

Quest

When going green backfires

Unintended consequences can include more energy consumption and emissions

DISCOVERY MAY REDUCE THE DAMAGE OF ASTHMA

La Jolla institute team says it has uncovered the cause of tissue scarring

KEITH DARCE • U-T

Most people with asthma can get relief from their symptoms by breathing in prescription steroids that reduce bronchial inflammation or other drugs that relax muscle tissue in the lungs.

But the drugs don't work in everyone, especially in those with severe cases of the breathing disorder.

One reason for the difference could be scarring that thickens muscles and the lining of air passages in the lungs.

Researchers at the La Jolla Institute for Allergy and Immunology believe they have discovered the key mechanism responsible for causing such tissue damage. The results of their work were published last week in the journal *Nature Medicine*.

If the scientists are right, their finding could lead to an entirely new class of drugs for treating the chronic disease.

That would be a major breakthrough for many of the 20 million Americans who suffer from asthma, said Dr. Dale Umetsu, an immunology researcher at Harvard University's Childrens Hospital in Boston.

"This is a big problem, and there are no good therapies that focus on this issue," he said. New therapies targeting the pathway identified in the study "could greatly improve asthma in patients with chronic asthma."

They also could generate big sales



Michael Croft led the research team.

for drug companies in a fast-growing disease category.

But that's still years away, if at all, said biologist Michael Croft, who led the team of scientists who conducted the basic-science research.

"There is a lot more work that needs to be done," he said.

Croft's laboratory focuses on special proteins that function as receptors on the surface of cells for certain types of cytokines that can cause cell death. Cytokines are disease-fighting molecules that are part of the body's immune response system.

In addition to asthma, Croft has studied the roles of various tumor necrosis factor receptors in multiple sclerosis, diabetes and cancer.

The work already has produced a promising drug candidate, OX40, which was licensed in 2009 to AstraZeneca subsidiary MedImmune for development as an asthma treatment.

In his latest work, Croft focused on a protein known as LIGHT, which binds to two particular receptors on the surface of cells.

SEE ASTHMA • E4

JOHN TIERNEY • NYT NEWS SERVICE

Energy-efficiency standards have been embraced by politicians of both parties as one of the easiest ways to combat global warming. Making appliances, cars, buildings and factories more efficient is called the "low-hanging fruit" of strategies to cut greenhouse emissions.

But a growing number of economists say the environmental benefits of energy efficiency have been oversold. Paradoxically, there could even be more emissions as a result of some improvements

in energy efficiency, these economists say.

The problem is known as the energy rebound effect. While there's no doubt that fuel-efficient cars burn less gasoline per mile, the lower cost at the pump tends to encourage extra driving. There's also an indirect rebound effect as drivers use the money they save on gasoline to buy other things that produce greenhouse emissions, like new electronic gadgets or vacation trips on fuel-burning planes.

Some of the biggest rebound effects occur when

SEE BACKFIRE • E3



While there's no doubt that fuel-efficient cars burn less gasoline per mile, the lower cost at the pump tends to encourage extra driving.

MARK MCGINNIS • SPECIAL TO THE U-T

EVOLUTIONARY FIND IS SUBJECT OF FREE PUBLIC LECTURE AT SCRIPPS

Paleoanthropologist Tim White will discuss latest discoveries in human evolution, the analysis of the data and its meaning

GARY ROBBINS • U-T

If you're curious about your roots, make plans to visit the Scripps Institution of Oceanography on Tuesday. Tim White, one of the world's most renowned paleoanthropologists, will discuss the latest findings in human evolution during a free public lecture.

White has helped clarify and explain how humans evolved, partly through groundbreaking work he did with Donald Johanson on the 3.2 million-year-old remains of the famed hominid Lucy.

Years later, White discovered a 4.4 million-year-old fossil skeleton

in Ethiopia, revealing that our human ancestors extended even farther back in time.

National Geographic hailed the discovery, saying that, "The fossil puts to rest the notion, popular since Darwin's time, that a chimpanzee-like missing link — resembling something between humans and today's apes — would eventually be found at the root of the human family tree."

Scripps decided to honor White for his work by naming him this year's recipient of the Richard H. and Glenda G. Rosenblatt Lecture-ship in Evolutionary Biology. In accepting the award, he will give

a lecture on human evolution at 3 p.m. Tuesday at the Scripps Seaside Forum, 8610 Kennel Way in La Jolla.

White, who is on the faculty at UC Berkeley, recently discussed his research in an interview done by email.

Q. Scientists have found the fossils of human ancestors that date back almost 6 million years. Do you think the evolutionary record goes back significantly farther? Say, 7 million years? What's plausible?

A. We have an excellent record of Miocene apes, SEE EVOLUTION • E4



Tim White, paleoanthropologist.
UC BERKELEY

EVOLUTION 'We had a treasure trove of data from a previously unknown time period'

FROM E1 stretching from 7 million years ago, back to circa 22 million years ago, in Africa, Eurasia. These are, however, all apes.

