NIAMS-FUNDED STUDY FINDS GUT MICROBES LINKED TO RHEUMATOID ARTHRITIS

The presence of a specific type of gut bacteria correlates with rheumatoid arthritis in newly diagnosed, untreated people. The finding suggests a potential role for the bacteria in this autoimmune disease.

Rheumatoid arthritis is a chronic inflammatory disorder that can cause pain, swelling, stiffness, and loss of function in the finger, wrist, and other joints. It occurs when the immune system mistakenly attacks the body’s own tissue, such as the membranes that line the joints.

The causes of rheumatoid arthritis aren’t completely known. Genes tied to the immune system may contribute. Environmental factors, such as cigarette smoking, diet and stress, may also play a role in triggering the disease. Treatments include medications to relieve pain and reduce inflammation.

The immune system is influenced by the microbiome, a network of microorganisms that live in and on the human body. These microbes outnumber the body’s cells by 10 to 1. Trillions of microbes—both helpful and harmful—reside in the digestive tract. The gut microbiome has been linked to arthritis in animal studies.

To see if these microbes might also be associated with rheumatoid arthritis in humans, Dr. Dan Littman of NYU School of Medicine led a team of researchers that examined DNA in 114 stool samples from both healthy people and those who had rheumatoid or psoriatic arthritis. The team identified gut bacteria by extracting DNA from the samples and then analyzing a bacteria-specific gene called the 16S ribosomal RNA gene.

The researchers found that 75% of people with new-onset, untreated rheumatoid arthritis had the bacterium Prevotella copri in their intestinal microbiome. In comparison, it was present in 12% of people with chronic, treated rheumatoid arthritis, 38% of people with psoriatic arthritis, and 21% of those in the control group. Increased levels of P. copri correlated with reductions in several groups of beneficial microbes, such as Bacteroides. The researchers performed more complete DNA sequencing on a subset of samples and identified unique Prevotella genes that correlated with rheumatoid arthritis.

To test whether P. copri could influence inflammation, the team administered the bacteria to healthy mice so that the bacteria became part of their gut microbiome. Mice were then given a chemical that induced colitis, a model of gut inflammation. Animals with P. copri developed more severe symptoms than the mice that hadn’t received the bacteria. The finding provides further evidence for a potential role for P. copri in inflammation.

“Our own results in mouse studies encouraged us to take a closer look at patients with rheumatoid arthritis, and we found this remarkable and surprising association,” Littman says. “At this stage, however, we cannot conclude that there is a causal link between the abundance of P. copri and the onset of rheumatoid arthritis. We are developing new tools that will hopefully allow us to ask if this is indeed the case.”

For more information, please click here.

“Our own results in mouse studies encouraged us to take a closer look at patients with rheumatoid arthritis, and we found this remarkable and surprising association.”
Focus on Rheumatology, Inflammation, Anesthesia, & Pain

UPDATES FROM NCATS

On January 16, 2014, the National Institutes of Health (NIH) held a joint meeting of the National Center for Advancing Translational Sciences (NCATS) Advisory Council and Cures Acceleration Network (CAN) Review board. This joint meeting featured presentations by NCATS leadership and invited guests. Presentations included a Director’s Report, a report from a CAN Review Board meeting on Flexible Research Authority, a portfolio analysis of current NCATS activities, an overview of advancements in rare disease research, and a discussion of pediatric study-researcher matching. Council subcommittees also reported on 1) patient engagement; 2) partnerships with pharmaceutical and biotechnology companies, and venture capital firms; and 3) medical technologies. For more information or a complete videocast of the meeting, please click here.

On February 28, 2014, the NIH will celebrate the seventh annual Rare Disease Day with a day-long celebration and recognition of the various rare diseases research activities supported by the NIH Office of Rare Diseases Research, the NIH Clinical Center, other NIH Institutes and Centers; the Food and Drug Administration’s Office of Orphan Products Development; other federal government agencies; the National Organization for Rare Disorders; and the Genetic Alliance. Attendance is free and open to the public.

In addition to the scheduled presentations, there will be Clinical Center tours as well as poster presentations and exhibits displayed by invited groups from the rare diseases research community. For more information, please click here.

