On a warm day in late spring, Kenneth Mann, Ph.D., sits at his desk at the University of Vermont’s Colchester Research Facility, poring over a paper written by one of his postdoctoral fellows. A self-described taskmaster — the manuscript he’s working on is filled with his handwritten marks and comments — Mann has counseled and supported a cadre of talented scientists who today are leaders in the field of blood coagulation. Working with fellows and post-docs and watching them evolve is one of the most enjoyable aspects of his work.

That work has spanned more than four decades, including 20 years as chair of the Department of Biochemistry at UVM, during which time Mann established himself as a pioneer in the field of blood coagulation. With nearly 500 published papers, more than 20 patents and 37 awards and honors (including two of the most prestigious in his field — the Chaigneau Prize from the Association Française des Hémophiles and the Pioneer in Hematology prize from the American Society of Hematology), Mann is internationally recognized and sought after by members of the medical profession.

From preventing a heart attack to treating hemophilia to saving the lives of trauma patients — understanding the process of how our blood clots is one of the most important functions of medical science today. UVM Professor and former Chair of Biochemistry Kenneth Mann, Ph.D., has been at the forefront of the science that seeks to understand this process. He has built a four-decade long legacy, and has brought the science behind clotting into the limelight, identifying the biochemical make-up of the factors in our blood that are essential for life.
At Manhattan College, chemistry professor William Batt asked Mann to work in his lab. It was there that Mann first received a letter from NIH not only rejecting his grant application, but disapproving it based on scientific merit. He was unpleasantly surprised — especially when he called up the NIH study section, and the administrative assistant recited all the flaws in his application that had been found.

Mann's NIH rejection galvanized him to move forward with his work independently and prove the reviewers wrong. Back in 1970, the NIH funding would have helped him buy a top-of-the-line $25,000 piece of equipment to process blood. Without it, he needed to find another way to break blood down into plasma and cells — and he needed to figure out where, and how, to get the raw blood in the first place. When he came home the day he'd received his rejection, agitated by the news, his wife Jeanette brought him buy a top-of-the-line $25,000 piece of equipment to process blood. Without it, he needed to find another way to break blood down into plasma and cells — and he needed to figure out where, and how, to get the raw blood in the first place. When he came home the day he'd received his rejection, agitated by the news, his wife Jeanette brought him a hand-cranked antique cream separator and the cooperation of a large slaughterhouse in St. Paul, from which he could get all the bovine blood he wanted, he was able to carry out his planned experiments. He and his laboratory colleagues — David Fais and Charles Heldebrant — developed isolation procedures for prothrombin and thrombin. They were the first to characterize the molecular weight, structure and activities of several active forms of thrombin — which were essential to understanding the process of blood clotting. One of their biggest breakthroughs was applying computational and mathematical models in looking at how blood clotting occurs. The following spring, they presented their findings at the Federation of American Societies for Experimental Biology (FASEB) meeting — showing scientists from throughout the country technologies that they had never seen before, to great acclaim.

Afterwards, when Mann resubmitted his application to the NIH, it was accepted and funded — and has continued to be renewed throughout his career.

A HOBBY BECOMES A LIFE’S WORK

At Manhattan College, chemistry professor William Batt asked Mann to work in his lab. It was there that Mann first became interested in enzymes and catalysis — and excited about science. “I became firmly convinced I wanted to be a biochemist,” he says.

From Manhattan College, Mann went to the University of Iowa for his biochemistry doctoral studies, followed by a postdoctoral fellowship at Duke University. At Duke, Mann received a letter from William Batt, who was doing work with thrombin, a protein in blood clotting that had been discovered in 1872 and used in World War II as a wound sealant to stop bleeding from battlefield injuries; but the protein had never been fully elucidated. Batt asked Mann to develop a full characterization of thrombin, which he did using newly developed biophysical techniques.

After Duke, Mann got a job as assistant professor at the University of Minnesota, with plans to study protein folding, or the process of how proteins fold into a three-dimensional structure. As a side activity, he continued to study prothrombin — the precursor to thrombin in the blood clotting process — using similar biophysical techniques to those he used at Duke.

That work — which started as a hobby — led to what became a major research focus for Mann. He received encouragement for his work from colleagues and decided to apply for research funding from the NIH. He assumed that he would be funded. But in this case, his lack of formal training in blood coagulation worked against him.

