NIAMS-SUPPORTED STUDY FINDS PROTEIN’S ROLE IN RHEUMATOID ARTHRITIS-INDUCED BONE LOSS

Investigators supported in part by NIAMS have shown how a protein called RBP-J controls a pathway that promotes bone degradation, a common complication of rheumatoid arthritis. The study also revealed that decreased levels of RBP-J are linked to the disease and could partly underlie the associated bone loss. The findings, which appeared in the Journal of Clinical Investigation, suggest that targeting the RBP-J pathway could be an effective strategy for preserving bone in people with rheumatoid arthritis.

Research was led by Baohong Zhao, Ph.D., assistant professor at the Weill Medical College of Cornell University, focused on a protein called RBP-J. Earlier work in Dr. Zhao’s lab had shown that RBP-J was involved in suppressing the formation of osteoclasts and restraining bone erosion. Osteoclast maturation and activity are regulated by a complicated network of signaling pathways that fine-tune the rate and degree of bone degradation. Dr. Zhao’s team wondered if RBP-J controlled this process by interacting with a pathway named RANK, another pathway named ITAM, or both.

While the earlier studies had indicated that both the RANK and ITAM pathways must be active in osteoclast precursor cells before osteoclasts develop, some evidence suggested that the ITAM pathway was not always essential. In the current study, Dr. Zhao’s team discovered that RBP-J controls whether the ITAM pathway needs to be involved. Cells from mice lacking both RBP-J and certain ITAM molecules could produce osteoclasts when investigators activated the RANK pathway. In contrast, when the precursor cells contained RBP-J, RANK stimulation did not promote osteoclast formation unless the cells also could engage the ITAM pathway.

To assess if RBP-J deficiency is associated with rheumatoid arthritis, the investigators next compared RBP-J levels in osteoclast precursor cells from rheumatoid arthritis patients and healthy individuals. They saw significantly less RBP-J in the patients’ cells than in controls. This finding, together with genetic studies that linked certain variants of RBP-J to rheumatoid arthritis susceptibility, suggests that RBP-J could be a key factor in the disease.

To read more, click here.
**Focus on Rheumatology, Inflammation, Anesthesia, & Pain**

### Updates from NCATS

On May 15 and June 5, 2015, NCATS released two new Clinical and Translational Science Awards (CTSA) program funding opportunity announcements (FOAs), one for Recruitment Innovation Centers (RICs) and the other for Trial Innovation Centers (TICs). Both are aimed at overcoming key roadblocks to multisite clinical trials. CTSA hubs form a national network of medical research institutions that work together to improve the translational research process.

The purpose of the RICs is to increase the likelihood of success for multisite clinical trials in two ways: (1) by developing informatics-driven approaches to assessing the site-specific availability of potential participants during trial planning and (2) by developing innovative approaches to participant recruitment during trial implementation. For these five-year awards, NCATS plans to fund up to two RICs in FY 2016 with up to $3 million each in total costs. The two RIC centers will work together with individual CTSA hubs to ensure that informatics approaches used to conduct feasibility assessments accurately reflect the local electronic health record environment, and that the collaboratively developed recruitment strategies are well-aligned with the local CTSA ethical and regulatory environment. The National Library of Medicine will co-fund the RICs.

For more information on these funding opportunities, please click [here](#).

On September 3-4, 2015 the NIH will hold a joint meeting of the NCATS Advisory Council and Cures Acceleration Network (CAN). This meeting feature reports from NCATS Director Christopher P. Austin, M.D., and others about the Center’s initiatives, policies, programs and future direction.

For more information, please click [here](#).

### Upcoming Meetings

| **Anesthetic & Analgesic Drug Products Advisory Committee** |
|__________________________________________________________________________|
| **July 7-8, 2015** |
| **Cellular, Tissue and Gene Therapies Advisory Committee** |
| ____________________________________________________________________________|
| **September 17-19, 2015** |
| **November 17-18, 2015** |
| **Arthritis Advisory Committee** |
| ____________________________________________________________________________|
| **October 23, 2015** |

### Dermatologic and Ophthalmic Drugs Advisory Committee

On March 9 the committee met for a morning session to discuss new drug application (NDA) 206333, deoxycholic acid injection, a cytolytic drug, submitted by Kythera Biopharmaceuticals, proposed for the improvement in the appearance of moderate-to-severe convexity or fullness associated with submental fat in adults.

