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By *Joanne Kotz, Senior Editor*

A California team has shown that monoacylglycerol lipase, which controls levels of a pain-reducing metabolite in the brain, also regulates neuroinflammation.¹ The researchers have proof of concept that a small molecule inhibitor of the target blocks inflammation and decreases neurodegeneration in a mouse model of Parkinson's disease, and they are now studying the compound in additional neurodegenerative and neurological diseases.

Newco **Abide Therapeutics** is exercising an option to license the monoacylglycerol lipase (MAGL) inhibitors.

MAGL is a serine hydrolase enzyme that degrades 2-arachidonoylglycerol (2-AG), a ligand of pain-relieving cannabinoid receptors in the brain. In 2008, a team led by Benjamin Cravatt identified a brain-permeable small molecule inhibitor of MAGL that causes 2-AG levels to increase in the brain, inducing analgesia in mice.²

Cravatt is chair of the Department of Chemical Physiology at **The Scripps Research Institute**.

At the time, Cravatt and collaborators observed that in addition to boosting 2-AG levels, MAGL inhibitors also triggered a decrease in brain levels of arachidonic acid, the precursor molecule to inflammatory prostaglandins.^{2,3} Phospholipase enzymes had previously been considered the principle regulators of arachidonic acid levels, and these observations suggested a link between MAGL activity and prostaglandin-mediated neuroinflammation.

Based on this, a team led by Cravatt and Daniel Nomura, an assistant professor in the Department of Nutritional Science and Toxicology at the **University of California, Berkeley**, has now looked more closely at the impact of blocking MAGL on brain inflammation.

In mice stimulated with lipopolysaccharide (LPS) to induce neuroinflammation, *Magl* deficiency or a MAGL inhibitor prevented increases in inflammatory prostaglandins and cytokines and blocked microglial activation compared with *Magl* expression or vehicle (see Figure 1, "Connecting cannabinoid and prostaglandin pathways").

Moreover, blocking *Magl* reduced LPS-stimulated increases in brain prostaglandin levels at least three-fold, whereas blocking

"Targeting MAGL might provide a combined pain and anti-inflammatory mechanism that could be interesting not only for PD but also for many other neurological diseases."

—*Johan Luthman, Merck & Co. Inc.*

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cPLA₂- α (phospholipase A₂ group IVA cytosolic calcium-dependent; PLA₂g4a), which is a known regulator of prostaglandin production in neuroinflammation, only resulted in an approximately 20% decrease in LPS-induced prostaglandins.

In a mouse model of neurotoxin-induced Parkinson's disease (PD), the MAGL inhibitor reduced neuroinflammation and dopaminergic neurodegeneration compared with vehicle.

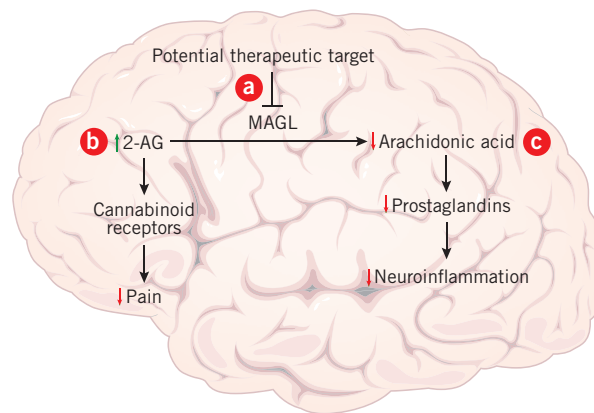
Finally, the team asked whether MAGL also controlled inflammation in peripheral tissues. In LPS-treated mice, Magl regulated prostaglandin levels in the liver and lung, whereas cPLA₂- α controlled levels in the gut and spleen. Neither Magl nor cPLA₂- α regulated prostaglandin production in the heart and kidney.

Results were published in *Science*.

"It's been thought since the early 1900s that phospholipases dominate the production of arachidonic acid," said Nomura. It now appears there are tissue-specific mechanisms that control production, he added.

Casting a MAGL net

The work "opens up another angle to approach inflammation in the brain," said Johan Luthman, leader of the Early Development Neuroscience and Ophthalmology Franchise at **Merck & Co. Inc.** "Targeting MAGL might provide a combined pain and

**Figure 1. Connecting cannabinoid and prostaglandin pathways.**

A team led by researchers from **The Scripps Research Institute** and the **University of California, Berkeley** have shown that monoacylglycerol lipase (MAGL), which controls levels of a pain-reducing metabolite in the brain, also regulates neuroinflammation. Thus, blocking MAGL could provide a therapeutic benefit in neurodegenerative disorders characterized by neuroinflammation.

