Physician-researcher Charles Dinarello, a member of the prestigious National Academy of Sciences, continues to study how to balance inflammation in ways that promote human health.

Isolating and cloning “fever molecule” makes Dinarello hot stuff

By Jim Spencer

Charles Dinarello’s search for the “fever molecule” began in 1965, the year he started Yale Medical School. Some scientists believed a human molecule existed that caused fever without infection. They wondered if the same molecule also caused other kinds of inflammation.

Dinarello set out to provide the facts that tested these theories.

It took decades for his work to translate into improved treatments for patients, but Dinarello’s research proved so important that in 2009 the University of Colorado School of Medicine professor won three of the world’s most prestigious medical science awards.

He finally isolated the fever molecule in 1977 at the National Institutes of Health. Then he headed the team that cloned the molecule in 1984 at MIT, while working at Tufts Medical School and the New England Medical Center.

As he isolated and cloned the fever molecule, Dinarello says he “lived in constant fear” that he was wrong because the concepts he and his colleagues were introducing were novel.

Dinarello’s work on the fever molecule—which the doctor and his colleagues eventually called Interleukin 1—led to better understanding and treatment of inflammation, diabetes, cancer, arthritis and autoimmune diseases.

Dinarello’s prizes in 2009 pay homage to the doctor’s persistence.

The Paul Ehrlich and Ludwig Darmstaedter Prize is among the most prestigious international prizes awarded in Germany in the field of medicine. Dinarello will accept the prize—worth $140,000—in a ceremony in Frankfurt on March 14, 2010, the birthday of the award’s namesake, Paul Ehrlich. Ehrlich won a Nobel Prize in medicine in 1908. Eighteen previous Ehrlich prize winners have gone on to win the Nobel.

“I’m just happy the field is getting recognized,” says Dinarello, who at 66 is considered the father of a subdivision of immunology called cytokine biology. “Many people have contributed to this.”

Dinarello is happiest because patients, such as those with Type 2 diabetes, now get relief because of the research he pioneered.

The Ehrlich prize was the third big recognition of Dinarello’s work in 2009. In the spring of 2009 Dinarello received a share of two other internationally prestigious awards—the Royal Swedish Academy of Sciences Crafoord Prize, presented to him by the King of Sweden, and the Albany Medical Center Prize in Medicine and Biomedical Research. In each case Dinarello split a $500,000 prize with two other researchers.

Dinarello, a professor of medicine in the medical school’s division of infectious diseases, gave away all the prize money. He will do the same with his Ehrlich prize winnings. All of the money will end up in the Interleukin Foundation, which Dinarello started to help fund biomedical researchers who had good ideas but no source of cash.

Dinarello chose not to use his prize money to pay off his home mortgage or replace his 13-year-old Volvo for one reason: He knows how lucky he was to discover a path to enlightenment on the unexplored edges of science.

“Some of my professional colleagues would say at scientific meetings that the fever molecule we isolated contained bacterial products,” he recalls. “Some called our fever molecule ‘lymphodreck’ from the German-Yiddish expression for dirty.”

In 1978 Dinarello and Dr. Lanny Rosenwasser stood at a beta counter in a National Institutes of Health lab and saw a sample of Dinarello’s best-purified molecule causing fever at one-millionth of the concentration they had begun testing.

He waited two years before publishing the data, using the time to check and double check his results.

While at Tufts-New England Medical Center Hospital, Dinarello asked to be relieved of clinical duties to try to clone Interleukin 1. At the time only three other molecules had been cloned—a human growth hormone, insulin and interferon.

“I was constantly aware of the potential of failure,” he says. “I estimate that we used 60 liters of human blood in the cloning project for Interleukin 1.”

Even when Dinarello and colleagues from MIT and Wellesley College finished cloning Interleukin 1 in 1984, enough professional skepticism persisted to cause the respected journal Nature to refuse to publish their findings. The Proceedings of the National Academy of Sciences published their results instead. The synthetic fever molecule turned out to be 100 percent pure. It did everything Dinarello claimed and more.

“In the end,” Dinarello says, “nothing beats proving a concept. More than any prize, that is the scientist’s dream.”