The committee also discussed pediatric development of systemic products for the treatment of atopic dermatitis with inadequate response to topical prescription therapy.

For more information about this meeting and meeting materials including agendas and briefing materials, please click [here](#).

### Anesthetic and Analgesic Drug Products Advisory Committee

On July 7, the committee will hold a joint meeting with the Drug Safety and Risk Management Advisory Committee.

The committees will discuss the results of post marketing studies evaluating the misuse and/or abuse of reformulated OXYCONTIN (oxycodone hydrochloride) extended-release tablets, supplemental new drug application (sNDA) 022272, manufactured by Purdue Pharma L.P. The committees will discuss whether these studies have demonstrated that the reformulated OXYCONTIN product has had a meaningful impact on abuse of OXYCONTIN.

For more information about this meeting, please click [here](#).

### Cellular, Tissue and Gene Therapies Advisory Committee and Oncologic Drugs Advisory Committee

On April 29, the committees met in a joint session to discuss talimogene laherparepvec, Amgen, Inc., BLA 125518, an oncolytic immunotherapy for the treatment of patients with injectable regionally or distantly metastatic melanoma.

Talimogene laherparepvec, is an attenuated replication-competent herpes simplex virus type 1 (HSV-1) that can constitutively express a biologically active form of human GMCSF, derived from a novel primary HSV-1 isolate that demonstrates enhanced oncolytic activity towards tumor cells, as compared to the commonly used laboratory strains and other primary isolates (Liu et al., 2003). To produce talimogene laherparepvec, the JS1 strain was genetically modified by deleting the virulence genes that code for ICP34.5 and ICP47.

For more information about this meeting and meeting materials including agendas and briefing materials, please click [here](#).
NIAMS FUNDING ANNOUNCEMENTS

PA-14-244 Research on Chronic Overlapping Pain Conditions (R01) - September 8, 2017
PAR-14-192 Exploratory Clinical Trial Grants in Arthritis and Musculoskeletal and Skin Diseases (R21) - March 2, 2017
PAR-15-146 Countermeasures Against Chemical Threats (CounterACT) Research Centers of Excellence (U54) - September 13, 2017
PAR-15-135 Advancing Mechanistic Probiotic/Prebiotic and Human Microbiome Research (R01) - May 8, 2018
PAR-15-165 NIAMS Clinical Trial Planning Cooperative Agreement (U34) - March 2, 2016

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

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

**Miniature System for Manipulating Small Animals in High-Throughput Screening Small Molecules**

The invention pertains to a miniaturized plating and feeding system based on a 96-well microplate base and is intended to reduce manipulation of organisms as well as amounts of test drug/anesthetic, thereby mitigating waste. The kit comprises a feeder plate, transfer adaptor and receiver plate. The feeder plate is defined by, for example, a plastic 96-well plate with rounded wells. The rounded bottoms can dispense to or permit access to the test organism of liquid food or drug through about 7 holes of approximately 350 microns in diameter. A top portion of the well provides test organisms (e.g., drosophila, daphnia) with sufficient space to enjoy normal life cycles without confinement stress. The feeder plate includes means for interfacing with complementary components of the transfer and receiver plates through receiving holes and complementary dowels or pins. A transfer adapter allows the interconnection of the feeder plate to the receiver plate. The transfer plate can be configured to be square or rounded for the transfer of organisms from the feeder plate to the receiver plate.

**LRKK2 Inhibitors: Novel Treatment for Intestinal Bowel Disorders**

Use of Leucine Rich Repeat Kinase 2 (LRRK2) inhibitors for the treatment of Intestinal Bowel Disorders (IBD) is disclosed. IBD is a broad term that describes conditions with chronic or recurring immune response and inflammation of the gastrointestinal tract. Crohn's disease and ulcerative colitis, two common forms of idiopathic IBD, are chronic, relapsing inflammatory disorders of the gastrointestinal tract. LRRK2 is a kinase encoded by a gene that contains a non-coding polymorphism (SNP). LRRK2 has been associated with and is a risk factor for inflammatory bowel disease. NIH inventors have shown that human cells expressing this SNP have increased levels of LRRK2 and, correspondingly, mice with increased levels of LRRK2 exhibit more severe Dextran Sulfate colitis. In various studies of the role of LRRK2 in cell signaling, NIH inventors have shown that increased levels of LRRK2 lead to increased pro-inflammatory cytokine secretion. Also, an inhibitor of LRRK2 is shown to abrogate the pro-inflammatory activity of LRRK2 both in vitro and in vivo.