Previous work from Scripps had shown that in mice, a small molecule inhibitor of MAGL [a] increased the levels of 2-arachidonoylglycerol (2-AG) in the brain, which acted through the cannabinoid receptors to decrease pain [b]. The team has now shown that in a mouse model of neuroinflammation, inhibiting MAGL lowers the production of arachidonic acid to decrease levels of inflammatory prostaglandins and blunt inflammation in the brain [c].

In a mouse model of neurotoxin-induced Parkinson's disease (PD), a MAGL inhibitor reduced neuroinflammation and dopaminergic neurodegeneration compared with vehicle.

anti-inflammatory mechanism that could be interesting not only for PD but also for many other neurological diseases.”

The weakness of the paper is the use of an acute, neurotoxin-based PD model, said Luthman. He noted that results from this model have not translated well into the clinic and suggested the authors should test MAGL inhibitors in newer PD models, such as the so-called MitoPark mouse, which better recapitulates the chronic neurodegeneration of the human disease.

Whether neuroinflammation is a cause or a symptom in PD and other chronic neurodegenerative diseases is still unclear, added Luthman. “The general idea is that neuroinflammation is a contributor and not causative, although this can be debated.”

Thus, Luthman said it is more likely that a MAGL inhibitor would improve symptoms but not affect the underlying disease process.

Luthman told *SciBX* that MAGL inhibitors also could be interesting to test in multiple sclerosis (MS), in which “the ongoing brain and spinal cord inflammation not only leads to physical disability but also commonly to sensory problems and pain.” Compared with current anti-inflammatory approaches, “the interesting angle is that this is a more brain-specific pathway,” he said.

The California team now is looking at the effects of MAGL inhibitors in genetic models of PD, as well as in MS and Alzheimer’s disease (AD) models, said Nomura.

He added that the team also would like to explore the therapeutic potential of blocking MAGL in acute neurological diseases. “An interesting avenue may be stroke or brain injury, where you could simultaneously enhance cannabinoid and decrease prostaglandin signaling in an acute treatment regimen.”

“An interesting avenue may be stroke or brain injury, where you could simultaneously enhance cannabinoid and decrease prostaglandin signaling in an acute treatment regimen.”

—Daniel Nomura,
University of California, Berkeley

Given MAGLs involvement in liver and lung inflammation, Nomura said inhibitors might also have a therapeutic benefit in fibrosis of those tissues.

Scripps holds patents on the MAGL inhibitor used in the *Science* paper. Abide Therapeutics, which was cofounded in 2011 by Cravatt to develop serine hydrolase inhibitors, is exercising its exclusive option to license patents covering MAGL inhibitors, according to CEO Alan Ezekowitz. “The MAGL program

is the most advanced program, and the company intends to explore MAGL inhibitors in the treatment of pain, neuroinflammation and potentially neurodegenerative diseases like Parkinson’s disease,” said Ezekowitz.

Kotz, J. *SciBX* 4(45); doi:10.1038/scibx.2011.1254
Published online Nov. 17, 2011

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SEMA4D in osteoporosis

By Lauren Martz, Staff Writer

Researchers from the **Tokyo Medical and Dental University** have shown that inhibition of the protein semaphorin 4D increases bone formation in a mouse model of osteoporosis.¹ By directly promoting bone formation, a semaphorin inhibitor could be more effective than existing osteoporosis therapies that work by preventing bone loss.

The semaphorins are a large class of membrane proteins that play a role in the CNS as axon guidance molecules. Semaphorins also have been implicated in immune cell function, tumor progression and tumor angiogenesis.²⁻⁴

In addition, studies have suggested that one of the semaphorins, semaphorin 4D (SEMA4D), plays a role in signaling between osteoclasts and osteoblasts,⁵ the two cell types that drive bone resorption and bone formation.

Thus, Hiroshi Takayanagi and colleagues at the Tokyo Medical and Dental University hypothesized that targeting SEMA4D could have a therapeutic effect in osteoporosis, which is caused by an imbalance in the activity of osteoclasts and osteoblasts. Takayanagi is a professor in the Department of Cell Signaling.

