Breathe

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FROM AFRICA TO ALBUQUERQUE: One Researcher's Journey

TOXICOLOGIST JANET BENSON: Biological and Chemical Threat Countermeasures


Dr. Tesfaigz

From Africa to Albuquerque

One researcher's journey

Addis Ababa is a long way from Albuquerque.

But Yohannes Tesfaigzi, Ph.D., says the high desert setting, mountains, and vegetation in New Mexico remind him of where he grew up in Ethiopia.

His path to a position as the Director of the COPD program at LRRI was set by decisions he attributes to chance. Although others might say that perhaps talent, intelligence and hard work have also contributed to his success.

Yohannes Tesfaigzi was just 15 years old when he went to Germany to visit his brother who was studying there. There was a change of government while he was traveling, so his father made the decision that Yohannes should stay put rather than come home to an unsettled Ethiopia. At the time it was tough for the teenager. He didn't know German very well, but had to finish high school studying all his subjects in that language.

Looking back, he knows now his father made a good decision. Some of his schoolmates back home had bad experiences as they had to interrupt their high school studies and teach rather than complete their education. The rural areas were not prepared for these newcomers; some were accepted but others weren't and faced severe hardships.

The boy who had loved animals, plants and biology from an early age finished growing up in Germany, and after completing high school went on to university there. He completed his Ph.D. in microbiology in 1988.

He was always thinking he would return to his country, but there was still conflict between Eritrea and Ethiopia, so going home didn't seem like a possibility. One option he considered was working for an international organization dealing with agriculture or health, such as the Food and Agriculture Organization of the U.N. (FAO) or World Health Organization (WHO). But the unstable political situation made that option less than ideal.

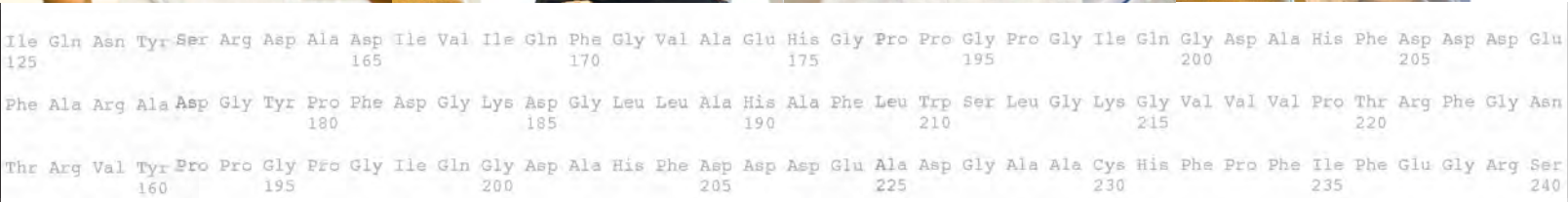
So Dr. Tesfaigzi followed the lead of some of his German colleagues and pursued postdoc research opportunities in the U.S. By chance, the first person he heard back from was Dr. Don Carlson at at the University of California, Davis, who wanted someone to work on airway epithelial cells. Dr. Tesfaigzi says, "I could have ended up in another lab, but thought, that looks interesting, so that's how I got into airway biology."

Dr. Tesfaigzi was looking initially at how airway epithelia differentiate, or how airway cells change from a type that produces mucus to a type that looks like skin cells. After joining LRRI, he found that the airway epithelial cells proliferate following exposure to environmental

<< Dr. Tesfaigzi and the LRRI COPD Program

Only 20 to 35 percent of heavy smokers eventually develop COPD and siblings of COPD patients have a higher risk of developing the disease. Therefore, it is generally believed that genetic factors make individuals susceptible to developing COPD. Recent studies suggest that variations in multiple genes underlie this susceptibility and research at LRRI is devoted to identification of these genes.

Shown across the top of this article are amino acid sequences that represent changes in proteins due to gene polymorphisms.