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

PATIENT ORGANIZATION EVENTS

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**BIO TESTIFIES ON XBRL REFORM LEGISLATION; HOUSE COMMITTEE APPROVES BILL**

On April 29, BIO provided testimony before a hearing of the House Subcommittee on Capital Markets, titled *Legislative Proposals to Enhance Capital Formation and Reduce Regulatory Burdens*. BIO was represented at the hearing by Shane Kovacs, CFO of BIO Board Member PTC Therapeutics. The hearing was focused on a package of bipartisan legislation designed to support the growth of emerging companies on the public market.

In his testimony, Mr. Kovacs stressed the importance of a strong public market for biotech capital formation. He also discussed the detrimental impact that costly regulatory burdens can have on groundbreaking R&D by diverting capital from science to compliance. In particular, Mr. Kovacs spoke about the impact that compliance with the eXtensible Business Reporting Language (XBRL) reporting requirement can have on pre-revenue biotechs.

BIO supports H.R. 1965, the Small Company Disclosure Simplification Act, sponsored by Rep. Robert Hurt (R-VA). This bill would grant emerging growth companies and low-revenue issuers a temporary exemption from XBRL compliance, allowing them to focus investment capital on research rather than an ineffective reporting requirement that is unused by investors.

Following the hearing, at which Mr. Kovacs endorsed H.R. 1965, the House Financial Services Committee passed the Small Company Disclosure Simplification Act with a bipartisan 44-11 vote.

To read Mr. Kovacs’s testimony, please click [here](#).

**REPS. MEEHAN, NEAL, KELLY, KIND, & LARSON INTRODUCE PARTNER ACT**

On April 30, Reps. Patrick Meehan (R-PA), Richard Neal (D-MA), Mike Kelly (R-PA), Ron Kind (D-WI), and John Larson (D-CT) introduced H.R. 2179, the PARTNER Act. The bill 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.

The innovation incentives in the current tax code do not benefit not-yet-profitable companies – yet these companies are the heart of America’s innovation ecosystem. The PARTNER Act would incentivize investment in groundbreaking R&D being conducted at companies across the country. The PARTNER Act is critical to the continued vitality of next generation innovators and is a much-needed step to ensure that America maintains its place as a leader in the 21st century global economy.

To learn more about the PARTNER Act, please click [here](#).

**SEC FINALIZES TICK SIZE PILOT PROGRAM**

In May, the SEC approved a finalized version of a tick size pilot program that will begin on May 6, 2016. The pilot will test the impact of a $0.05 tick (an increase from the existing $0.01) on certain small company stocks. Eligibility for the pilot will be limited to companies with a market cap below $3 billion, an average daily trading volume of less than 1 million shares per day, and a share price above $2.

The pilot will last for two years and evaluate 1,200 companies. BIO has long been a supporter of increased trading increments for growing companies on the market, and we view this as a huge step toward that goal. BIO commented on the initial pilot proposal from the SEC and the national exchanges, and we will continue to engage with members and the SEC as the pilot start date approaches.

To learn more about the upcoming pilot program, please click [here](#).
**BIO Releases Emerging Company Financing Report**

On June 11, BIO released a new report – Emerging Therapeutic Company Investment and Deal Trends – highlighting ten years (2005-2014) of biotechnology funding and deal making across five areas: venture capital, IPOs, follow-on public offerings, licensing, and acquisitions. The report also offers a first-time look at the degree of collaboration across the industry’s clinical pipeline.

“Accessing capital and forming strategic alliances is vital to today’s emerging biotechnology companies in their search for cures and treatments for patients suffering from devastating and life-threatening diseases,” said Carter Esham, PhD, BIO’s Executive Vice President, Emerging Companies. “This data is helpful as we seek to improve our understanding of investor and deal making trends in order to inform future policy development activities intended to bolster the industry’s ability to develop the next generation of innovative medicines.”

Key findings include:
- A decade high in 2014 for US venture capital in Novel R&D lead programs. However, Series A investments went to fewer companies and with fewer dollars vs 2013. Additionally, some disease areas affecting large populations continue to see declines.
- A decade high in 2014 for U.S. emerging company IPOs.
- A decade high in 2014 for upfront payments in R&D-stage licensing deals.
- R&D-stage acquisition volume is returning to levels not seen since 2008.
- Nearly 70% of the industry clinical pipeline is attributed to small emerging companies. A significant portion of the emerging company pipeline (43%) is partnered.

