Lasker Awards for 2002

Synergy and symbiosis à la Matisse-Picasso

Advances in the sciences and the arts often result from synergistic interactions and symbiotic relationships between pairs of individuals. Perhaps the most remarkable example in the arts is the synergy and symbiosis that developed over a 50-year period between Henri Matisse and Pablo Picasso. No two twentieth-century artists influenced modern art more than Matisse and Picasso. In the early stages of their careers, their styles were vastly different. Matisse was the master of bold color and flat decorative patterns, painting realistic images that were calm and lovely. Picasso was the master of lines and angles, painting fragmented images that seethed with turbulence and emotion. Yet despite this innate difference in styles, they inspired and influenced each other's work for half a century.

The synergistic–symbiotic nature of the Matisse–Picasso relationship was explored in a recent exhibition at the Tate Modern in London with a side-by-side display of 130 works from 1906 to 1955. The Matisse-Picasso show (in Paris 25 September 2002 to 6 January 2003 and then in New York City 13 February to 19 May 2003) demonstrates how the two artists understood each other, borrowed from each other and tried to outdo each other. In the final analysis, their synergy and symbiosis produced a magnificence of 'matissean Picassos' and 'picassoesque Matisses' that largely defined modern art.

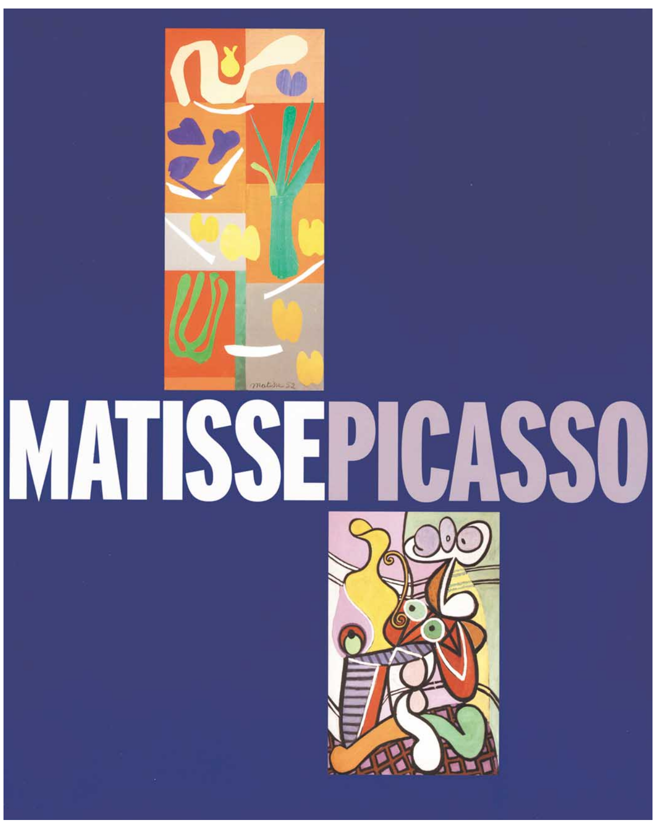

Fig. 1 Matisse-Picasso catalogue cover. Tate Modern summer exhibition, London 2002.

This year's Albert Lasker Awards in Medical Research honor two pairs of individuals, one in basic research and the other in clinical research, whose accomplishments illustrate the power of scientific synergy and symbiosis, echoing the artistic synergy and symbiosis of Matisse and Picasso.

The Lasker Award in Basic Medical Research is given each year in celebration of a fundamental discovery that opens up a new area of biomedical science. This year's recipients, James E. Rothman of Memorial Sloan-Kettering Cancer Center and Randy Schekman of the University of California at Berkeley, identified and characterized the universal molecular machinery that orchestrates the budding and fusion of membrane vesicles, a fundamental process essential to organelle formation and membrane trafficking in all eukaryotic cells.

In a eukaryotic cell, the ingestion of nutrients from the outside and the secretion of hormones, neurotransmitters and antibodies from the inside are mediated by an elaborate internal membrane system that involves lipid vesicles pinching off from one organelle and fusing with another organelle. This process of membrane trafficking was first visualized and conceptualized by George Palade in the early 1970s in his pioneering studies of the secretory pathway in the exocrine pancreas.

The research of Rothman and Schekman, beginning in the late 1970s, transformed the mystery of cellular membrane trafficking into molecular reality. In the beginning, Rothman developed an ingenious biochemical strategy to identify the protein machinery that mediates vesicular budding and fusion in mammalian cells, whereas Schekman pioneered a powerful genetic strategy in yeast cells. But after several years, each of them began to inspire and influence the other, establishing a Matisse–Picasso-like synergy and symbiosis that culminated in the discovery of SECs, COPs, NSF, SNAPs, v-SNAREs and t-SNAREs. The work of Rothman and Schekman is awesome in that they have essentially taken the membrane trafficking system apart and put it back together from its component molecules in a test tube.

The Lasker Clinical Medical Research Award is given each year in celebration of a scientific contribution that has had a profound influence on improving the clinical care of patients. This year's award honors the two individuals who developed renal hemodialysis, a technological advance that changed kidney failure from a fatal to a treatable disease. This accomplishment constitutes one of the monumental life-saving advances in the history of modern medicine, prolonging the useful lives of more than 1.5 million people in the last 35 years. The two recipients are Willem J. Kolff of the University of Utah School of Medicine and Belding H. Scribner of the University of Washington School of Medicine in Seattle.

