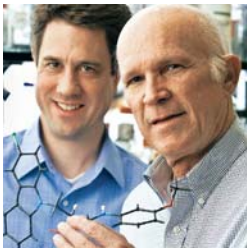
UT SOUTHWESTERN MEDICAL CENTER

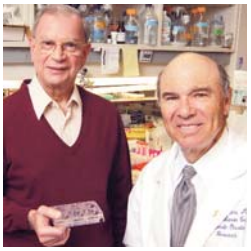
OUR DISCOVERIES MAKE A DIFFERENCE

Aging/Alzheimer's



- Drs. Steven McKnight and Andrew Pieper have found a compound, called P7C3, that preserves newly created brain cells and boosts learning and memory in an animal study, funded by a $2.5 million National Institutes of Health Director's Pioneer Award to Dr. McKnight.
- In animal studies, scientists led by Dr. Roger Rosenberg have created an experimental vaccine against beta-amyloid, the small protein that forms plaques in the brain and is believed to contribute to the development of Alzheimer's disease. Compared with similar so-called DNA vaccines tested in a 2010 animal study, the new experimental vaccine stimulated more than 10 times as many antibodies that bind to and eliminate beta-amyloid.

Cancer



- Drs. John Minna and Adi Gazdar have spent the past 30 years elucidating the genetic and epigenetic changes associated with the development and treatment of lung cancer. Their work seeks to discover these changes and use them as biomarkers – molecular signatures of disease – both to detect lung cancer earlier and to develop new therapies. Their approach also bodes well for so-called personalized medicine, which aims to target the unique characteristics of an individual's tumor with the best current therapies.
- Dr. Jonathan Uhr investigates some of the enigmas of breast cancer. About 10 years ago, he developed a technique to detect cancer cells that are shed from a primary tumor and go on to circulate in the blood. The test has been commercialized and now is used routinely in laboratories to selectively pluck circulating cancer cells out of the bloodstream for further analysis and characterization.
- Dr. Xiaodong Wang was awarded the 2006 Shaw Prize in Life Science and Medicine, sometimes referred to as the "Nobel Prize of the East," for his discovery of the biochemical basis of programmed cell death, a vital process that balances cell birth and defends against cancer.

Cardiology

- Drs. Helen Hobbs and Jonathan Cohen are among the world's leading experts on the genetic factors associated with heart disease. They are not only making tremendous progress in identifying specific genetic links to disease, but also are translating that information from the laboratory to develop strategies to combat heart disease in patients. Drs. Hobbs and Cohen published a study in 2005 showing that humans with mutations in a gene called PCSK9 had low-density lipoprotein (LDL) cholesterol levels 40 percent lower than individuals without the mutation.
- The pioneering work of Dr. Eric Olson is regarded as a major step in finding genetic targets for treatment of congenital heart defects and adult heart disease, and it has illuminated the fundamental principles of organ formation. He and his team have discovered networks of genes that orchestrate the formation of the heart and have shown how inherited genetic mutations in these genes cause congenital heart disease, the most frequent form of birth defect.
- Working with mice, researchers, including Drs. Eric Olson and Hesham Sadek, have discovered that the mammalian newborn heart can heal itself completely. The researchers found that within three weeks of removing 15 percent of the newborn mouse heart, the heart was able to completely grow back the lost tissue and, as a result, looked and functioned just like a normal heart.
- UT Southwestern-based research indicates that lowering "bad" blood cholesterol earlier in life, even by a modest amount, confers substantial protection from coronary heart disease. The 2006 findings were based on 15 years of data tracking more than 12,000 multi-ethnic subjects and reported in *The New England Journal of Medicine*.
- The Dallas Heart Study, a groundbreaking investigation of cardiovascular disease involving thousands of Dallas County residents, was launched in 1999. Nearly 6,000 Dallas County residents participated in the study, in

which researchers used molecular and clinical research techniques to examine a large multi-ethnic group of individuals to develop new biotechnology and to establish a novel training program for scientist-physicians.

- In association with NASA, Dr. Gunnar Blomquist explored the adaptation of the heart to spaceflight. Dr. Blomquist's bold and innovative experiments (including placing the first heart catheter in an astronaut) made him the world's premier expert about the effects of gravity on the cardiovascular system. He was the principal investigator of numerous experiments on the Space Shuttle as well as the Russian Mir Space Station and sent three of his trainees into space as NASA Payload Specialists.

Cholesterol

- UT Southwestern researchers have identified nearly 30 disease-causing genes, including in 1983 the gene responsible for familial hypercholesterolemia, an inherited condition that causes extremely high levels of cholesterol and heart attacks at an early age. That discovery by Drs. Michael Brown and Joseph Goldstein contributed to the pair winning the Nobel Prize in physiology or medicine for their research uncovering the underlying mechanisms of cholesterol metabolism.
- Researchers led by Dr. Jay Horton have shown that a protein responsible for regulating “bad” cholesterol in the blood works almost exclusively outside cells, providing clues for the development of therapies to block the protein’s disruptive actions.

Depression

- UT Southwestern researchers led the $35 million, six-year STAR*D (Sequenced Treatment Alternatives to Relieve Depression) study, which began in 2001 and was the largest study on treatments for depression. STAR*D was the first benchmark investigation to implement specific step-by-step medication treatment guidelines based on patients’ symptoms and medication side effects.

Diabetes

- Using mice, UT Southwestern researchers led by Dr. Roger Unger showed that insulin becomes completely superfluous and its absence does not cause diabetes or any other abnormality when the actions of glucagon are suppressed. These new findings may lead to an alternative to insulin as a treatment for type 1 diabetes, which affects about 1 million people in the U.S.
- Dr. Roger Unger also has pioneered research into the actions of the hormone leptin against diabetes. He and his team, using mouse models, found that leptin administered instead of insulin showed better management of blood-sugar variability and lipogenesis, the conversion of simple sugars into fatty acids.
- In a mouse study, researchers led by Dr. Roberto Coppari found that resveratrol, found in the skin of red grapes, may offer some protection against diabetes.

Metabolism and nutrition

- In a landmark study published in 2002 in *The New England Journal of Medicine*, a team of researchers led by Dr. Abhimanyu Garg reported that leptin replacement therapy not only controlled severe insulin resistance and lowered triglyceride levels in patients with severe lipodystrophy but also decreased fat accumulation in the liver, an abnormality for which there has been no effective therapy.
- The research in the Center for Human Nutrition is significant for everyone. Center investigators, led by Dr. Scott Grundy, were the first to prove the "Mediterranean diet" healthy, discover that antioxidants help prevent atherosclerosis and define the varieties of fatty foods that are harmful.

Osteoporosis/kidney stones

- Dr. Charles Y.C. Pak and his research team have played a critical role in the development of several drugs used worldwide – including Citracal for the prevention of osteoporosis and Urocit-K for the control of kidney stones – as well as widely recognized diagnostic methods for measuring the risk factors for kidney stones.

Ricin

- RiVax, an experimental vaccine developed by Drs. Ellen Vitetta and Joan Smallshaw for the prevention of ricin intoxication, received an orphan drug designation from the Food and Drug Administration in 2011. “Orphan drug” status means that a drug will be available on the open market more rapidly than most in development.

Transplants

- Dr. Peter Stastny is pushing past conventional testing with new methods that may allow doctors to predict whether an organ recipient will develop antibodies rejecting the transplant. Collaborating with colleagues in Germany, Dr. Stastny for the first time identified antibodies associated with transplant rejection of otherwise healthy kidneys, research that appeared in *The New England Journal of Medicine*.