The earliest hominids will be difficult to recognize; some colleagues do not even accept the fossils you cite as being hominid at all (the subject of my seminar following my lecture). One issue is figuring out when the fork between our lineage and the chimpanzee lineage happened, and the molecular data are calibrated on a poor fossil record, so we can't get at it that way very easily. I think that the Late Miocene fossils from Ethiopia, Chad, and Kenya dated from 5.7 to 7 million years ago are very close to that fork, but they are poorly representative, so far, of the creatures that evolved into *Ardipithecus ramidus* that we found at 4.4 million years ago.

Q: You've written that Charles Darwin "creatively but incorrectly hypothesized that our earliest ancestors would appear to be a halfway house between chimpanzee and human." In what ways was he wrong?

Details

Paleoanthropologist
Tim White's lecture on human evolution
When: 3 p.m. Tuesday
Where: Scripps Seaside Forum, 8610 Kennel Way, La Jolla
Cost: Free



Tim White, professor of integrative biology at UC Berkeley.

A: Actually, Darwin was more right about this than many of his contemporaries and intellectual descendants, because he appreciated so well that it was a dangerous game to use living animals as proxies for ancient ones. It turns out that many things that separate chimpanzees from humans arose along the chimpanzee line AFTER the fork in the evolutionary road. They are highly specialized, frugivorous, knuckle-walking apes with social systems highly evolved from the common ancestor we shared with them at the time of the fork.

Q: The development of such scientific tools as DNA sequencers has profoundly deepened the study of human evolution.

It is inevitable that other tools will arise as your career continues. Do you have a sense of what such tools might tell scientists about evolution?

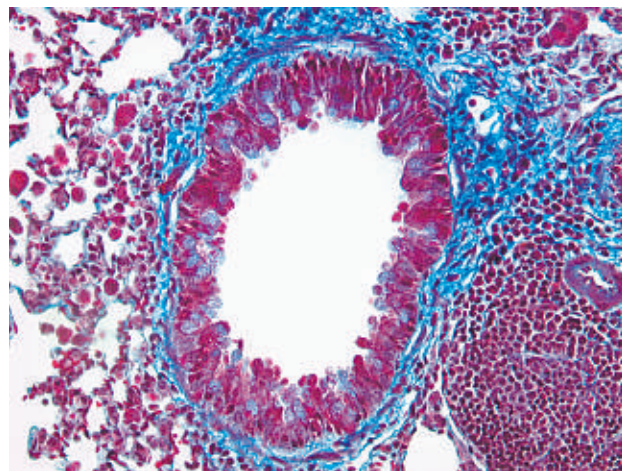
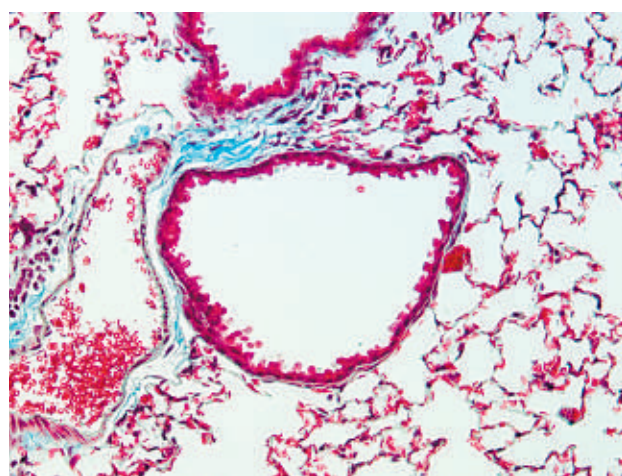
A: We use many tools, from satellites to mCT scanners, to do our work of discovery and analysis. I wouldn't have been able to predict the ways that these have helped us understand *Ardi*, so I won't hazard a guess. Paleontologists are better at figuring out what happened than they are at predicting what is going to happen!

Q: You're well known for the lengthy, deliberate pace of your research. Are you ever bothered by the time it takes to go from initial discovery to peer-reviewed publication?

A: If I were bothered by that, I shouldn't be doing science. The whole point is to get the right answer. For the *Ardi* analysis, as I'll demonstrate in my lecture, we had a treasure trove of data from a previously unknown time period. So it took a long time to assemble the data in the field, assemble the team to analyze it, let these scientists do their work, get thorough reviews, and then publish, as the largest special issue of *Science* since Apollo 11.

I'd be bothered by any scientist who thought that good science came from fast, shoddy, in-deliberate analysis, and I am concerned about increasing pressures in that direction, that have only increased in the decade after I wrote the article on the state of the field.

ASTHMA • The work already has produced a promising drug candidate licensed in 2009



Microscopic views of a cross section of bronchial tube that has been thickened by collagen built-up. DR. TAYLOR DOHERTY

FROM E1

LIGHT is the shortened version of this long description: "homologous to lymphotoxins, exhibits inducible expression, competes with HSV glycoprotein D for HVEM, a receptor expressed by T lymphocytes." The protein was first identified in 1998 by Carl Ware, a former

La Jolla Institute faculty member who now directs the Infectious and Inflammatory Disease Center at the Sanford Burnham Medical Research Institute in La Jolla.

