

# NIH...

## Turning Discovery Into Health

### ADVANCES IN KNOWLEDGE

NIH-funded research leads to thousands of new findings every year. These incremental advances and technological developments are the building blocks that ultimately yield significant improvements in health. Highlighted below are just a few of the many recent advances from NIH-supported research.

- ***Treating Type 2 Diabetes in Youth*** – Rising childhood obesity in America has brought more cases of type 2 diabetes in youth, however, because type 2 diabetes has been primarily an adult illness, information about how to treat youth effectively has been limited. A new study now indicates that a combination of two diabetes drugs, metformin—currently the only approved oral medication for treating young people—and rosiglitazone—a drug with limited use for treating adults—was more effective in treating youth with type 2 diabetes than metformin alone. The study, funded by NIH's National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), compared long-term blood glucose control in randomly assigned treatment groups of youths. The group treated with the metformin and rosiglitazone (sold as Avandamet) maintained acceptable long-term blood glucose control superior to metformin alone or when combined with intensive lifestyle changes. The results may be a starting point for a more aggressive approach to treating youth with type 2 diabetes.
- ***Treating HIV Early Prevents Transmission*** – Treating HIV-positive patients with anti-retroviral therapy early—before their T-cell counts start to drop—can lower significantly the risk of transmitting HIV. In a large NIH-funded clinical trial, researchers selected over 1,700 couples from around the world in which one partner was HIV-positive. Half the HIV-positive patients started anti-retroviral therapy immediately, while the other half received standard clinical treatment. Early therapy reduced the rate of HIV transmission by 96 percent. The study demonstrates that antiretroviral medications can treat and prevent the transmission of HIV infection among individuals. The clinical trial was chosen by the journal *Science* as the 2011 Breakthrough of the Year, recognizing the extraordinary public health significance of the study results.
- ***Targeted Therapy for Cystic Fibrosis*** – In a significant step towards personalized medicine, the FDA in January approved Kalydeco, the first drug to treat an underlying cause of cystic fibrosis (CF). NIH-supported basic research, including the discovery of the CF gene, laid the foundation for development of this drug by Vertex Pharmaceuticals. Mutations in the CF gene cause mucus to build up in the lungs and digestive tract, eventually leading to death. Kalydeco counters a mutation that affects just 4 percent of CF patients, but research is underway to see if combining Kalydeco with an experimental compound, called VX-809, can help people with the most common CF mutation. Interim results from a Phase 2 clinical trial, released in early May, showed a significant improvement in lung function in patients receiving the combination therapy. Complete results of that trial are expected this summer.

