

## Tribute

# John Denis McGarry, PhD

**D**enis McGarry died peacefully at his home in the presence of his family on the evening of 27 January 2002. The cause of death was a glioblastoma multiforme, diagnosed after the sudden appearance of expressive aphasia in late April 2001.

Denis was born in Widnes, England, in 1940. He did his undergraduate and graduate work at the University of Manchester, receiving his PhD in 1966. He did two years of postdoctoral fellowship at the University of Liverpool and the University College of Wales before joining the University of Texas Southwestern Medical Center in Dallas as a postdoctoral fellow in 1968. He was appointed assistant professor of internal medicine in 1969 and reached full professorship in internal medicine and biochemistry in 1977. He was named to the Clifton and Betsy Robinson Chair in Biomedical Research in 1996.

Denis was a gifted teacher who was regularly judged outstanding by medical students who attended his lectures on metabolism in the biochemistry course. He also taught in the graduate school and lectured internal medicine residents and endocrine fellows.

Research, however, was his passion. He had an uncanny knack of making discoveries that changed the way other scientists thought about metabolism. He defined the malonyl CoA regulatory system operating through carnitine palmitoyltransferase one (CPT1) and showed that the ketosis of starvation and the ketoacidosis of type 1 diabetes were the consequences of a glucagon-induced fall in malonyl CoA. A solution to the problem of ketogenesis had eluded such illustrious names as Krebs, Wieland, and Lehninger. Denis subsequently showed that the malonyl CoA/CPT1 system operated in heart, skeletal muscle, adipose tissue, sperm, and other tissues. Under his leadership the laboratory cloned and sequenced the involved genes and unequivocally proved that CPT1 of liver was distinct from CPT1 of muscle and that CPT1 and CPT2 were separate enzymes derived from different genes.

Denis devoted considerable energy to the mechanism by which glycogen was synthesized from glucose after a fast. In contrast to conventional wisdom, he showed that the indirect pathway (glucose→lactate→glucose-6-PO<sub>4</sub>→glycogen) was dominant over the direct pathway (glucose→glucose-6-PO<sub>4</sub>→glycogen).

In 1992, he published a famous paper in *Science* entitled "What if Minkowski Had Been Ageusic?" (1). In this paper he suggested that scientific concentration on abnormal glucose metabolism had masked the critical importance of abnormal fat metabolism, especially in type 2 diabetes. Subsequent to this paper there was a huge swing by

investigators toward the key role of abnormal lipid metabolism in insulin resistance and lipotoxic damage to tissues as diverse as the heart and the β-cell of the pancreas.

Denis received the American Diabetes Association's 2001 Banting Medal for Scientific Achievement for his research. In the recently published Banting Lecture 2001 (2), he emphasized studies on the role of dysregulated fatty acid metabolism in the diabetic state. Although Denis was unable to deliver the address (it was given beautifully by American Diabetes Association president Bob Sherwin), he felt blessed that he was able to be present and receive the medal.

In addition to the Banting Medal, Denis had previously received the Lilly Award, the Herman O. Mosenthal Award, the Joslin Medal, the David Rumbough Scientific Award, and the Grodsky Award.

A remarkable thing about Denis McGarry was the vast number of deep friendships he had in the world of diabetes and the scientific community. I thought these friends, and others who know him only from the literature, might like to share in comments made at his memorial service by one of his colleagues:

He was not just a premier scientist, he was a premier person. His essence was nowhere more visible than in the illness. He was brave. I never heard him ask, 'Why me?' I only saw a tear one time, and that was when he realized he would not be able to give the Banting Lecture. He was calm, even when as an eloquent man he could not complete a sentence. He was calm as death approached.

At the beginning of the 7th century, Isadore, Archbishop of Seville, gave his prescription for a good life. This is what he said: 'Learn as if you were to live forever. Live as if you would die tomorrow.'

Denis did. He learned all his life in science. When death came he was ready.

His colleagues here and elsewhere have established and funded the John Denis McGarry, PhD Chair in Diabetes and Metabolic Research in his honor. That will continue to remind us of this wonderful man.

DANIEL W. FOSTER, MD

## REFERENCES

1. McGarry JD: What if Minkowski had been ageusic? An alternative angle on diabetes. *Science* 258:766-770, 1992
2. McGarry JD: Banting Lecture 2001: Dysregulation of fatty acid metabolism in the etiology of type 2 diabetes. *Diabetes* 51:7-18, 2001