JOINT MEETING OF THE ARTHRITIS ADVISORY COMMITTEE AND DRUG SAFETY AND RISK MANAGEMENT ADVISORY COMMITTEE

On February 10-11, 2014, the FDA will hold a joint meeting of the Arthritis Advisory Committee and Drugs Safety and Risk Management Advisory Committee.

The committees will discuss data and analyses published in 2006 or later that are relevant to further understanding the relationship between nonsteroidal anti-inflammatory drugs (NSAIDs) and cardiovascular thrombotic risk that is currently described in NSAID class labeling.

For more information on this meeting, including an agenda and briefing materials, please click here.

ANESTHESIOLOGY AND RESPIRATORY THERAPY DEVICES PANEL OF THE MEDICAL DEVICES ADVISORY COMMITTEE

On February 20, 2014, the Anesthesiology and Respiratory Therapy Devices Panel of the Medical Devices Advisory Committee will discuss, make recommendations, and vote on information related to the premarket approval application regarding the Inspire II Upper Airway Stimulator, sponsored by Inspire Medical Systems, Inc. The Inspire II Upper Airway Stimulator is a permanently implanted device intended to treat moderate to severe obstructive sleep apnea in patients who are not effectively treated by continuous positive airway pressure devices. The device stimulates the hypoglossal nerve synchronous with inspiration in order to contract the patient’s upper airway muscles and help maintain airway patency during sleep.

Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Written submissions may be made to the contact person on or before February 10, 2014. On February 20, 2014, oral presentations from the public will be scheduled between approximately 1 p.m. and 2 p.m. Those individuals interested in making formal oral presentations should notify the contact person and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time requested to make their presentation on or before January 31, 2014.

For more information on this meeting, including an agenda, briefing materials, and contact information, please click here.
NIAMS FUNDING ANNOUNCEMENTS

PAR-14-060  Pilot and Feasibility Clinical Research Grants in Arthritis and Musculoskeletal and Skin Diseases (R21) – November 4, 2014
PAR-13-382  Analysis of Genome-Wide Gene-Environment (G x E) Interactions (R21) – February 15, 2014
PAR-13-233  Chronic Inflammation and Age-related Disease (R01) – September 8, 2014
PA-12-132  Improving Translational and Basic Research to Control Itch in Humans (ITCH) (R21) – May 8, 2015
PA 12-019  Mechanisms Mediating Osteoarthritis in Aging (R01) – January 8, 2015

For more information or to find more funding opportunities, please click here.

NEW TECHNOLOGIES AVAILABLE FOR LICENSING FROM THE NIH OFFICE OF TECHNOLOGY TRANSFER

AAV-Aquaporin-1 Gene Therapy for Sjögren’s Syndrome
Sjögren's syndrome is a chronic inflammatory disease affecting over 2 million Americans, whereby moisture-producing glands are attacked by the body's immune system. The disease is marked by disabling dryness of the mouth and eyes as well as fatigue and pain. Researchers at the National Institute of Dental and Craniofacial Research have developed a therapy that alleviates xerostomia in an animal model of Sjögren's syndrome. This technology consists of local delivery of adeno-associated virus (AAV) mediated aquaporin-1 (AQP1) fusion protein to salivary glands. Using a murine model that mimics Sjögren's dry mouth symptoms, it was discovered that treatment restored salivary fluid movement upon expression of AQP1. Targeted delivery of the AAV-AQP1 system makes this invention a novel and potential long-term therapeutic for restoration of exocrine gland function and prevention of xerostomia-associated pain associated with Sjögren's syndrome.

Amelioration of Inflammatory Arthritis Targeting the Pre-ligand Assembly Domain (PLAD) of Tumor Necrosis Factor Receptors
The invention relates to compositions of matter and methods for treating arthritis by modulating Tumor Necrosis Factor Alpha (TNF-alpha) signaling. TNF-alpha plays a key role in the pathogenesis of numerous diseases including rheumatoid and septic arthritis, and other autoimmune and inflammatory diseases. TNF-alpha mediates its effects through receptors that contain a Pre-ligand Assembly Domain (PLAD). The inventors have discovered compounds that interfere with PLAD can block the effects of TNF-alpha in vitro. Treatment of mice with these compounds in vivo ameliorated disease in several models of arthritis. Therefore, the compositions and methods of the current invention may lead to novel arthritis treatments.