- ***Bypass Surgery Shows Advantage*** – A study supported by the NIH’s National Heart, Lung and Blood Institute (NHLBI) found older adults who received bypass surgery to open blocked coronary arteries had better long-term survival rates than those who had angioplasty. The new findings will help patients and their health care providers decide which approach is best for them. Coronary heart disease affects about 14 million men and women nationwide and is most common in people over 65. Bypass surgery is the most common type of heart surgery in the United States, where a healthy artery or vein from elsewhere in the patient's body is used to bypass the blocked coronary artery and improve the blood supply to the heart. Angioplasty, another common procedure that is less invasive, involves the insertion of a thin tube (catheter) with a balloon at its tip used to open blocked arteries. A stent, or small mesh tube, is then usually placed in the opened arteries to allow blood flow to continue into the heart muscle. In the study, investigators analyzed hospital data comparing older adults who underwent bypass surgery to those who underwent angioplasty. While there was no difference in mortality one year after treatment, at four years there was less mortality with bypass surgery than angioplasty. The study results provide comprehensive, large-scale, national data to help doctors and patients decide between these two treatments.
- ***Drug Improves Alzheimer's-like Condition in Mice*** – Alzheimer’s disease also stands to benefit from translational research by way of drug rescuing and repurposing. Recently, a team that included NIH-supported investigators reported that bexarotene, a drug compound originally developed for treating T-cell lymphoma (a type of skin cancer) was capable of clearing the protein beta-amyloid quickly and efficiently after only a short exposure to the compound in Alzheimer’s disease mouse models. Beta-amyloid accumulates in the brain of Alzheimer’s patients due to an impaired ability to clear the protein, leading to a build-up of beta-amyloid plaques and ultimately neuronal death. These findings are exciting because they could in time benefit patients with Alzheimer’s disease especially since the drug compound used in the study has already been studied in humans, leaving a wealth of information already known about dosage and toxicity.
- ***Insights into MRSA Epidemic*** – A research team of NIH scientists from the National Institute of Allergy and Infectious Diseases (NIAID) and their colleagues in China identified a gene that’s been playing a pivotal role in epidemic waves of methicillin-resistant *Staphylococcus aureus* (MRSA) infections in Asia, suggesting a potential target for novel therapeutics. MRSA strains are a leading cause of severe infections in hospitals and community settings—in the US the estimated deaths due to MRSA infections exceeds that due to HIV/AIDS. The newly identified gene, called *sasX*, is more prevalent in MRSA strains than thought and its frequency is increasing. The resulting protein coded for by *sasX* helps the MRSA bacteria colonize the nose and causes skin abscesses and lung disease in mice. The protein also helps the bacteria evade human immune defenses. Taken together, these findings establish *sasX* as a crucial factor in MRSA's virulence and a probable driving force of the Asian MRSA epidemic.
- ***Up Close With Opioid Receptors*** – Researchers have taken the closest-yet look at the structures of opioid receptors, which play key roles in pain relief and addiction. The findings

might aid development of safer painkillers and addiction-fighting medications. Opioid drugs—including codeine, morphine and brand name medications like Vicodin and Oxycontin—act by binding to receptors found on the surfaces of certain cells, mostly in the brain. Two research teams, both supported by NIH’s National Institute on Drug Abuse along with significant support from the National Institute of General Medical Sciences (NIGMS) for one of the teams, independently tackled the challenge of uncovering structural details of two different opioid receptors. The structural details of these receptors could aid in the development of effective medications for the treatment of depression, anxiety and drug addiction, particularly to stimulants like cocaine, for which there are no medications currently available.

- ***Clues to HIV Protection*** – A new study gives insight into the workings of the first vaccine ever reported to modestly prevent HIV infection in people. In 2009 a landmark clinical trial of adult volunteers in Thailand who received an experimental HIV vaccine had a lower chance of becoming infected with HIV than those who received a placebo. Since then, scientists have been seeking to explain why the vaccine showed a modest protective effect. New analysis of blood samples from vaccinated participants, some of whom later became infected with HIV, show differences in levels of two families of antibodies to HIV. Vaccinated patients with high levels of immunoglobulin G (IgG) were significantly less likely to become infected than those who made IgG at lower levels or patients with high levels of a second type of antibody, IgA, that might interfere with the protective IgG antibodies. The results of this analysis, partly funded by NIH’s National Institute of Allergy and Infectious Diseases (NIAID), provide hints about what types of human immune responses a preventive HIV vaccine may need to induce.
- ***Drugs Equally Effective for Age-Related Vision Loss*** – A 2-year clinical trial launched by NIH’s National Eye Institute (NEI) showed that the drugs Avastin and Lucentis lead to similar vision improvements in patients with age-related macular degeneration (AMD). AMD is the leading cause of vision loss and blindness in older Americans. The study, called the Comparison of AMD Treatments Trials (CATT), compared Lucentis, a drug approved for treating AMD and Avastin, a similar drug used for cancer treatment. Both drugs are widely used to treat AMD. The first-year results, published in May 2011, found that both drugs were equally effective in preventing vision loss from AMD. The new report describes the findings from the trial’s second year where patients were assigned to either monthly or as needed regimens. Both drugs led to similar improvements to vision with at least 60 percent of patients in all groups achieving 20/40 vision or better—the level needed for driving. Treatments given monthly were slightly more effective than when given as-needed.