Philip W. Majerus, MD: Bristol-Myers Squibb Award

Philip W. Majerus, MD, who first proposed that low-dose aspirin could be used to treat people at risk of heart attack, stroke, and other ailments associated with blood clots, has been awarded the Eighth Annual Bristol-Myers Squibb Award for Distinguished Achievement in Cardiovascular Metabolic Research. His proposal that low-dose aspirin could protect those at risk of clot formation is credited with saving thousands of lives a year.

But that is not his only achievement. Dr Majerus’ research into the role played by platelets in blood clotting and thrombosis is considered groundbreaking.

Dr Majerus, a professor of medicine and biochemistry and molecular biophysics at the Washington University School of Medicine in St Louis, Mo, received the acclaim of his colleagues at the time of the award. “Phil Majerus, more than any other individual, has produced the most original body of work on biochemistry of platelets as it relates to thrombosis,” said Joseph L. Goldstein, MD, professor of genetics at the University of Texas Southwestern Medical Center in Dallas. Dr Goldstein is a Nobel laureate.

“Philip Majerus made some of the earliest breakthroughs in preventive cardiovascular treatment and set the stage for many more,” said Hubert Pouleur, MD, vice president of cardiovascular research and development at Bristol-Myers Squibb. Dr Majerus received a $50 000 award and a silver medallion at a dinner in New York on May 13, 1998.

Dr Majerus’ work delineated the role of platelets in the clotting process. Until the results of his research became known, scientists thought that platelets merely formed the substance of blood clots. Dr Majerus proved that they precipitate the clotting process. He discovered receptors on the surfaces of platelets that are the site of action for the clot-promoting factors in blood. When the factors bind to the receptors, they accelerate 300 000-fold the activation of another clot-promoting substance, prothrombin. The activation of prothrombin results in rapid and specific blood clotting in the local area.

He is also credited with demonstrating the mechanism behind the clot-inhibiting effect of aspirin. He showed that low doses of aspirin modify cyclooxygenase, an enzyme that leads to the formation of thromboxane. Thromboxane is a platelet-made molecule that causes the constriction of blood vessels and aggregation of platelets.

More than that, Dr Majerus showed that aspirin changes platelets for their entire 2-week lifespan. His work with aspirin was persuasive in encouraging the use of medication in low doses to reduce all kinds of destructive blood-clotting events.

His work on clotting led to the description of a lipid called phosphatidylinositol, which consists of inositol with various numbers of phosphate molecules added or subtracted. The phosphates change in response to the extracellular signals. The changes in phosphate act as signals that are part of a variety of behaviors, from the aggregation of platelets in the blood to our ability to move our fingers together. Dr Majerus has cloned many of the genes involved in this inositol system. Other researchers are now trying to link these genes to various diseases. “Ultimately, I believe a very large number of human genes—as many as 500 to 1000—will turn out to be involved in the inositol system,” he said.

Some of the changes in phosphates result in Lowe’s syndrome, which causes mental retardation and eye and kidney disorders. Another gene from this system is inhibited by lithium, which could lead to a less toxic form of the chemical that could be used in the treatment of mental disorders.

Dr Majerus received his bachelor’s degree from Notre Dame University in 1958 and his medical degree from the Washington University School of Medicine in 1961. He performed his internship and residency at Massachusetts General Hospital and then was a research associate at what was then the National Heart Institute. He joined the Washington University Medical School faculty in 1966 and quickly achieved full professorships in medicine and biochemistry.

He has previously received the Dameshek Prize for Research from the American Society of Hematology, the Distinguished Career Award for Contributions to Hemostasis from the International Society for Thrombosis and Hemostasis, and the Robert J. and Claire Pasarow Foundation Award for Cardiovascular Research. He serves on the editorial advisory board of the journal *Biochemistry* as well as the editorial boards of the *Proceedings of the National Academy of Sciences of the United States of America* and the *Journal of Biological Chemistry*.

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