Achievements and beyond: Scientific trajectory of Professor Mohammad A. Rafi

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Summary

This biography highlights the scientific trajectory of Professor Mohammad A. Rafi, Ph.D., who, in particular, has greatly advanced the field of neurodegenerative disorders during his long and successful tenure at Jefferson Medical College, Thomas Jefferson University. This Editorial recognizes, above all, Professor Rafi’s significant contributions to the study of lysosomal storage disorders as they relate to Krabbe Disease.

Authors’ Biosketch

Abass Alavi, MD is a distinguished professor in the Department of Radiology at the Hospital of the University of Pennsylvania (Philadelphia). Professor Alavi is internationally known for his exceptional achievements in the field of PET as well as the structural imaging with MR and CT, including groundbreaking studies in cardiovascular diseases, neurologic disorders, and inflammation. He was awarded two honorary degrees from the European universities in 2016. Professor Alavi has been listed among the top 1% scientists of the world.

Yadollah Omidi, Pharm.D., and Ph.D. is a Professor of Pharmaceutical Sciences at Nova Southeastern University College of Pharmacy, working on the development of advanced multifunctional nanobiosystems used for drug delivery and targeting, biosensing and tissue engineering. Having work experience in Cardiff University, TUOMS Faculty of Pharmacy, and the University of Pennsylvania, Professor Omidi is the recipient of several awards and has published over 250 papers and 20 book chapters. He has been listed among the top 2% scientists of the globe.

Professor Mohammad A. Rafi (Persian: محمد رفیع), Ph.D. in Neurology, from the Department of Neurology, Thomas Jefferson University (TJU), who has been serving BioImpacts journal as the Editor for almost a decade, revealed his retirement decision in September 2020. We learned that he was also nominated for the lifetime position of “Emeritus Professor of Neurology” at TJU. In honor of Professor Rafi’s retirement, we briefly review his prolific scientific journey in the field of Lysosomal Storage Disorders (LSDs), and in particular his role in unraveling Krabbe Disease (KD).

When we look back at our lives, we literally picture the main dimensions disappear within the fog and specks of dust collected over the years, simply forgetting ourselves, and maybe lost in memories! We see past the path and look instead to the nested memories of scattered occasions. Many memories of our lives are important because they relate to our abilities and accomplishments over the years. However, the remembrance of good and bad memories makes us decide what actions to take next. While aging slows down this potential, our experience helps us to see changes often go unnoticed, and problem-solving skills, planning, and abstract and critical thinking become challenging. Once there, we coalesce many memories by looking at our achievements and positively seeing further aspirations. These opening words were written to illustrate this path for every one of us studying scientific matters and to pave the way for younger successors.

Young Mohammad started his path through higher education at the University of Tabriz (Tabriz, Iran), where he received his first M.Sc. degree in Animal Biology. Having been awarded a scholarship from the International Center for Advanced Mediterranean Agronomic Studies, he then traveled to Montpellier, France to be trained in Environmental Science. While in Montpellier, he enrolled in a second M.Sc. degree program in Pathology and Parasitology at the University of Montpellier, School of Sciences and Technology. This led to his Ph.D. (Docteur-Ingénieur) in Animal Biology (Pathology and Parasitology).

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in 1970, earned “with first-class honors” (avec mention très honorable) as a result of his outstanding research accomplishments.

Professor Rafi was then recruited in 1971 by the University of Tabriz, Department of Animal Biology, as a faculty member, and remained a faculty member there until 1987. While at the University of Tabriz, he established the Cytology and Cell Biology Laboratory, with tissue culture facilities, as well as students’ hands-on microscopic sections. Professor Rafi taught Cell and Molecular Biology, Histology, and Human Genetics for several years and was selected as an Outstanding Professor by students in two different school years. He served as the Chair of the Department of Animal Biology for about 10 years and was also the Head of the Educational Science School of the University, offering evening classes and lectures.

At the University of Tabriz, Professor Rafi had the opportunity to take two sabbatical leaves, each for one academic year. He spent his first sabbatical leave, in 1974-75, at the University of Paris-Sud, Orsay, France. During this time, he studied the interaction of prolactin and thyroxin on the development of the thyroid gland in *Xenopus laevis*, which resulted in an innovative method of organotypic culture of the thyroid gland of this amphibian. He also earned his third M.Sc. degree in the field of Experimental Biology, allowing him to gain an in-depth vision of Cell and Molecular Biology. He spent his second sabbatical leave, in 1986-87, at the Department of Nutrition, University of California-Davis, USA. During this time, he studied Teratogenic Effects on Fetal Renal Morphology in Malnourished and Benomyl-Exposed Rats. All of this education and scholarship has enabled him to be a well-trained scientist with a multi-disciplinary perspective.

Overall, Professor Rafi has spent over 50 years (1970-2020) of his life on academic activities, of which he has spent over 33 years (1987-2020) at TJU. In 1987, he joined Professor David Wenger’s research group at Jefferson Medical College, Department of Medicine, Division of Medical Genetics, at TJU. There, he was able to pursue his dream research on inherited brain diseases and their molecular and biochemical bases. Given that the research was related to leukodystrophies and myelination, Professor Rafi, along with Professor Wenger, moved to the Department of Neurology in 1998.