The researchers first looked at semaphorin expression in the osteoclasts and osteoblasts of healthy mice and found that *Sema4d* levels were greater in osteoclasts than levels of other semaphorin family members.

Based on that finding, the researchers created *Sema4d* knockout mice to better understand the function of the protein in bone remodeling. In those animals, bone volume, trabecular thickness and bone strength were higher than those in wild-type mice, suggesting that the presence

Figure 1. SEMA4D released by osteoclasts blocks osteoblast formation. Whereas most osteoporosis drugs on the market work by curbing the destruction of bone, inhibiting semaphorin 4D (SEMA4D) could go a step further and promote bone growth.

SEMA4D is expressed on osteoclasts as a transmembrane protein, which is released upon activation by proteolytic cleavage [a]. Active SEMA4D binds plexin B1 (PLXNB1) on the osteoblast surface [b]. PLXNB1 forms a complex with HER2 (EGFR2; ERBB2; neu), causing ERBB2 autophosphorylation and activation. ERBB2 activation then causes PLXNB1 phosphorylation (P).

Rho guanine exchange factors (RhoGEFs) bind to and are activated by phosphorylated PLXNB1 [c]. RhoGEFs activate Ras homolog gene family member A (RHOA), which induces RHOA-Rho-associated coiled-coil containing protein kinase (ROCK) signaling [d]. The activated RHOA-ROCK pathway inhibits phosphorylation of insulin receptor substrate 1 (IRS1) by the insulin receptor (INSR), which prevents downstream synthesis of insulin-like growth factor-1 (IGF-1) and ultimately prevents osteoblast differentiation and proliferation [e]. Activated proteins are indicated by an asterisk.

“Therefore, it is expected that blocking SEMA4D would be a direct and efficient way to treat bone loss.”

—Atsushi Kumanogoh,
Osaka University Graduate School
of Medicine

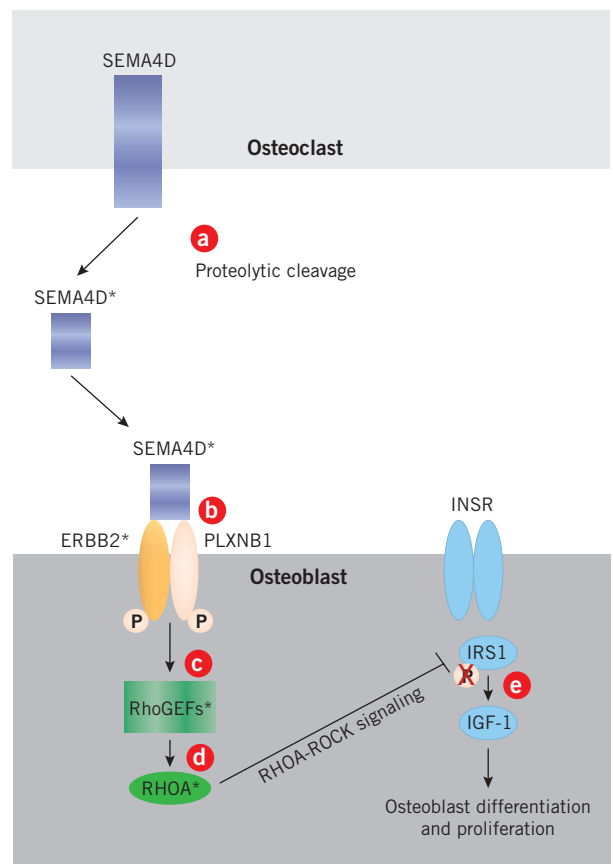
of *Sema4d* in osteoclasts serves to suppress bone formation.

Subsequent mouse studies fleshed out a mechanism: osteoclast-derived *Sema4d* binds its receptor, plexin B1 (Plxnb1), on osteoblasts, which then decreases osteoblast motility and ultimately inhibits bone formation (see Figure 1, “SEMA4D released by osteoclasts blocks osteoblast formation”).

The real question for the researchers was whether blocking *Sema4d* would trigger bone formation and treat osteoporosis. In an ovariectomized mouse model of postmenopausal osteoporosis, an anti-*Sema4d* mAb protected against bone loss by promoting bone formation compared with saline control. The antibody was given both prophylactically and therapeutically.

