In Memoriam

Kappiareth Gopal Nair
1931–2010

Dr Kappiareth Gopal Nair, who died in India on March 12, 2010 at the age of 78, was a gifted scholar who was at home in the research laboratory, at the bedside, and in the humanities. He was among the first to demonstrate that adult cardiac myocytes have little or no ability to proliferate and that sympathetic stimulation can modify gene transcription.

Dr Nair, who was known to his friends as “Raj,” was born in Kollengode, Kerala State, India, on July 2, 1931. He received his MBBS from the University of Bombay in 1953 and was subsequently awarded an MD degree by examination and thesis. After internship and residency in India, he came to Boston in 1956 for advanced training in Cardiology at the Massachusetts General Hospital and West Roxbury VA Hospital. He then became a graduate student in the Department of Physiology at the University of Chicago, and in 1962, received his PhD for work carried out in the laboratory of Murray Rabinowitz; his thesis described the isolation, purification, and several key properties of a cAMP phosphodiesterase from cardiac muscle.¹

Raj returned to India as Assistant Professor of Medicine at the Seth G. S. Medical College but was drawn back to basic research when, in 1963, he went to the National Institute of Medical Research, Mill Hill, London, as a Visiting Research Scientist with H. R. V. Arnstein. The following year, he rejoined the Rabinowitz laboratory in Chicago as an Assistant Professor of Medicine and Physiology. It was here that he carried out his major work on protein synthesis and myocardial cell growth.

In 1969, Raj moved to the University of Pennsylvania as Associate Professor of Medicine, and 2 years later, he returned to India, where he assumed the highly prestigious position of Professor–Director of Medicine and Head of the Department of Medicine at the King Edward Memorial Hospital in Mumbai (Bombay). He spent the remainder of his life in India, where he became one of the leaders in Indian Medicine and Cardiology.

Dr Nair’s first postdoctoral research project, carried out in London, was a description of the role of mRNA in regulating protein synthesis in a cell-free system.² The key finding, that high molecular weight reticulocyte mRNA stimulates amino acid incorporation, added to a growing body of evidence that mRNA, together with ribosomes, participates directly in peptide chain elongation. Raj continued this work after his return to the Rabinowitz laboratory, which was then studying protein synthesis in the heart. His first publications as a member of this group indicated that interactions between ribosomal aggregates and newly formed peptide chains stabilize polysomal structure.³–⁴ He also characterized the RNA synthesized by these polysomes.⁵

The first paper describing Dr Nair’s work on cardiac hypertrophy, which was published in Circulation Research in 1968, demonstrated that stimulation of RNA polymerase activity is one of the earliest molecular responses of the heart to pressure overload.⁶ He subsequently contributed to 2 landmark papers that represented the centerpiece of the work then in progress in the Rabinowitz laboratory. The first⁷ showed that although DNA concentration does not change significantly when the heart is overloaded, DNA content increased by more than 50% at a time that heart weight had also increased 50%. Overload was found to cause about a 10-fold increase in the mitotic index, which is the number of mitoses per 10 000 nuclei determined by “counting 25,000 or 50,000 total nuclei per heart in sections from left ventricular muscle of several hypertrophied and control hearts.” However, of the 86 mitotic figures seen in this study, only 1 could have been in a cardiac myocyte; all of the others were in connective tissue and endothelial cells. A greater number of polyploid myocytes was also found in the overloaded hearts, but the increased ploidy was estimated to account for no more than 1% of the increased DNA content. The companion paper⁸ counted the number of nuclei containing [³H]thymidine as a second method to determine whether overload caused the number of myocyte nuclei to

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increase; the frequencies of labeled nuclei were determined by “counting, in each heart, 100 labeled nuclei or 500 fields, whichever came first.” The conclusion of the first paper that the overload-induced increase in DNA content was attributable almost entirely to proliferation of connective tissue cells, was confirmed by the finding that muscle nuclei rarely contained [3H]thymidine, and that the hydroxyproline content of the hypertrophied hearts was approximately doubled. The authors’ conclusion, that “there is little or no division of cardiac muscle cells following a stimulus to cardiac growth,” is consistent with today’s consensus that adult mammalian cardiac myocytes rarely divide.

At the University of Pennsylvania, Raj observed that the overload-induced increase in RNA polymerase activity he had reported several years earlier is paralleled by an increase in adenyl cyclase activity,9 which led him to suggest that cAMP plays a crucial role in activating transcription in overloaded hearts. This hypothesis was a generation ahead of its time and is in accord with current understanding of the importance of sympathetic stimulation as a cause of maladaptive hypertrophy in failing hearts and that β-adrenergic receptor blockers improve prognosis in patients with heart failure by inhibiting the proliferative response that is responsible for progressive left ventricular dilatation (“remodeling”).

After returning to India in 1971, Raj published more than 150 articles on a variety of topics. These include reviews of calcium channel blockers, the pathogenesis and treatment of rheumatic fever, a possible role for taurine in cardiac disease, and the contributions of free radicals and homocysteine in the pathogenesis of cardiac damage and coronary artery disease. Toward the end of his life, Raj returned to molecular biology when, with his long-time colleague Tester F. Ashavaid, he published a series of reports on the role of gene mutations and polymorphisms in cardiovascular diseases.

Raj combined the analytic skills of a scientist with the art of a physician. Above all, he was a scholar. While a student, he earned many prizes, and he graduated from medical school with the highest aggregate marks in the University. In high school, he won a Latin Prize; this was evident when, in the early 1970s, he spent several hours in a long, detailed, and fascinating discussion of Greek and Roman culture with my wife, who is a classicist.

Raj and I crossed paths briefly in 1957, when I was a medical intern at the Massachusetts General Hospital, and we subsequently became close friends after I joined the Department of Medicine at the University of Chicago in 1967. Our children attended school together, and his wife, Sumati, taught my wife, who was then becoming a skilled Indian cook, some of the secrets of great Indian cuisine. I visited Raj and his family several times after his return to India, and in 1981, I had an opportunity to observe Raj practice the art of medicine at the King Edward Memorial Hospital. At that time, when technology was coming to dominate cardiology in the United States, most Indian cardiologists, including Raj, did not have access to the resources needed to take every patient to the cath laboratory. Instead, Raj and his colleagues were master clinicians who relied on their clinical skills to identify those patients whose problems required the use of high technology; this allowed them to reserve the limited diagnostic resources for those patients for whom the technological data would make the most difference. For the majority, the care that they provided depended on data obtained from the history, physical examination, and such simple tools as the ECG and chest x-ray.

Dr Nair, who is survived by his wife, his son, Rajeev, and his daughter, Sunita, balanced enthusiasm for basic research and academic medicine with a love for the culture of his native India. Successful as both a laboratory scientist and clinician, he was among the pioneers who helped form the link between molecular biology and cardiology. His death marks the loss of a unique individual whose personal warmth and powerful intellect will be missed by his many friends and admirers.

Arnold M. Katz
University of Connecticut School of Medicine
Farmington, Connecticut
Dartmouth Medical School
Hanover, New Hampshire
and
Harvard Medical School
Boston, Massachusetts
E-mail arnold.m.katz@dartmouth.edu

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Arnold M. Katz

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