cluster of Excellence of the German Research Foundation. In its biomedical research, the MAP Cluster pursued the strategic concept that laser physics has the potential to reduce cancer mortality significantly. The idea was to apply sensitive screening methods and laser-generated phase-coherent X-rays for detection and imaging of early non-metastasized tumors and to eradicate the tumors by localized laser-based radiation treatment with protons or heavy ions.

In a first proof-of-principle experiment, the group was able to irradiate a monolayer of cancer cells with laser-generated protons. Laser-generated protons are pulsed and have an extremely high dose rate. The Molls group built on this basis to compare pulsed nanosecond proton irradiation with 150-millisecond continuous proton irradiation (a difference of eight orders of magnitude) by investigating chromosomal aberrations and double-strand DNA breaks. Measuring these types of cellular damage, which lead to cell death, the researchers found no significant differences in relative biological effectiveness.

The MAP Cluster also built the framework for the Center for Advanced Laser Applications (CALA) at LMU and TUM. Ferenc Krausz of LMU and Michael Molls of TUM jointly initiated the CALA project. Funding for the 63 million-euro project was recommended by the German Council of Science and Humanities (WR).

A further project of the Molls group was the initiation of the European radiobiology research network CARDIORISK, which investigated effects of low and moderate

radiation doses in the hearts of mice (EU-funded). One major conclusion of the experimental observations was that low-dose radiation exposure and related minor changes (clinically not significant) are likely to be permissive for the development of a cardiovascular disease, e.g., a reduced heart ejection fraction after application of cardiotoxic cytostatic drugs. Thus low-dose radiation can potentially reduce the capacity of the heart to recover from adverse events.

In summary, the scientific ideas and commitments of Michael Molls have stimulated and contributed to the more extensive integration of biological and physical research into the field of radiation oncology.

Scientifically, the Molls group has collaborated with international colleagues from the MD Anderson Cancer Center Houston of the University of Texas, the Department of Oncology (Radiation Oncology) of the University Hospital Aarhus, Denmark, the Department of Radiotherapy of the Medical University of Vienna, Austria, the Croatian Academy of Sciences and Arts (Zagreb), the Department of Radiation Oncology, University of Florence, Italy, the Department of Radiation Oncology of the Japanese National Cancer Center, Tokyo, and other institutions. International guests working in the Molls laboratories and clinic have come from Japan, Malaysia, India, Iran, Egypt, Russia, Serbia, Croatia and Italy.

Michael Molls has served on numerous scientific, national, and international commissions: German Council of Science and Humanities (WR); Scientific Program Committee of the International Congress of Radiation Oncology in Beijing (1997); Peer Review College of the Danish Council for Strategic Research; Advisory Board for the Extreme Light Infrastructure Beamlines (ELI) Facility Prague, Czech Republic (a pan-European project); Advisory Council for the Oscar Lambret Comprehensive Cancer Center in Lille, France; and others. He was an elected member of the Review Board on Medicine of the German Research Foundation (DFG) for the areas of Radiation Oncology and Radiation Biology as well as Medical Technology. He also chaired or was member of many academic review committees in medicine, physics, and engineering.

Michael Molls has served as a reviewer for a number of highly ranked scientific journals in the fields of radiation oncology, radiation biology, and medical physics, and as a member of the editorial boards of several national and international journals. He is the author or co-author of about 500 reviewed publications and an editor of textbooks, monographs, and book series (MEDICAL RADIOLOGY – Diagnostic Imaging and Radiation Oncology, Springer).

Michael Molls has supervised 14 professorial teaching qualification processes (habilitations). Eight of his colleagues (female and male) have achieved appointments as professors and clinical directors in Germany and internationally, two have achieved professorships and leading positions in the field of radiation biology.

2014 - 2021

After retirement, Michael Molls became a member of the International Scientific Advisory Board of the German National Center for Tumor Diseases. In 2016, he was elected as the chairperson of the TUM Senior Excellence Faculty, with a seat on the TUM Extended Board of Management and the Board of TUM: Junge Akademie. Since 2020, he serves as Director of the TUM Institute for Advanced Study, and since

2021 he is a board member of the International Graduate School of Science and Engineering (IGSSE) at TUM.

In recent years, the scientific interests of Michael Molls shifted toward the topic of sustainability. His related activities are manifold, including the organization of symposia and book editions (e.g., *Sustainable Risk Management*, 2018, Springer; *Strategies for a Sustainable Interaction with the Earth System*, 2021, Springer; and *Science, Rationality & Sustainability - Food for thought for the time after Corona*, TUM University Press 2021; *Circular Economy*, TUM University Press 2022).

Awards

Hans Langendorff Award (1979); Member of the German National Academy of Sciences “Leopoldina” (1998); President of the Joint Annual Congress of the German and Austrian Societies of Radiation Oncology and the German Society of Medical Physics (2000); Honorary Award of the Munich Tumor Center (2007); Chairman of the Alfred Breit Award Committee (since 2013); honorary member of both the Austrian and the German Societies of Radiation Oncology (2004, 2014); TUM Emeritus of Excellence (2013); Paul Harris Fellow of Rotary International (2017); Doctor Honoris Causa of the Cyprus University of Technology (2019); Dr. h.c. of the Dimitrie Cantemir Christian University Bukarest (2021); Member of the European Academy of Sciences and Arts (2021).

(Michael Molls, January, 2023)