Results were published in *Nature Medicine*. The paper also included researchers from **The University of Tokyo**, the **Mount Sinai School of Medicine** and **The University of Western Australia**.

“Existing strategies to treat bone loss are indirect—they suppress functions of osteoclasts, which absorb bone, resulting in increased bone mass,” said Atsushi Kumanogoh, professor and chair of the Department of Respiratory Medicine, Allergy and Rheumatic Diseases at the **Osaka University Graduate School of Medicine**. By contrast, he said, blocking SEMA4D promotes the activity of osteoblasts, which form bones, directly increasing bone mass. “Therefore, it is expected that blocking SEMA4D would be a direct and



efficient way to treat bone loss.”

The only marketed osteoporosis drug that acts by increasing bone formation rather than preventing bone loss is parathyroid hormone (PTH). **Eli Lilly and Co.** markets Forteo teriparatide, an injectable recombinant PTH fragment.

Takeda Pharmaceutical Co. Ltd.’s **Nycomed** subsidiary markets Preotact recombinant PTH (NPSP558) in Europe. The hormone is in registration in the U.S. under the name Preos by **NPS Pharmaceuticals Inc.**, which developed the drug and licensed rights to Nycomed.

Good to the bone

Takayanagi said his team plans to study anti-SEMA4D antibodies in arthritis and bone

metastasis. He added that the researchers will look closely at any side effects related to the immune system.

“SEMA4D plays important roles in the immune system, and a lack of SEMA4D results in immunodeficiency. Therefore, too much blocking of SEMA4D may affect the immune system,” said Takayanagi.

He noted that SEMA4D is recognized by a different receptor, CD74, in immune cells than in osteoblasts, which have PLXNB1. “It may be a good strategy to develop antibodies or small molecules that specifically block the interaction between SEMA4D and plexin B1,” he said.

Takayanagi told *SciBX* that the Tokyo Medical and Dental University has filed a patent application for bone-forming agents targeting SEMA4D and PLXNB1. The IP is available for licensing.

Vaccinex Inc. has a humanized anti-SEMA4D mAb in Phase I testing in cancer, and the company plans to begin an additional Phase I study

in multiple sclerosis (MS) next year.

“The Vaccinex anti-SEMA4D antibody has been shown to have potent anti-inflammatory as well as antiangiogenic and antimetastatic activity in animal disease models,” said President and CEO Maurice Zauderer. “Extending development to osteoporosis is an interesting opportunity, which, because of the need to score relatively low-frequency bone fractures as the major clinical endpoint, would be a major undertaking.” He said that based on the endpoints, a large clinical trial would be required in order to accrue a significant number of events.

Zauderer said the company does not have current plans to move into osteoporosis.

Martz, L. *SciBX* 4(45); doi:10.1038/scibx.2011.1255
Published online Nov. 17, 2011

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Cancer matchmaker

By Lev Osherovich, Senior Writer

As pharma increasingly look to offload early stage R&D expenses, **Cancer Research Technology Ltd.**, the commercial arm of biomedical charity **Cancer Research UK**, has seen more uptake of its partnered consortium model for commercializing the discoveries of its stable of academic researchers. This year, Cancer Research Technology has expanded its anchor collaboration with **AstraZeneca plc** by brokering two more deals between the pharma and academic teams.

CRT brings together researchers across the U.K. with similar interests and organizes them into teams to work on specific discovery projects, said CSO Clive Stanway. CRT's academic consortia focus on mechanisms in cancer that are potentially targetable but require additional tool building and proof-of-concept work before entering pharma pipelines.

Each consortium consists of academic researchers at four to six laboratories across the U.K. "We pick leaders and work with them to create plans and select other team members. There's a joint management team, and CRT has rights to the IP that comes out," said Stanway.

"We aim to have four or five consortia going at any given time," added CEO Keith Blundy. "Some of these projects might be about validating a target, some might be about medicinal chemistry."

Discovery work is done primarily at team member institutions. CRT provides administrative support and technical services such as medicinal chemistry on an as-needed basis. CRT is putting about \$1 million into each consortium to cover at least 2 years of work.

According to Blundy, CRT wants to be a one-stop shop for pharma and biotechs seeking expertise and services in the cancer space. In exchange for upfront cash, a company receives the right of first refusal to new IP emerging from a given consortium.

In effect, the consortia serve as outsourced R&D units for pharma. This arrangement "aligns well with current pharma strategy to externalize research activity but retain access to early research, keeping an eye on a mix of projects in a variety of areas," said Blundy.