To access a copy of BIO’s emerging company financing study, please click [here](#).

**SEC Finalizes Regulation A+ Rule**

On March 25, the SEC [issued a final rule](#) implementing the Regulation A changes directed by the JOBS Act. The rule took effect on June 20; companies are now able to conduct offerings of up to $50 million under the revised reporting and disclosure requirements of Regulation A+. Prior to the passage of the JOBS Act, Regulation A offerings were limited to $5 million. The new SEC rule creates a similar offering pathway, Regulation A+, for offerings of up to $50 million. Importantly, Regulation A+ offerings will not be subject to state-level securities law, but will instead be held to a single national standard of review.

Reforming Regulation A in order to make it a viable capital formation tool for emerging biotech companies has been a key advocacy priority for BIO. To read BIO’s comment letter to the SEC on its Regulation A+ proposal, click [here](#). To read BIO’s press release applauding the finalized rule, please click [here](#).

**BIO Provides Testimony for Senate Banking Hearing**

On March 24, the Senate Subcommittee on Securities, Insurance, and Investment held a hearing titled *Capital Formation and Reducing Small Business Burdens*. BIO provided testimony for the hearing supporting the Subcommittee’s efforts to enhance capital formation for growing companies. Specifically, BIO’s statement stressed the importance of a public market that supports capital formation while also reducing capital diversions from science to compliance. BIO also provided support for a number of specific bills, including reforms to the XBRL and SOX 404(b) compliance requirements.

For more information, please click [here](#).

**Rheum/Inflamm/Anesthesia/Pain-Focused Legislation**

**H.R. 2138—Medicare Access to Rural Anesthesiology Act**

This bill would amend the Social Security Act to provide payment under Medicare part A on a reasonable cost basis for anesthesia services furnished by a physician who is an anesthesiologist in certain rural hospitals.

- **Sponsor:** Rep. Lynn Jenkins (R-KS)
- **Status:** Referred to the House Committee on Ways and Means

**S. 1509—Treat and Reduce Obesity Act**

This bill would amend title XVIII of the Social Security Act to provide for the coordination of programs to prevent and treat obesity.

- **Sponsor:** Sen. Tom Carper (D-DE)
- **Status:** Referred to the Senate Committee on Finance
On May 21, BIO released the following statement regarding the approval of the 21st Century Cures Act by the House Energy and Commerce Committee:

"BIO is pleased that the legislation prioritizes placing patients at the center of the drug development process, which we believe will help spur the development of therapies for the most prevalent conditions, as well as encourage development of treatments focused on unmet medical needs. We strongly support establishing a framework for incorporating patient views into the development and regulatory review processes in a more structured and transparent way with respect to both patient input for benefit-risk assessments and use of patient experience data in regulatory decision-making.

"BIO supports modernizing clinical trials to expedite and accelerate drug development through the use of alternative clinical trial designs, biomarkers and surrogate endpoints, and modern scientific approaches and greater utilization of post-market validation and other confirmatory techniques, including the use of real-world data. We support enhancing the FDA’s scientific capacity by improving access to adequate funding. We especially note the important inclusion in this legislation of provisions to ensure privately-paid user fees to FDA are protected from the effects of any future sequestration.

"BIO looks forward to working with Chairman Upton and Rep. DeGette to ensure that the 21st Century Cures Initiative expedites the delivery of the next generation of modern medicines that will save lives and reduce and eliminate suffering."

For more information on the 21st Century Cures Act, please click here. To read BIO’s statement, please click here.

On June 5, BIO released the following statement regarding the mark-up of the PATENT Act:

"BIO appreciates the efforts of members of the Senate Judiciary Committee to include needed reforms to the PTO’s inter partes review (IPR) and post-grant review (PGR) proceedings, aimed at addressing our concerns about the basic fairness of these proceedings to patent owners. We remain committed to working with all Senators engaged in the process to include further IPR improvements necessary to ensure that the PATENT Act reflects an appropriate balance between the interests of those who seek to enforce patent rights and those who are accused of infringement.

"Biotechnology companies rely upon the strength of their patents to raise and invest the hundreds of millions of dollars needed to develop and bring to market the next generation of innovations. Without strong patent protections, revenue streams will dry up, degrading our industry’s ability to provide solutions to the most pressing medical, agricultural, industrial and environmental challenges the world faces."

To read BIO’s statement, please click here.