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pollutants such as bacterial components or ozone, and the new cells make more mucus to protect the airways. Under conditions of cancer the increase in cell numbers continues, but under typical conditions the number of cells is reduced to normal levels once the injury has healed.

Dr. Tesfaigzi started looking into the mechanism that gets rid of the extra cells. How does the airway epithelium get rid of up to 30 percent of its cells in two weeks under normal conditions?

It turns out there is a resolution process regulated by the Bcl-2 family of proteins that is crucial in the elimination of hyperplastic epithelial cells. This knowledge has led to findings that are likely to help regulate epithelial cell numbers in people who have chronic bronchitis, asthma or cystic fibrosis.

"We can see that there are similar changes in people with these chronic diseases in that there are deficiencies in regulating the proteins that help resolve airway epithelial hyperplasia," Dr. Tesfaigzi explains. When they lack sufficient levels of the protein that handles the resolution of proliferated cells, the hyperplastic condition does not resolve after injury. The extra mucus-producing cells create too much mucus, and airways become clogged so that breathing becomes a problem.

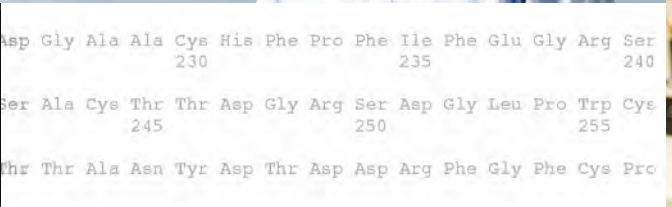
How do we restore Bcl-2 family protein levels in those epithelial cells so we can reduce the number of mucous cells? This is one of the questions Dr. Tesfaigzi and his colleagues at the LRRI COPD program are working on.

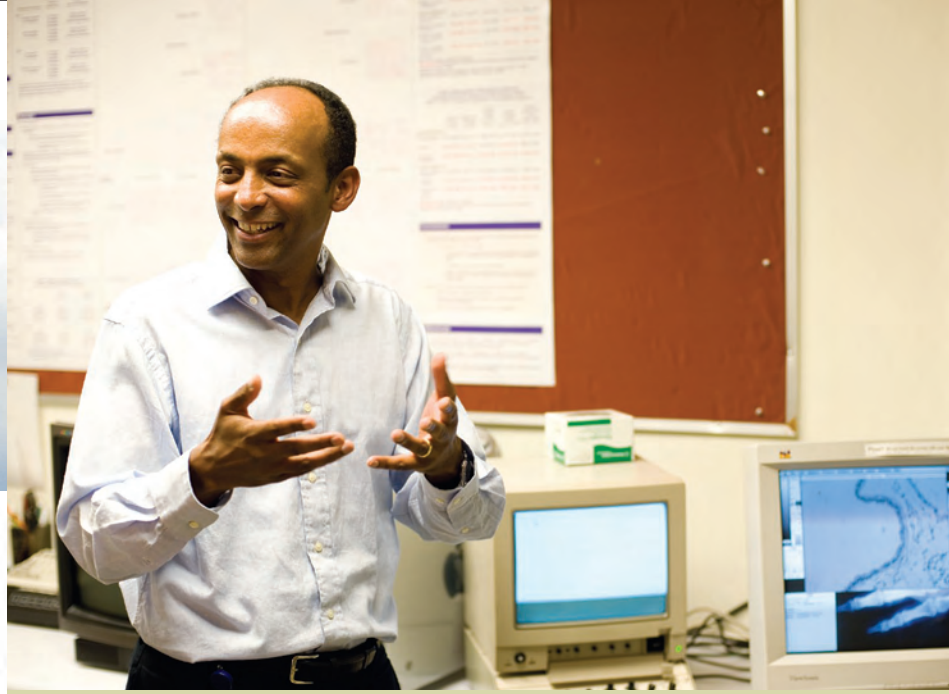
Now they are at the stage where they are looking at how delivery of proteins can be optimized for patients with a variety of disease conditions. Which protein would work best for which condition? They are also looking at single nucleotide polymorphisms (or SNPs) that affect the regulation of Bcl-2 family members in a cohort of smokers.