The story begins in 1938 in the Netherlands when Kolff, a newly minted physician, was assigned care of a 22-year-old man in uremic coma caused by glomerulonephritis. Kolff watched helplessly for 4 days as the young man died. He had no treatment to offer—if only he could find a way to remove the toxic metabolites that accumulated in blood when the kidney failed. To make a long story short, after 7 years of working under the adverse circumstances of the Nazi-occupied Netherlands, Kolff miraculously succeeded, in 1945, in constructing the first artificial kidney. This machine, known as the 'rotating-drum hemodialyzer', consisted of 130 feet of cellophane tubing made from sausage casing, wrapped 30 times around a horizontal drum made of aluminum strips. Despite the primitive nature of this contraption, it unambiguously saved the lives of patients whose kidneys suddenly failed because of acute insults such as traumatic injuries. Such patients recover kidney function after being dialyzed only one or two times.

But what about the thousands of patients with chronic end-stage renal disease caused by diabetes or hypertension for whom prolongation of life requires repeated dialysis three times a week forever? In the late 1950s, conventional wisdom held that chronic intermittent dialysis would never be possible because of the formidable technical problem of vascular access: Every time a patient was hooked up to the artificial kidney, veins and arteries were damaged, and after six or seven treatments, physicians would run out of blood vessels to connect to the machine.

This is where Belding Scribner enters the story. Scribner, a physician, was influenced and inspired by Kolff's heroic accomplishments in developing the artificial kidney. In agonizing over the fate of one of his patients who was slowly dying of end-stage renal disease, Scribner figured out, in 1960, how to solve the problem of vascular access. The basic idea was elegant in its simplicity: Sew plastic tubes into an artery and a vein in the patient's arm for connection to the artificial kidney. After each dialysis treatment, keep the access to the circulation open by hooking the two tubes together outside the patient's body through a U-shaped Teflon device, called the Scribner shunt, which serves as a permanently installed extension of the patient's own circulatory system. Whenever the patient needed to be dialyzed again, no new incisions in blood vessels had to be made. The shunt was simply disconnected from the tubes in the patient's arm, and the patient was hooked up again to the machine. The fifth patient to receive a Scribner shunt was dialyzed repeatedly for 36 years, undergoing 5,700 cycles of hemodialysis before dying several years ago.

The original Scribner shunt, although now replaced by improved types of permanent vascular access, was the pioneering breakthrough that converted Kolff's artificial kidney from a rescue device in acute renal failure into a long-term instrument of organ replacement that has prolonged the lives of millions of patients throughout the world, another wonderful example of scientific synergy and symbiosis reminiscent of Matisse and Picasso.

The contributions of Kolff and Scribner not only revolutionized the treatment of kidney disease, but also launched the discipline of medical bioethics in the mid-1960s. For the first time in medicine, physicians had a technology that would save the lives of thousands of people; yet there were not enough machines or money to treat every patient. Dealing with such dilemmas, unique in the early days of hemodialysis, is now the 'bread and butter' of ethics committees that handle complex issues stemming from organ transplantation, gene therapy, *in vitro* fertilization and therapeutic cloning.

The Lasker Special Achievement Award in Medical Science is a relatively new award that was inaugurated in 1994 and is given periodically to honor a scientist whose lifetime contributions to biomedical research are universally admired and respected for their creativity, importance and impact. Previous recipients include Maclyn McCarty (1994), Paul C. Zamecnik (1996), Victor A. McKusick (1997), Daniel E. Koshland, Jr. (1998), Seymour Kety (1999) and Sydney Brenner (2000).

The recipient of this year's award is James E. Darnell of The Rockefeller University. Darnell is cited for an exceptional career in which he opened two fields in biology, RNA processing and cytokine signaling, and fostered the development of many creative scientists. In the first half of his 45-year career, he pioneered studies of mRNA biosynthesis in animal cells and viruses. This work led to the discovery of poly(A)$^+$ RNA and set the stage for the discovery of mRNA splicing by Roberts and Sharp in 1977. In the last half of his career, Darnell unraveled the JAK–Stat pathway by discovering the Stat family of transcription factors that transduce information from the cell surface to the nucleus. This pathway explains how many cytokines (including interferons, interleukins 2, 4 and 6, erythropoietin and so on) activate gene expression.

As an academic leader, Darnell has excelled in three arenas: as an influential editor of several major textbooks in virology and molecular cell biology; as an esteemed mentor to more than 125 postdoctoral fellows and graduate students, including an exceptionally large number of creative scientists such as Sheldon Penman, David Baltimore, Jonathan Warner, Ronald Evans, Joseph Nevins and Jeffrey Friedman; and as an indefatigable and indispensable advocate for building a strong independent junior faculty at The Rockefeller University.

JOSEPH L. GOLDSTEIN
Chair, Lasker Awards Jury

Lasker Award recipients receive an honorarium, a citation highlighting their achievements and an inscribed statuette of the Winged Victory of Samothrace, which is the Lasker Foundation's symbol of humankind's victory over disability, disease and death.

To read the formal remarks of speakers at the Lasker ceremony, as well as detailed information on this year's awardees, please refer to the Lasker web site at www.laskerfoundation.org.

doi:10.1038/nm768