

FROM TUBERCULOSIS SANATORIUMS TO 21ST CENTURY MEDICINE



It began as a medical myth: tuberculosis patients in the 1890s believed Denver's abundant sunshine and dry air would cure them. Of course it wasn't true, but as patients flocked to the area, hospitals arose that now rank amongst the world's premiere respiratory centers.

The 113-year-old **National Jewish Research and Medical Center** stands among them. After tuberculosis-killing antibiotics arrived with the Second World War, National Jewish refashioned itself into a pulmonology and immunology center of excellence.

Today, National Jewish has been ranked the No. 1 respiratory hospital in the nation by U.S. News & World Report for eight years in a row. While small, with only 125 researchers and three academic departments – immunology, medicine and pediatrics – the institute is home to world-class researchers and clinicians. Those include Drs. Philippa Marrack and John Kappler, whose ongoing research has revealed the pivotal role the T cells play in detecting and fighting infection, and Dr. Erwin

Gelfand, a pediatric immunologist who built one of the earliest animal models for asthma.

To get a sense to the institution's influence, consider this. From 1993 to 2003, work done by National Jewish molecular biology and genetics researchers was the 13th most cited in the world in other scientist's papers. The hospital's biology and biochemistry research was ranked 15th in the world, and immunology ranked 22nd, in terms of citations in other scientist's papers.

And, as if a testament to the hospital's success, more than a half a dozen Denver-based biotech and medical device companies work nearby on cures for lung and immune system ailments.

"There are a large number of very prominent researchers in asthma and inflammation at National Jewish," said Dr. Woodruff Emlen, president of Denver-based Taligen Therapeutics. "They are definitely a resource for company like us."

Gelfand, who has served as National Jewish's chair of pediatrics for the past 19 years, says, "I cannot imagine a better place to be surrounded by colleagues who collaborate, who are open. We have among the best scientists, among the best clinicians."

In recent years, National Jewish has attracted \$40 million to \$50 million in grants annually. A quarter of its funds come from industry, and licensing deals have grown each year. Technology transfer will become even more important in light of recent changes at the National Institutes of Health, Gelfand predicts.

The NIH has shifted funds toward biodefense, away from the formerly popular areas of asthma and immunology. Increasingly, he predicts, research at National Jewish will be funded by collaboration with the pharmaceutical industry and through outlicensing good ideas.

One example of such outlicensing is **Taligen Therapeutics**, founded in March 2004. The company, headquartered at the Colorado Bioscience Park in Aurora, is based on research done by Gelfand and Dr. V. Michael Holers, who chairs the department of rheumatology at the University of Colorado School of Medicine.

Holers identified a cascade of protein reactions in the immune system that leads to inflammation, a key aspect of asthma. The doctor discovered that by blocking a particular molecule early in the chain reaction, he could limit inflammation. He tested the idea using Gelfand's animal models.

The idea has attracted significant interest. If successful, a resulting product could treat the estimated 5 to 10 percent of asthma sufferers who don't respond to milder treatments, a market size of 10 million people worldwide. Taligen has won more than \$800,000 in Small Business Innovation Research (SBIR) grants, as

well as \$100,000 proof-of-concept financing from the University of Colorado. In September 2005, the company announced it had raised \$3.75 million in Series A venture financing. Of that, \$240,000 came from the state of Colorado itself, through a new state-backed venture capital program designed to fuel emerging bioscience companies.

The next step is for the company to take its antibodies and turn them into a product, explains Dr. Woodruff Emlen, Taligen's president. Then comes a long series of clinical trials followed by application to the FDA for drug approval.

A SINGLE PNEUMONIA-CAUSING BACTERIUM GROWING AND DIVIDING IN 60 MINUTES INTO A CLONE, AS ANALYZED BY ACCEL8'S BACCER8R™ INSTRUMENT. THE BACCER8R ELIMINATES CULTURING BY MEASURING THE RESPONSES OF INDIVIDUAL BACTERIAL CELLS TO DIFFERENT TESTS, A METHOD ACCEL8 CALLS QUANTUM MICROBIOLOGY™.

