National Heart, Lung, and Blood Institute

NHLBI Science Advances

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Science Advances in Heart Research

Key Protein Found in Molecular Pathway Linked to Hypertension

PCSK6

High blood pressure, or hypertension, is a major risk factor for heart attacks, strokes, and heart failure. Results from an NHLBI-funded study uncovered a key molecular player in regulating blood pressure: PCSK6. This protein is the long-sought master switch in a molecular pathway that was only partially understood: scientists knew that a protein called corin activates atrial natriuretic peptide, which in turn has effects that lower blood pressure. However, scientists had been searching for the protein that activates corin and discovered that it was PCSK6. Now, investigators can study this pathway to identify potential approaches to lowering high blood pressure.

NIH Study Confirms That a Lower Blood Pressure Target Can Save Lives, Reduce Cardiovascular Disease

SPRINT

High blood pressure, or hypertension, is a major public health problem that affects 1 in 3 American adults. The condition, also called the “silent killer,” is an important risk factor for health problems including heart attack, heart failure, stroke, chronic kidney disease, and cognitive function decline. Many patients have difficulty keeping their blood pressure under control. In 2015, results from an NIH-supported study of hypertension revealed that achieving a lower blood pressure target below the target commonly recommended can save lives and reduce the risk of cardiovascular disease in non-diabetic adults 50 years and older with high blood pressure. The SPRINT (Systolic Blood Pressure Intervention Trial) study, which included more than 9,300 people from throughout the U.S. and Puerto Rico, used blood pressure medications to achieve targeted blood pressure goals. The study found that, in this group of older adults with high blood pressure, targeting a systolic blood pressure of less than 120 millimeters of mercury (mm Hg) reduced rates of cardiovascular events, such as heart attack and heart failure, as well as stroke, by 25 percent. Additionally, this target reduced the risk of death by 27 percent — as compared to a target systolic pressure of 140 mm Hg. The study could lead to new, more stringent guidelines for the treatment of hypertension in older adults.

Scientists Develop Nanoparticles With Potential to Protect Against Atherosclerosis

annexin A1 protein

Chronic inflammation plays an important role in the development of atherosclerosis, the process by which plaque builds up inside arteries and which can lead to heart attack or stroke. A protein called annexin A1 has been shown to play a role in reducing inflammation. NHLBI-funded investigators found that nanoparticles containing a short, 27-amino-acid sequence from annexin A1 can effectively resolve the inflammatory response in a hypercholesterolemic mouse model of advanced atherosclerosis as measured by an increase in the protective collagen layer over plaque lesions, suppression of oxidative stress, and a decrease in plaque necrosis. The results suggest that nanoparticles containing annexin A1, or other inflammation-reducing mediators, might play a therapeutic role in resolving inflammation associated with atherosclerosis.

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Science Advances in Lung and Sleep Research

Study Provides More Evidence for Association Between Sleep, Obesity

CHARGE

An NHLBI-funded multinational study, from the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium, has provided new evidence that short sleep duration is associated with prevalent obesity. Researchers analyzed sleep and dietary data from 15,000 adults, who enrolled in several cohort studies, and found that longer sleep duration in young adults was associated with a lower intake of saturated fatty acids, and a lower intake of carbohydrates in older women. The findings suggest that longer sleep duration may facilitate compliance with cardioprotective dietary and health recommendations. Genomic analyses of the study population suggest that some geographic variation in the analysis of dietary intake may be explained by genetic mutations that change the duration of circadian rhythm.

Key Components Found in Molecular Pathway Leading to Pulmonary Emphysema

microRNA

Pulmonary emphysema is a chronic inflammatory lung disease in which airflow becomes limited. Together with other forms of smoking-related chronic obstructive pulmonary disease (COPD), it represents the third leading cause of death in the U.S. NHLBI-funded researchers found that microRNAs (miRNAs) — lesser known partner molecules of DNA — are key components of the molecular pathway leading to pulmonary emphysema. The investigators specifically found that the miRNA known as miR-22 was essential for the development of emphysema resulting from inhalation of cigarette smoke or nanoparticulate carbon black. As mice deficient in miR-22 did not develop emphysema, the researchers concluded that a potentially effective therapy for pulmonary diseases, as well as other inflammatory diseases, might be selective inhibition of miR-22.