AstraZeneca is the first pharma to come on board. In 2010, AstraZeneca and CRT launched a jointly funded, three-year discovery-stage collaboration in cancer metabolism. Work on that project is underway at CRT's Discovery Laboratories facilities in London and Cambridge and at AstraZeneca's facility in Cheshire.

This year, the company signed deals with two CRT-managed academic research consortia focused on tumor cell senescence and lipid metabolism.

Essence of senescence

The first of AstraZeneca's 2011 CRT deals was with **Senectus Therapeutics Ltd.**, an academic consortium that spun out into a company. Senectus is seeking ways to trigger senescence or nonapoptotic growth arrest in tumor cells.

Senectus had its origins as a CRT-managed collaboration between researchers at the **University of Glasgow**, the **University of London**, **Cold Spring Harbor Laboratory** and research tool developer **Horizon Discovery Ltd.** In 2009, Senectus was incorporated. The company has since raised £1.2 million (\$2 million) from CRT.

"Cell senescence is a normal process that's a barrier to cancer

development. It limits the growth of normal cells," said consortium leader W. Nicol Keith, a professor of molecular oncology at University of Glasgow. "Senescent cells don't die, but they don't divide. Cancer cells have latent senescent signaling, but it's either not at a high enough level or it's not engaging the final steps. We want to force cancer cells to reengage the senescence program."

Senectus is screening for markers of senescence in tumor cells, potentially targetable pathways and, with AstraZeneca's help, small molecules that hit undisclosed targets involved in senescence.

Keith said it is difficult to clearly define which cells in a tumor are undergoing senescence, thus making it hard to screen for agents that induce the process. The partnership with AstraZeneca provided access to the pharma's compound library, which Keith said allowed Senectus to validate its proposed screening strategy using newly identified markers.

"There was initially a barrier to convincing pharma that senescence was interesting, so we needed to generate the evidence," said Keith. After gaining access to AstraZeneca's small molecule library, "we showed them that we could get something sensible using their own reagents and they came on board."

Accelerated metabolism

In September, AstraZeneca and CRT assembled an academic research consortium focused on abnormal lipid metabolism in tumor cells.

That team is headed by Eyal Gottlieb, professor of molecular cell biology at **The Beatson Institute for Cancer Research**, and includes researchers at the **University of Oxford**, the **Babraham Institute**, **Imperial College London** and Cancer Research UK's **London Research Institute**.

"Rapidly growing cancer cells need to build a lot of lipids for cell membranes and organelles," said Gottlieb. The consortium aims to identify the specific lipids that are aberrantly produced in tumor cells and to find targets involved in their biosynthesis.

CRT and AstraZeneca each invested £300,000 (\$476,500) to fund discovery-stage work for 2 years, with AstraZeneca retaining right of first refusal to new discoveries.

A third CRT-managed consortium launched in January and is unpartnered. It is focused on cancer stem cells and received £500,000 (\$794,000) from CRT. That team is led by Fiona Watt, professor of molecular genetics and deputy director of Cancer Research UK's **Cambridge Research Institute**.

Osherovich, L. *SciBX* 4(45); doi:10.1038/scibx.2011.1256

Published online Nov. 17, 2011

COMPANIES AND INSTITUTIONS MENTIONED

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Babraham Institute, Cambridge, U.K.

The Beatson Institute for Cancer Research, Glasgow, U.K.

Cambridge Research Institute, Cambridge, U.K.

Cancer Research Technology Ltd., London, U.K.

Cancer Research UK, London, U.K.

Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.

Horizon Discovery Ltd., Cambridge, U.K.

Imperial College London, London, U.K.

London Research Institute, London, U.K.

Senectus Therapeutics Ltd., London, U.K.

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MD Anderson's private screening

By Kai-Iye Lou, Staff Writer

Less than two years after **The University of Texas MD Anderson Cancer Center** carved up the IP for its *in vivo* phage display screening platform, the two biotech licensees have preclinical proof-of-concept data and preliminary patient validation for products based on the technology. **Alvos Therapeutics Inc.** is now determining optimal peptide-payload combinations for use in cancer, while **Ablaris Therapeutics Inc.** is developing follow-on formulations of its lead compound for obesity-related indications.