To learn more about these technologies and to find others available for licensing, please click here.

PATIENT ORGANIZATION EVENTS

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<th>American Academy of Pain Medicine</th>
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<td>59th Annual Update in Anesthesia</td>
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Click here for more details.
On November 6, Senators Robert Menendez (D-NJ) and Pat Toomey (R-PA) introduced S. 1658, the Start-up Jobs and Innovation Act. On January 28, Sen. Pat Roberts (R-KS) showed his support for this legislation by officially joining Sens. Menendez and Toomey as a co-sponsor. S. 1658 would modernize the U.S. tax code to encourage the private sector to invest in breakthrough research being conducted at growing biotechs and other innovative small businesses across the country.

Specifically, the legislation would relax the passive activity loss (PAL) limitations for R&D-focused pass-through entities. Under this bill, small innovative companies would be able to enter into a joint venture with an R&D project’s investors via R&D Partnership Structures. The losses and credits generated by the project would then flow through to the company and investors, who would be able to use the tax assets to offset other income.

A study commissioned by the Coalition of Small Business Innovators and conducted by Ernst & Young found that the R&D Partnership Structures proposal would increase investment by an estimated $10.3 billion per year, resulting in 156,000 additional jobs at affected companies.

The Start-up Jobs and Innovation Act also includes important reforms to the capital gains treatment of small business stock, as well as business expensing for growing companies and rules governing small firm accounting methods. In addition to making the permanent the provision in Section 1202 that allows investors to exclude from taxation 100% of their gain from the sale of qualified small business (QSB) stock held for at least five years, the bill would change the QSB definition by raising the gross assets limit to $150 million.

Improving the capital gains treatment and relaxing the PAL rules to allow investors to enjoy a more immediate return on their investment, despite the long and risky timeline usually associated with groundbreaking research, would incentivize them to invest at an earlier stage, when capital is most needed. By making targeted changes for small, R&D, intensive companies, the Start-up Jobs and Innovation Act would stimulate capital formation for growing innovative businesses and speed the development of groundbreaking technologies.

"Senators Menendez and Toomey have taken an important step to help drive the next generation of scientific advancement," said BIO President and CEO Jim Greenwood. "BIO supports this Act because it will encourage important investments, support vital research, and stimulate the U.S. economy."

To access the full text of the Start-up Jobs and Innovation Act, please click here; for a summary of the bill, click here.

On December 12, the Coalition of Small Business Innovators (CSBI) hosted “Promoting the Innovation Economy,” a policy forum on tax reform and innovation. The forum featured a discussion on the need to simplify the tax code and eliminate specific deductions and credits while simultaneously encouraging and supporting small business innovation, the potential for comprehensive tax reform in 2014, and recent legislative proposals.

The forum was moderated by Paul Stimers, Partner at K&L Gates, and panelists included: Doug Doerfler, President and CEO of MaxCyte; Ed Mathers, partner at New Enterprise Associates; Katherine Hamilton, Policy Director at the Energy Storage Association; and Darrell West, Vice President and Director of Governance Studies, Douglas Dillon Chair, and Founding Director of the Center for Technology Innovation at the Brookings Institution.

A complete broadcast of the forum, as well as selected highlights, can be viewed here. For more information on the Coalition of Small Business Innovators, please visit smallbusinessinnovators.org. The Coalition also has Facebook and Twitter accounts.
**BIO COMMENTS TO THE SEC ON TICK SIZE**

On January 31, the SEC’s Investor Advisory Committee (IAC) voted in favor of a recommendation that the SEC take no action to adopt a tick size pilot program. BIO provided comment to the SEC opposing the IAC’s recommendation and endorsing a tick size pilot program for growing companies.

BIO supports flexibility in tick size for smaller issuers in order to address the needs of growing companies hamstrung by decimalization. The SEC adopted decimalization in 2000, changing the standard tick to one cent. As large companies enjoyed an influx of new investors under the one-size-fits-all rule, small issuers experienced a corresponding decrease in liquidity. BIO supports a pilot program to allow growing issuers to choose larger trading increments (either $0.05 or $0.10) in order to support small company liquidity, stimulate job creation, and maintain the vital role that public financing plays in the ongoing search for lifesaving therapies.