While working on several LSDs (including research related to Sphingolipid Activator Protein, Metachromatic Leukodystrophy, GM1-gangliosidosis, and Niemann-Pick diseases), Professor Rafi focused primarily on Globoid cell Leukodystrophy (GLD), or KD, and treatment trials in the Twi mouse, the murine model of this disease. He concentrated mostly on a gene therapy approach, alone or in combination with other treatment strategies, testing the effectiveness of many viral vectors, such as lentiviral vectors and different serotypes of adeno-associated viral (AAV) vectors, alone or in combination with other treatment methodologies, such as neuro-stem cell transplantation and bone marrow transplantation (BMT).

The following highlights show his research outcomes:

- In 1993, in collaboration with outstanding colleagues, he succeeded in the cloning and expression of cDNA encoding human galactocerebrosidase (GALC), the enzyme deficient in GLD. This achievement led the way for potential treatment strategies for KD patients.
- In 1994, the chromosomal location of the GALC gene was determined (14q31). Such a finding, and the finding of the complete cDNA sequence and gene organization, allowed the laboratory and other laboratories around the world to engage in mutation analysis of human patients and to study polymorphic changes.
- In 1995, he published the structure and organization of the human GALC gene. Then, in 1996 and 1997, he managed to clone and sequenced the GALC cDNA in the rhesus monkey model and the canine model of KD.
- In 2012, he brought to the lab the idea of gene therapy using mouse tail vein injection from the meeting of the American Society of Gene and Cell Therapy (ASGCT), and Professor Wenger, who had attended another meeting in Paris, brought to the lab the idea of using the AAVrh10 serotype, which was newly developed at that time, instead of other serotypes. The successful outcome of each of these ideas was a turning point in the research on the treatment of the Twi mice.
- In 2015, the combination of gene therapy using AAVrh10 expressing GALC cDNA following bone marrow transplantation resulted in unprecedented outcomes in the treatment of the Twi mice. This combinational method of treatment is currently under investigation by the National Institutes of Health (NIH) for a human trial.
- In 2020, he demonstrated the importance of viral dose in combinational therapy.

As for publications and presentations, his research accomplishments have resulted in over 80 peer-reviewed articles and book chapters as an author and co-author. He was invited to present talks in multiple national and international meetings and academic institutions and has presented over 50 abstracts and poster presentations. He has a total citation number of 3378 in the Science Citation Index. The total h-index of the publications, at this time, is 36 (21 since 2015).

Along with most other colleagues in the research community, he has served as a reviewer of many journal articles and research proposals. He is also part of the...
editorial board of several scientific journals, such as *Avicenna Journal of Medical Biotechnology* (http://www.ajmb.org/En/Default.aspx). Currently, he is actively involved in the editorial board of *BioImpacts* (http://bi.tbzmed.ac.ir/) and has been since 2011. After having contributed several editorials, research, and review articles, the journal’s impact factor has reached 3.475 in the latest Clarivate analysis (2019).

He is currently a grant reviewer for the European Leukodystrophy Association (ELA), American Institute of Biological Sciences (AIBS), Scientific Peer Advisory and Review Services (SPARS), New York State Department of Health, and the Empire State Stem Cell (NYSTEM).

While at Jefferson, Professor Rafi served as the founding member of different scientific associations, including the Iranian Academic Association (IAA), the Middle East Genetic Association (MEGA), and the Iranian Biomedical Society (IBS). He also chaired several meetings and review panels of these associations. Alongside these activities, he was an active member of the American Society of Human Genetics (ASHG) and the American Society of Gene and Cell Therapy (ASGCT).

Professor Rafi has been awarded the Outstanding Student Travel Award of Tour de France, University of Tabriz, Iran (1966); the scholarship award from the International Institute for Mediterranean Studies, Montpellier, France (1967-68); and the scholarship award for graduate study, French Government, France (1968-70). He has earned the designation of Honorary Professor of Tabriz University of Medical Science (TUOMS), Iran; Honorary Member of Research Center for Pharmaceutical Nanotechnology (RCPN) at TUOMS; and Adjunct Professorship of the Aging Institute of TUOMS. While over 95% of his curriculum at TJU was research-related activities, Professor Rafi also taught in the Summer Science Programs offered by the Department of General Studies at TJU. He enjoyed the training and supervising graduate and M.D. and Ph.D. students who chose to join the laboratory for their rotations or thesis programs.

On this occasion of Professor Rafi’s retirement, we wanted to highlight his fruitful scientific journey by detailing his work and emphasizing that his voyage has transcended routine research towards not only the philosophy of science, but also the philosophy of life. So long as his scientific journey continues, Professor Rafi’s work, as a senior editor of *BioImpacts*, is deeply appreciated.

**Competing interests**

The authors of this editorial are the current Editors of the journal. This biography is written in appreciation of Prof. M.A. Rafi for his contribution to neurology, in particular LSDs, over the three last decades.

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