The instruction wasn’t what I was looking for — it wasn’t the hands-on science and working with mechanical things that I loved,” he recalls. To Mann, educational life at MIT seemed to be mostly focused on memorization, instead of the deductive reasoning and synthesis he had grown to love in high school.

So Mann got a job in a machine shop as a tool and die maker’s apprentice. After six months, however, he decided that his future didn’t lie on that route, either. He applied and was accepted at Manhattan College, where he planned to study physics.

He received a letter from NIH not only rejecting his grant application, but disapproving it based on scientific merit. He was unpleasantly surprised — especially when he called up the NIH study section, and the administrative assistant recited all the flaws in his application that had been cited by the reviewers.

THE EARLY DAYS

Mann is the youngest of six children born to Arthur and Helen Mann in Brooklyn and Long Island. From his earliest days, it was drilled into him that he was going to go to MIT and be an engineer.

His father was abandoned when he was three years old, and lived independently from age 11. But as a child, the elder Mann was befriended by a mining engineer and through his influence became convinced of the importance of engineering as a career. While he didn’t go to school as a boy, he eventually put himself through grammar school, high school and two years of college while raising six children.

Mann’s two oldest brothers became engineers. His second oldest brother, the late Robert W. Mann, a long-time professor of engineering at MIT, is considered one of the founders of bioreengineering. Because money was tight, young Kenneth needed to get a scholarship to a private Catholic high school and then to MIT — which he did. But after just three months in Cambridge, he quit.

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CREATIVE SOLUTIONS

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THE MANN FILE
Kenneth C. Mann, Ph.D.

Professor, Departments of Biochemistry and Medicine, 1984–Present
Chair of Department of Biochemistry, 1984–2003
Professor of Biochemistry, University of Minnesota, 1980–1984
Professor of Biochemistry, Mayo Medical School, 1978–1984
Vice Chairman, Department of Internal Medicine, Mayo Clinic, 1977–1984
Consultant in Hematology Research, Mayo Clinic and Mayo Foundation, 1972–1984
Founder, Haematologic Technologies, Inc., Essex Junction, VT

• Author of more than 500 peer-reviewed published papers.
• Holder of 22 patents on blood and bone-related items.

EDUCATION
Manhattan College, Riverdale, New York, B.S., Chemistry, 1963
University of Iowa, Iowa City, Iowa Ph.D., Biochemistry, 1967
University of Iowa, Iowa City, Iowa Postdoctoral, 1967–1968

SELECTED HONORS
Henri Chauveau Prize, Association Française des Hémosthètes, 2010
Pioneer in Hematology, American Society of Hematology, 2008
Special Recognition Award in Thrombosis, American Heart Association, 2007
Distinguished Alumnus Award, Mayo Foundation, 2004
Exemplary Service Award — American Society of Hematology, 1999
The Novo Nordisk Haemostasis Award, 1999
Robert P. Grant Medal — International Society on Thrombosis and Haemostasis, 1997

SUCCESES AND DISCOVERIES
Following the success of the FASEB presentation, Mann was asked to join a research group at the Mayo Clinic, run by one of his primary mentors, Walter Bowie.

At Mayo, Mann first became convinced of the importance of his work from a clinical point of view. Prior to that he had mainly thought of it as an intellectual puzzle. “It was the moment I realized that if it’s translatable to improving the human condition, you should do it,” Mann says. With Bowie’s encouragement, Mann joined the Department of Medicine and eventually became Mayo’s vice chairman of research for medicine.

A number of breakthroughs occurred while he was at Mayo, but perhaps the most noteworthy was the isolation and characterization of a blood-clotting protein called Factor V. Factor V had first been identified in 1942, but throughout decades of work no one had successfully been able to isolate it.

By chance, a graduate student named Michael Nesheim had come to Mann’s lab. Mann took Nesheim on as a temporary technician, advising the young investigator and enabling him, through his mentoring, to complete his thesis and find a post-doctoral position. Nesheim succeeded in isolating and characterizing Factor V. It was a major breakthrough, one that allowed Mann and his colleagues to assemble and fully understand the catalysts that cause coagulation to occur.

