Conferment of the Degree of Doctor of Science, honoris causa A Citation

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Professor Ferid Murad MD, PhD, Nobel Laureate in Physiology or Medicine

As is well known, it was the nineteenth-century Swedish scientist Alfred Nobel who invented dynamite and who bequeathed the fund for the annual Nobel Prizes. What may be less well known is that the chief active ingredient of dynamite, nitroglycerin, has also been used for over a hundred years in the treatment of angina pain. When Nobel himself was taken ill with heart disease, he found it "ironic" that his doctor prescribed nitroglycerin. It is doubly ironic, in fact, because it was a recent Nobel Prize laureate for Medicine who first discovered the reason why nitroglycerin is effective in the relief of angina pain. The researcher was Professor Ferid Murad, and the discovery was the action of nitric oxide, which relaxes smooth muscle cells.

The discovery of the action of "nitric oxide as a signalling molecule in the cardiovascular system", which Professor Murad shared with two other scientists, has been both surprising and profound in its implications. It is surprising partly because nitric oxide is totally different from any other known signal molecule and partly because it is such a simple and common compound, which is formed whenever nitrogen burns, as in a motor car engine, for example. The discovery is extremely important because it has implications in so many areas of medicine, such as the treatment of heart disease, bacterial infections, high blood pressure in the lungs of infants, cancer and, last but by no means least, erectile dysfunction in men.

At first glance Professor Murad's background does not seem very promising soil to produce a Nobel Prize winner. His father came from a family of shepherds in Albania and had less than a year's formal schooling, though he could speak seven languages. He emigrated to the United States in 1913, where he met his wife, who had only primary school education. Professor Murad believes that the childhood poverty and minimal education of his parents had a beneficial influence on him and his brothers, one of whom became a dentist, the other a professor of anthropology.

Another powerful influence on Professor Murad was his parents' restaurant business in Whiting, Indiana. From an early age he worked in the restaurant beside his parents, who worked 16 to 18 hours a day. His mother cared for the tenants of the building, many of whom were old, preparing their meals when they were sick. From her Professor Murad learned compassion, and this influenced his choice of medicine as a career. From his father he learned about business and systematic analysis, and these too seemed to have played a part in Professor Murad's career, in which research project management and fund-raising have been so important.

Professor Murad's career goals were firm early in life. He wrote an essay in the eighth grade putting down as his first three choices, physician, teacher and pharmacist. "Today I do just that," he says, "as I am a board certified physician and internist doing both basic and clinical research with considerable teaching in medicine, pharmacology and clinical pharmacology." After completing high school he became the first member of his extended family to enter college when

he won a scholarship to DePauw University, a small liberal arts university in Indiana. Here he became a premed major, and when he graduated in 1958 he applied to an innovative MD-PhD programme at Western Reserve University in Cleveland, Ohio. After an interview by the whole Pharmacology Department, he was awarded full tuition and a stipend of \$2000 per year.

Entering the new programme at Western Reserve set Professor Murad on the course that would lead to his ground-breaking research of the 1970s. Under the mentorship of Earl Sutherland Jr and Theodore Rall he was set to work on the role of the cyclic AMP molecule as a cell messenger. "This work," he says, "subsequently influenced my desire to work with cyclic GMP as described in my Nobel lecture." This was an exciting time to be participating in a new and rapidly growing area of biology, and it was here that he came to love the life of research. His mentors were visionary in drawing together researchers of many disciplines in a way that produced new data. At the same time, Professor Murad undertook Western Reserve's experimental integrated organ-system approach to medical education. He found that, because of his simultaneous PhD work, he approached every aspect of his medical training with a sense of genuine inquiry because he realised that every piece of knowledge could have research significance.

Meanwhile Professor Murad had married Carol and had started a family. To make ends meet he had to moonlight at the Cleveland Clinic, working one or two nights a week in the Obstetrics and Gynaecology service, assisting at deliveries and Caesarian sections and scrubbing tables and floors after each delivery. For the 12 hours' work from 7 pm to 7 am he earned \$20 per night. Then he would often have a full day of classes the next day. He was absent from his family as often as 4 or 5 nights a week, though he tried to have dinner at home as frequently as possible. That the children have turned out well in spite of his absence, he says, is a tribute to the mothering of Carol.

In 1965-67 he did his internship and residency in medicine at Massachusetts General Hospital, where he met some of the world's leading medical scientists, teachers and clinicians. He missed research, however, and soon took up an appointment as a clinical associate at NIH in the Heart Institute, where he worked for three years. In 1970 he was recruited by the University of Virginia to develop a new Clinical Pharmacology Division in the Department of Medicine. Here he began his important work on cyclic GMP as a possible new "second messenger" to mediate hormone effects. The experiments that won him the Nobel Prize were done at Virginia. In 1971 he became Director of the Clinical Research Center there; in 1973 Director of Clinical Pharmacology and in 1975 he became one of the youngest full professors at the University. He remained at Virginia until 1980. As he looks back on these highly productive years in which he built up a research programme with clinical and basic medical studies, he sees the 82 students and fellows he worked with and trained as among his greatest achievements. Of these some 20 are now professors, chairmen, research directors and division chiefs around the world. "There is no question," he says, "that one of my greatest accomplishments is to have participated in the training of such successful scientists in my own laboratory and also influenced the careers of many talented medical students, graduate students and house staff."

In 1981 Professor Murad took up a position at Stanford as Chief of Medicine of the Palo Alto Veterans Hospital. Here he was able to continue the work he was doing at Virginia and at the same time to recruit many young faculty and students from all over the world. After some productive years at Stanford he became Vice President of Abbott Laboratories, where he supervised drug discovery and development on a large scale and with access to a very large research budget. Under his management about 24 new compounds were brought forward for clinical trials. Meanwhile he continued his own work on nitric oxide and cyclic GMP. When he left Abbott he had a huge managerial load that included the supervision of 1500 scientists.

After a brief period as President and CEO of a new biotech company, Professor Murad returned to academia in 1997, to his present position at the University of Texas-Houston, where he is the first chairman of a newly combined basic science department, Integrative Biology, Pharmacology and Physiology. Professor Murad is happy, he says, back in his laboratory in the University, where his love of research began, with the freedom and the intellectual environment of academic medicine – and with bright young students and fellows a "daily joy" to him.

Among the distinguished positions Professor Murad currently holds at the University of Texas-Houston Medical School are those of Director, Institute of Molecular Medicine for the Prevention of Human Diseases, the John S Dunn Sr Distinguished Chair in Physiology and Medicine and Director of Clinical Pharmacology, Department of Internal Medicine. He is Professor (Adjunct), Department of Pharmacology, Northwestern University School of Medicine. He is also the Honorary Director of the Epithelial Cell Biology Research Centre of The Chinese University of Hong Kong in collaboration with the Chinese Academy of Military Medical Sciences.

Apart from the Nobel Prize, Professor Murad has won the Baxter Award for Distinguished Research in Biomedical Sciences (2000), the "Honour of the Nation" Award, Albania (1999), the Albert Lasker Award for Basic Medical Research (1996) and the Ciba Award, American Heart Association (1988).

Professor Murad is a truly distinguished man of science, and it is my privilege to present him to you, Mr Chairman, for the award of the degree of Doctor of Science, *honoris causa*.

This citation is written by Professor David Parker

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