To read BIO’s comment letter, please click [here](#). BIO has also [endorsed](#) legislation, the Small Cap Liquidity Reform Act, that would institute a tick size pilot program.

**SEC PROPOSES REGULATION A+ RULE**

On December 18, the SEC proposed a rule that would implement the reforms to Regulation A directed by the JOBS Act. The JOBS Act requires the SEC to create a new pathway, called Regulation A+ and modeled after the existing Regulation A, for offerings of up to $50 million – a significant increase from the $5 million limit under current law. The proposed rule would circumvent state regulatory authority for Regulation A+ offerings, an important provision that will simplify the registration process and keep growing issuers from being bogged down by 50 disparate regulatory regimes. BIO was a strong supporter of the Regulation A reforms authorized by the JOBS Act and will engage with the SEC to ensure that it effectively implements Regulation A+ to bolster emerging biotech capital formation.

**NASAA COORDINATED REVIEW PROPOSAL**

In November, BIO commented to the North American Securities Administrators Association (NASAA) on its proposed coordinated review program for Regulation A+ offerings conducted under the new rules authorized by the JOBS Act. If implemented the program could govern the review of offerings under the new Regulation A+, which will allow a raise of up to $50 million. NASAA’s proposed program could take effect if the SEC grants jurisdiction to the states. BIO is concerned that the cost burden associated with complying with 50 sets of state regulations could be prohibitive. BIO’s letter cautions NASAA to be mindful of the harm that costly regulations can cause for pre-revenue biotechs considering an offering.

To read BIO’s comment letter, please click [here](#).

**RHEUMATOLOGY / INFLAMMATION / ANESTHESIA / PAIN-FOCUSED LEGISLATION**

**H.R. 1366—Stop Oxy Abuse Act of 2013**  
Bill would the Commissioner of Food and Drugs (FDA), within 90 days, to take such actions as may be necessary to modify the approval of, and limit any subsequent approval of, any drug containing controlled-release oxycodeine.  
Status: Referred to the House Subcommittee on Health

**H.R. 1429—Scleroderma Research and Awareness Act of 2013**  
Bill amends the Public Health Service Act to authorize the NIH Director to expand, intensify, and coordinate NIH activities relating to scleroderma, with emphasis on research on etiology and development of new treatments.  
Sponsor: Rep. Lois Capps (CA-24)  
Status: Referred to the House Subcommittee on Health

**S. 557—Medication Therapy Management Empowerment Act of 2013**  
Bill would amend title XVIII (Medicare) of the Social Security Act to require CMS to provide a report to HHS and Congress on whether an expanded definition of targeted beneficiaries would reduce Medicare spending.  
Sponsor: Sen. Kay Hagan (NC)  
Status: Referred to the Committee on Finance
BIO has authored a white paper, “The Future Policy Landscape for Emerging Biotechnology Companies,” in an effort to highlight promising policy legislation and its impact on the biotech sector.

Innovative biotech companies are working toward creating the next breakthrough technology. Many of these innovative, research-intensive companies rely on private investment to support their groundbreaking R&D. Therefore, favorable legislation, such as the JOBS Act, is essential in fostering the biotech pipeline, which ultimately supports the next generation of breakthrough technologies. In addition to a strong policy landscape, a healthy public market is paramount to the success of the biotech industry, as growing innovators often turn to an IPO to fund late-stage clinical trials. BIO’s white paper discusses these issues as well as the key policies that could have a positive impact on the future of the biotech sector.

Please click here to access a copy of BIO’s white paper.

BIO Comments on Proposed PCAOB Accounting Rules

In December, BIO provided comment to the PCAOB urging it to reconsider its proposed audit rules that would substantially burden growing public biotech companies. The comment letter opposes the PCAOB’s recommendations to institute an onerous critical audit matters standard in small company audit procedures. BIO’s letter also urges the PCAOB and the SEC not to apply the proposed rule to the audits of emerging growth companies as defined by the JOBS Act.

To read BIO’s comment letter, please click here.