MICHAEL S. BROWN Biographical Sketch

Michael S. Brown was born in Brooklyn, New York in 1941. In 1962 he graduated from the College of the University of Pennsylvania and in 1966 from its School of Medicine. He then was a resident in internal medicine at the Massachusetts General Hospital in Boston, where he met Joseph L. Goldstein, a fellow resident. The two established the friendship and mutual respect that led to their long-term scientific collaboration.

Brown spent 1968–71 training in biochemistry at the National Institutes of Health. In 1971, he joined the Department of Internal Medicine at the University of Texas Southwestern Medical School in Dallas where he succeeded in purifying the enzyme HMG CoA Reductase, which participates in cholesterol biosynthesis. He and Goldstein collaborated to elucidate the biochemical and genetic mechanisms that regulate the level of this enzyme. In 1974, the two young scientists discovered that human cells possess on their surfaces a protein that they called the low-density lipoprotein (LDL) receptor. The receptor carries LDL into the cell by a process that they called receptor-mediated endocytosis. Within the cell LDL turns off HMG CoA reductase, stopping cholesterol synthesis. Subjects with familial hypercholesterolemia (one in 500 people) have defective LDL receptors and suffer early heart attacks

The work of Brown and Goldstein established the first cause of heart attacks that could be traced to the molecular level, providing a strong scientific foundation for the theory that cholesterol-carrying LDL particles are a major cause of heart attacks. Building on their work, scientists in the pharmaceutical industry developed drugs called statins that inhibit HMG CoA Reductase, increase the activity of LDL receptors, and lower LDL-cholesterol.

In the early 1980s, Brown, Goldstein and their colleagues purified the LDL receptor, isolated its gene, and traced the mutations to the molecular level. As a result, familial hypercholesterolemia is among the best understood of all human genetic diseases.

During the following decade, Brown and Goldstein turned their attention to the feedback process that regulates the genes for the LDL receptor and the enzymes of cholesterol synthesis. They discovered a family of proteins, designated sterol regulatory element binding proteins (SREBPs), that control these genes. The SREBPs also control the process by which the body converts sugars to fats and thus they are important in obesity and diabetes mellitus.

Throughout the 1970s, when their scientific work was most intensive, Brown and Goldstein continued to function as academic physicians, each performing clinical attending rounds on the

general medicine wards of Parkland Memorial Hospital.

Brown is married to the former Alice Lapin. They have two daughters, Elizabeth (born 1973) and Sara (born 1977).

Brown currently is Regental Professor at the University of Texas Southwestern Medical School where he holds the W.A. Moncrief Chair and directs the Jonsson Center for Molecular Genetics.

Brown has received honorary degrees from eight institutions. With Goldstein, he has shared 21 major awards, including, in 1985 the Nobel Prize in Medicine or Physiology, in 1988 the National Medal of Science, and in 2003 the Albany Medical Center Prize.