By understanding the pathways and the proteins involved that reduce hyperplastic mucous cells, they hope to identify therapies for chronic mucus hypersecretion. They are also trying to reduce the size of the proteins that are effective in reducing mucous cell hyperplasia, because smaller molecules can be developed as drugs that can be administered with an aerosol inhaler.

"Some drugs currently used by COPD patients reduce the viscosity of mucus," Dr. Tesfaigzi says. But, as he explains, they really don't address the underlying cause of the excess mucus. "What we're doing is working to understand the mechanism in detail first, and then develop drugs that are specific for the unwanted cells and that will leave other cells alone." These more targeted drugs would help reduce side effects in patients.

Even though the number of patients is very high, COPD wasn't taken as seriously or researched as much as some other diseases until recently. It is primarily an age-related disease that mainly affects smokers. Dr. Tesfaigzi explains that by





2020, it will rise to the third most common cause of death in the world. "While early detection and treatment have helped cancer decline, with COPD we still don't have a good understanding of the basic science behind it."

These days, in addition to his own research, Dr. Tesfaigzi is also helping to coordinate the efforts of other members of the recently developed LRRI COPD Program. Working as a manager does take time, Dr. Tesfaigzi acknowledges, but he knows in the long run it will benefit everyone. He feels he gains by interacting with other researchers both inside and outside LRRI, and has seen the interest that the pharmaceutical industry has in the program already. He is working to balance his own research with managing other projects, and in the next two years, he plans to write a program project grant for the NIH.

Dr. Tesfaigzi has not been back to Ethiopia or Eritrea in several years. The unsettled political situation makes travel difficult. But he's found a way to help. "There's little I can do, but one thing I can contribute is to train young people from Africa," he says. Dr. Tesfaigzi has begun training postdocs from Africa at LRRI and plans to continue the program. He hopes the knowledge they take back to their countries might be a small step in improving the disparity in healthcare between the U.S. and Africa. ■

What is COPD?

Chronic obstructive pulmonary disease (COPD) is a diagnosis referring to two lung diseases: chronic bronchitis and emphysema. Both diseases cause obstruction of airflow into and out of the lungs, and frequently exist together.

According to the Lung Association, COPD is the fourth leading cause of death in the U.S., claiming the lives of 127,049 Americans in 2005.

In recent years, the number of women dying from the disease has increased, becoming more than half of the total.

Smoking is the primary risk factor for COPD. Other risk factors include exposure to air pollution, second-hand smoke and occupational dusts and chemicals, a history of childhood respiratory infections, and heredity.

LRRI COPD Program

The COPD Program was developed in January 2007 to facilitate the interaction of investigators at LRRI and the University of New Mexico who are addressing key problems related to COPD and maximize the use of existing resources to improve research.

Ongoing studies with the Lovelace Smokers Cohort (LSC) compare risk of chronic airflow obstruction in Hispanics and non-Hispanic whites, investigate the association of obesity with decline in pulmonary function and chronic bronchitis, and determine risk factors for developing COPD exacerbations.

Based on the mechanistic studies of cigarette smoke-induced chronic bronchitis, DNA polymorphisms in genes involved in apoptosis, DNA methylation, and DNA damage/repair pathways are being screened in the LSC. Findings from these studies will be compared with findings from ongoing experiments on cigarette smoke-induced emphysema and chronic bronchitis in susceptible and resistant mouse strains and cell and organ culture models of chronic bronchitis.

The COPD Program investigators have contributed to the understanding of regulation of mucus secretion, resolution of mucous cell metaplasia, and the role of gene polymorphisms in regulating mucous cell metaplasia. Studies on nutrition and obesity, vascular congestion, and the role of C-fibers on attenuated ventilatory responses are ongoing in mouse models of COPD.