In an industrial park on the other side of Denver, 14-employee **Accelr8** (pronounced "accelerate") is developing a machine to rapidly diagnose strains of pneumonia acquired in hospital intensive care units. The machine uses slides, lasers and statistical analysis to marry classical microbiology with high-tech micro-array technology.

In the ICU, mechanical ventilators "breathe" for a patient, involving placing a tube in the patient's windpipe so air can be delivered to the lungs. Sometimes ventilation can lead to pneumonia, a serious

bacterial infection. Doctors typically use X-rays or sputum cultures to diagnose the disease, but these methods can take hours or days. Accelr8 aims to identify the strains in eight hours, allowing doctors to prescribe optimal antibiotics. That, the firm says, will save thousands of lives and millions of dollars in costly hospital stays.

"The problem is that antibiotic resistance has become so widespread and it moves so fast," says David Howson, president of Accelr8. "You have to get it right the first time." The company is working with Denver Health, the city's public safety-net hospital, and already has its first diagnostic prototype in the lab.

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“Denver probably has more world-class expertise in pulmonology than any other city in the world,” Howson says. “Because we’re focused on respiratory infections, and there is such a history of pioneering in respiratory medicine, the expertise here is just phenomenal.”

Pulmonology and immunology are naturally connected at National Jewish, as the institution specializes in asthma and allergies. Allergies are an immunological disorder, and asthma concerns both the lungs and the immune system. Therefore, immunological diseases are the focus of several local companies.

Still at a very early stage of development, **Sentry Biosciences** has licensed technology from the University of Colorado to develop treatments for many diseases, including stroke and autoimmune diseases. Sentry’s science focuses on how to regulate the chromosomal DNA associated with apoptosis, or planned cell death.

Many parts of healthy human bodies are naturally programmed to die, such as old or damaged skin and other cells. But when under attack by disease, the body’s process goes awry, with cells living longer or dying sooner than they should. The cell’s DNA regulates this process, and Dr. Ding Xue of the University of Colorado at Boulder has discovered a set of enzymes associated with the process.

Sentry, which licensed Xue’s enzymes from the University of Colorado, hopes to validate them as clinical targets and then identify, develop and commercialize small molecules that can modify the enzymes.

“From a scientific perspective, there’s reason to believe it could be a very valuable technology,” says Randy Swenson, Sentry’s founder.

Amgen, one of the largest and oldest biotechnology companies in Colorado, has facilities in Longmont and Boulder. It manufactures its rheumatoid arthritis treatment, Kineret, in Boulder.

Rheumatoid arthritis, an autoimmune disease, is characterized by excess production of interleukin-1, which leads to pain, swelling and joint stiffness. Kineret is a second-line therapy that helps manage excess levels of interleukin-1 in the body. It is manufactured in E. coli bacteria; the bacteria are grown to produce a protein that forms the basis of the injectible drug.

The product received FDA approval in 2001 and reached worldwide sales of \$70 million by 2002. Kineret was Amgen’s first product to be exclusively manufactured in Colorado.

The 25-year-old company is headquartered in Thousand Oaks, Calif., and no longer undertakes any research in Colorado. But as a manufacturing entity, the company has been on a recent hiring spree for manufacturing experts, quality control managers and process

development engineers. By mid-2006, more than 1,000 people will work for Amgen in Boulder and Longmont. Amgen has found that attracting talent to Colorado has been easy.

“People have found, in general, that the quality of life and the location is a plus,” says Debbi Ford, Amgen’s Colorado spokeswoman. “The opportunity for recreational activities, obviously the proximity to the mountains and the cost of living are all considered a plus for people who want to relocate here.”

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— DEBBIE FORD, AMGEN

OTHER FIRMS with respiratory care product divisions in Colorado include BioStar and Ferraris Respiratory.