Nanoparticles Deliver Synthetic Nucleotide Analogs to Correct Cystic Fibrosis Mutation

F508del & PNAs

Cystic fibrosis (CF) is a life-threatening disorder caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene; the most common mutation is designated as F508del. NHLBI-funded investigators corrected F508del by using biodegradable polymer nanoparticles linked to synthetic nucleotide analogs, called peptide nucleic acids (PNAs), which are able to induce DNA repair at targeted sites. In vitro studies using human cells showed that the PNA nanoparticle corrected chloride ion flow, the dysfunction of which is a hallmark of CF. Furthermore, intranasal delivery into a CF mouse model produced CFTR gene correction in nasal epithelium as well as in the mouse lung. Results of this study suggest a possible role of PNA nanoparticles in direct in vivo repair of CFTR mutations in human CF.

Integrin Suppression Reduces Tissue Fibrosis

alpha V beta 1

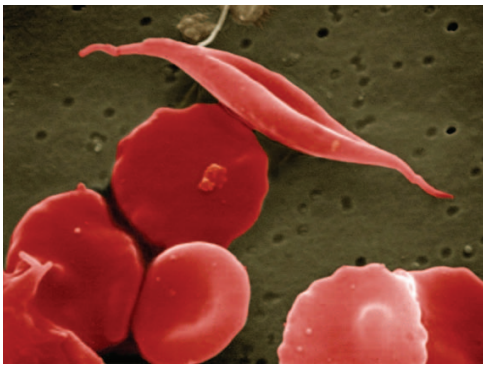
Integrins are transmembrane proteins that play roles in cell adhesion and tissue integrity. NHLBI-funded investigators designed and synthesized a small-molecule inhibitor of a little-studied integrin, called alpha V beta 1. They determined that this integrin can mediate activation of tissue growth factor beta, which is important in cell proliferation and differentiation, and that inhibition of the integrin suppressed the growth factor. Furthermore, the investigators looked at two models of chemically induced tissue fibrosis (formation of excess, scar-like tissue) in mice, bleomycin-induced pulmonary fibrosis and carbon tetrachloride-induced liver fibrosis, and found that inhibition of alpha V beta 1 reduced the amount of fibrosis in both cases. This study suggests that in some cases, inhibition of integrin by specifically designed small-molecule inhibitors might be useful for treatment of diseases characterized by fibrosis.

Science Advances in Blood Research

Scientists Take Another Step Forward in Gene Editing for Sickle Cell Disease

SCD & iPSCs

Sickle cell disease (SCD) affects 70,000 to 100,000 people in the U.S., causing extreme pain in the affected individuals and other serious conditions such infections, acute chest syndrome, and stroke. NHLBI-funded researchers have developed a method to target and correct the SCD gene mutation in patient-specific induced pluripotent stem cells (iPSCs) — stem cells created from adult cells that have been genetically reprogrammed to an embryonic stem cell–like state. The researchers were able to then transform the iPSCs into red blood cells with corrected copies of the SCD gene. During their study, they found that CRISPR/Cas9 — a tool for cutting and inserting small pieces of DNA at precise areas along a DNA strand — was more efficient than zinc finger nucleases and transcription activator-like effector nucleases, or TALENs. The researchers concluded that their study is a significant step toward the clinical use of genome editing using patient-derived iPSCs to produce disease-free cells for therapies.



Research Shows Hydroxyurea as Viable Treatment for Children With Sickle Cell Disease at Risk for Stroke

TWiTCH

Children with sickle cell disease live with an increased risk of stroke. Although standard treatment with regular blood transfusions has been an effective therapeutic option, health care providers have to monitor patients closely for iron overload. Results from the Transcranial Doppler With Transfusions Changing to Hydroxyurea (TWiTCH) study found that the drug hydroxyurea is as good as standard treatment for stroke prevention. The TWiTCH study was stopped early due to positive results.

Age of Transfused Blood Does Not Appear to Affect Results of Cardiac Surgery in Adults

RECESS

For years, doctors have wondered whether the length of time red blood cells are stored impacts a patient's clinical outcome after transfusion. Some studies suggested that red blood cells stored for longer periods have a decreased capacity to deliver oxygen to tissues and may adversely affect surgical patients. While addressing this medical mystery, an NHLBI-funded study found that the duration of red blood cell storage (age of transfused blood) appears to have no significant impact on the clinical outcome of adult patients undergoing cardiac surgery. The study, known as RECESS (Red Cell Storage Duration Study), evaluated 1,098 cardiac surgery patients who received either red blood cell transfusions with blood stored for short-terms (up to 10 days) or blood stored for longer periods (21 or more days). The researchers did not find any significant difference between the two groups in terms of changes in organ dysfunction (including the heart), adverse effects, or survival. The study results do not support the need to modify current transfusion practices in heart surgery, the researchers noted. The results provide a measure of reassurance that the age of transfused blood will not impact clinical outcomes in adult patients undergoing cardiac surgery, the authors noted.

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