Scientists knew at that time that there was an enzyme that activated prothrombin and thrombin (key clotting proteins) called Factor Xa. They also knew that to make that reaction occur, other things were needed, including calcium and Factor V. The thought was that when you added “accessories” such as calcium and Factor V, it would increase the rate that thrombin was activated. But what Nesheim, Mann and their colleagues discovered was that when you added Factor V, the reaction rate actually skyrocketed from 1 to 300,000.

“We realized that the only enzymes that were biologically relevant were the ones that were formed in these big complexes,” Mann says. “That was the starting point of our really important accomplishments.”

Other studies in Mann’s lab led to the identification of Factor Va, the active form of Factor V, which is required in the coagulation process. Later, in the 1990s, researchers in Mann’s lab at the University of Iowa were the first to understand the molecular defect of Factor V Leiden, a genetic mutation of Factor V that causes increased abnormal cloting, or thrombophilia. The presence of Factor V Leiden, which is present in 5 percent of the Caucasian population, increases a person’s chance for developing deep vein thrombosis.

BUILDING A TEAM
Those discoveries, and many others in Mann’s lab at Mayo and then at the University of Vermont, were possible because of the team of talented scientists and collaborators he formed. In 1984, Mann was recruited to chair UVM’s Department of Biochemistry, a post he held for the next 21 years. Mann recruited Paula Tray, Ph.D., and Russell Tray, Ph.D., from Mayo, and helped bring together a group of scientists who included current chair of pathology Edwin Bovill, M.D. — a group that informally called itself “the Clotters.”

“He brought people into the lab, gave them a general feel for what was going on and let them go to it,” says Srimat Krishnaswamy, Ph.D., a former UVM postdoctoral fellow with Mann, who is now at the University of Pennsylvania School of Medicine.

Michael Kalafatis, another fellow of Mann’s at UVM, now at Cleveland State University. Mann, who is now at the University of Pennsylvania School of Medicine.

Michael Kalafatis, another fellow of Mann’s at UVM, now at Cleveland State University, said his work with Mann influenced his career 100 percent. Today, he is an international scholar and active researcher in blood coagulation, thrombosis, cancer, and apoptosis, or programmed cell death. Kalafatis says his chemistry students refer to Mann as “the grandfather of coagulation.”

Mann not only facilitated collaborations in his lab, but encouraged scientists and physicians from different disciplines to work together on blood clotting. “He has a multidisciplinary translational approach,” says Russell Tray, Ph.D., professor of biochemistry and former senior associate dean for research and academic affairs in the College of Medicine. “Early on, he had teams of physicians, scientists, clinical laboratory folks, all working on the same problem and taking away from it different things they could use in their own fields.”

Mann has also continued a strong focus on communicating his work to a wider audience. He developed a DVD that fully explains the elements and functions of the blood coagulation system — complete with a colorful, animated movie illustrating the clotting process. The NIH uses his DVD on its Web site, and the American Society of Hematology has distributed it to its members.

Mann’s work has also spawned a commercial enterprise, Haematologic Technologies. Mann founded this maker of plasma proteins for in-vitro research uses in a small commercial space in Essex Junction. It has since grown to encompass most of the building in which it is housed, and is a leader in its field.

RECENT WORK
Mann’s work today is focused on helping to prevent blood disorders — both bleeding and clotting problems — by identifying and categorizing risk factors in the blood.

Over the years, he and his colleagues have developed increasingly sophisticated models to hypothesize how chemical reactions will occur — based upon and validated by studies of biological systems. Those measurements then are translated into mathematical models, which are used to predict what will happen in a given blood sample. These methods eventually may be used to predict a person’s increased risk for stroke or heart attack, or to identify what type of drug would be effective in preventing blood clots.

“I think we’re getting close to doing those sorts of things,” Mann says.

Ongoing research in his lab today includes studies that focus on helping to improve clinical management of bleeding diseases, such as hemophilia. Another project involves working with the U.S. military to improve diagnosis and treatment of certain bleeding defects in trauma, a key area of study for Mann. Since most causes of death today — such as heart attack, stroke, pulmonary embolism and hemorrhage in trauma — are associated with formation of blood clots, this work has widespread implications for clinical treatment in the future.

“Blood is everywhere,” Mann says. “... All of our work is based on very fundamental chemistry. But it’s quite exciting when you translate that into human care.”

A long way from the cream separator: Dr. Mann now uses powerful lasers in research at his Colburn lab.