However, the molecule's role in asthma had not been previously defined. In the study by Croft's team, LIGHT was blocked

from binding with the two key receptors in one set of mice suffering from chronic asthma. Another group of asthmatic rodents were genetically altered so that they lost the ability to make LIGHT.

In all of the mice, the production of two cytokines tied to tissue thickening was reduced along with the damage, or "remodeling," usually caused by the molecules.

"It wasn't completely absent, but it occurred to a much lower degree," Croft said.

"This previously unknown role for LIGHT in airway remodeling may lead to strategies targeting this molecule in asthmatic airway remodeling or other diseases involving fibrosis and remodeling," the researchers concluded in their report on the work.

Since Croft's lab focuses on basic immunology research, the scientist is hoping that other scientists will conduct more research on how blockage of LIGHT affects disease and that drug developers will take up the task of searching for molecules or compounds that effectively shut down the protein.

"There is a lot we don't know," he said. "I think this is just the tip of the iceberg."

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RESERVOIR OF DRY ICE FOUND UNDER SURFACE OF RED PLANET

Carbon dioxide was once in atmosphere, making it more dense

ALICIA CHANG
ASSOCIATED PRESS

LOS ANGELES

Think Mars today is a hostile place? It was worse 600,000 years ago, according to new research that suggests the planet had a dustier, stormier atmosphere.

"It was an unpleasant place to hang out," said lead researcher Roger Phillips of the Southwest Research Institute.

The evidence comes from the discovery of a huge underground reservoir of dry ice, or frozen carbon dioxide, at its south pole — much more than scientists realized. They suspect some of that store of carbon dioxide was once in Mars' atmosphere, making it denser.

In the recent geologic past, when Mars' axis tilted, sunlight reached the southern polar cap, melting some of the frozen carbon dioxide. This release would have made the atmosphere thicker and caused more dust to loft into the air, creating severe storms. Other times, carbon dioxide cycled back into the ground as part of a seasonal cycle.

There is an upside to that stormier climate: The thicker atmosphere back then meant there were more regions on the planet where liquid water probably existed. Water is considered an essential ingredient for life.

Still, "it was not the balmy, tropical Mars" that existed even billions of years earlier, Phillips said.

Mars today is frigid, arid and constantly bombarded by lethal radiation. Its atmosphere, made up mostly of carbon dioxide, is many times thinner than the top of Mount Everest on Earth. In fact, the Martian atmosphere is less than 1 percent of Earth's.

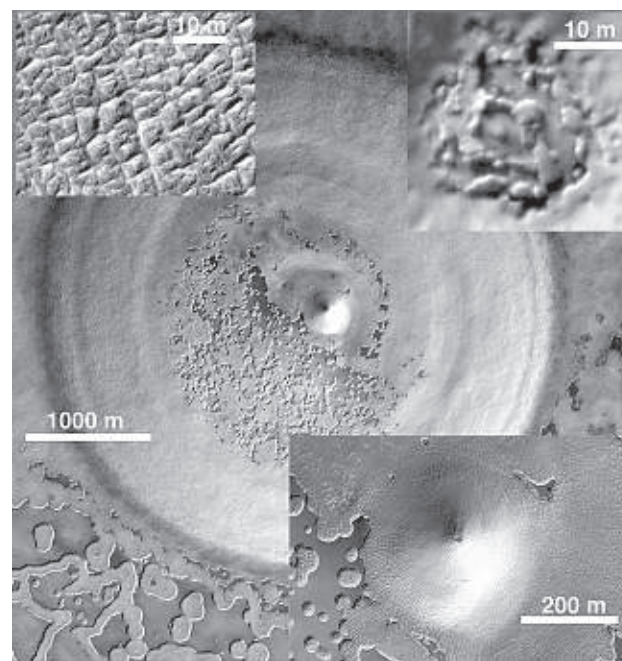


Image taken by the NASA Mars orbiter shows a recently discovered underground deposit of carbon dioxide ice. NASA

The red planet wasn't always this unforgiving. A maze of gullies, canyons and river channels on the surface points to a warmer and wetter past very early in the planet's history.

The underground dry ice deposit, roughly the size of Lake Superior, was discovered using ground-piercing radar aboard the NASA Mars Reconnaissance Orbiter designed to probe below the crust. Researchers estimate it represents 30 times more carbon dioxide than previously believed. Its presence may help explain how most of the Martian atmosphere disappeared.

"It really is a buried treasure," said Jeffrey Plaut of the NASA Jet Propulsion Labora-

tory who was part of the discovery team reporting online last week in the journal *Science*. "We found something underground that no one else realized was there."

Though the newfound store sounds like a lot, it's only enough carbon dioxide to double the mass of the feeble Martian atmosphere if released — not enough to warm up the planet substantially or allow water to pool.

"The atmosphere would still be quite thin and would not have the density necessary to warm things up enough to have liquid water stable on the surface," said Peter Thomas of Cornell University who had no role in the mission.

The mystery of what happened to Mars' atmosphere has long intrigued scientists. NASA plans to explore the upper atmosphere and study how gases are lost to space with a new spacecraft in 2013.

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