MD Anderson spent more than a decade developing its *in vivo* patient-based screening platform.¹ The technology involves injecting terminally ill cancer patients with a large-scale phage display library of peptides that circulate for a short time before life support is terminated. Follow-up biopsies and phage rescue reveal which peptides home to which tissues and the receptors the peptides bind.

Peptides significantly enriched in diseased tissues could be used to deliver a therapeutic payload to those tissues. According to Alvos COO Pete Leone, screening in patients is important because, unlike conventional screening platforms, it can determine whether a target is on the surface or inside of a human cell. This is difficult to determine with proteomic approaches and cadaveric tissue samples, he said.

Late last month, the MD Anderson group published a study in the *Proceedings of the National Academy of Sciences* that provided additional human validation for the screening platform licensed to Alvos and Ablaris.² The study identified two ligand-receptor pairs common to the vasculature of multiple human tissues and a pair specific to bone metastases.

The study also provided mechanistic and functional validation for the target of Ablaris' lead compound adipotide, a peptidomimetic consisting of a prohibitin 1 (PHB; PHB1)-targeting peptide coupled to a proapoptotic helical peptide that disrupts mitochondrial membranes. The researchers found an annexin A2 (ANXA2)-PHB ligand-receptor pair specific to the vasculature for normal white adipose tissues and showed that the targeting peptide domain of PHB mimicked a region on ANXA2.

This month, the academics published in *Science Translational Medicine* that adipotide caused weight loss and increased insulin resistance in obese nonhuman primates.³

The two studies were co-led by Renata Pasqualini and Wadih Arap, who are both professors in the Department of Genitourinary Medical Oncology at MD Anderson and cofounders of Alvos and Ablaris.

Ablaris in obesity

In the *Science Translational Medicine* study, the MD Anderson researchers showed that obese nonhuman primates receiving

daily adipotide injections for 28 days had lower body weight, BMI, abdominal circumference and total body fat percentage than controls given saline ($p < 0.0001$ for all). Adipotide also improved insulin resistance compared with saline ($p = 0.006$).

"The biggest impact of the *Science Translational Medicine* study is in demonstrating the pharmacological efficacy of our lead compound in a primate system," said James Hulvat, director of R&D at Ablaris and coauthor on the paper. "Most drug candidates in our space fail when going from rodents to humans or other primates because the physiology of food intake and metabolism are very different."

Because white adipose tissue produces factors that can promote prostate cancer growth,^{4,5} MD Anderson has submitted an IND for a Phase I trial of adipotide in obese men with castration-resistant prostate cancer. The center plans to start patient recruitment early next year.

In this trial, Hulvat expects adipotide will be dosed daily for 28 days via subcutaneous injection.

Ablaris is taking a different tack with the molecule and is developing adipotide as a lead-in therapy to treat morbidly obese patients planning to undergo bariatric surgery. The compound is in preclinical development for the indication.

According to Hulvat, a decrease in body weight prior to bariatric surgery is associated with a decrease in surgery-related complications and mortality.⁶

The dosing schedule for the MD Anderson-sponsored trial would not be

optimal for broader obesity-related indications, and as a result Ablaris also is developing follow-on formulations of adipotide.

The goal, said Hulvat, will be formulations that could be dosed weekly or given as a subdermal implant. The company also is working to broaden adipotide's therapeutic index by improving the adipotide-receptor interaction to increase potency and by altering the compound's renal clearance to decrease toxicity risk.

The company hopes to submit an IND for a follow-on adipotide formulation in late 2012 or early 2013.

Parent company **Arrowhead Research Corp.** launched Ablaris in December 2010 to commercialize the technology licensed from MD Anderson. Arrowhead holds a majority stake in Ablaris.

Alvos in oncology

While Ablaris is focused on obesity, Alvos is using peptides identified with the MD Anderson screening platform to target therapeutic payloads to cancer cells. The company also is using the platform to identify additional targeting peptides and their corresponding receptors.

Alvos was founded in July 2010 as Mercator Therapeutics. The following month, the biotech closed a \$2 million venture round and announced the licensing deal with MD Anderson.

Alvos' programs include peptides that target IL-11 receptor, heat shock 70 kDa protein 5 (glucose-regulated protein, 78 kDa; HspA5; GRP78) and v-crk sarcoma virus CT10 oncogene homolog (avian)-like (CRKL). Leone said Alvos is determining the optimal peptide-payload combinations for various tumor types and is about two years away

"We'll provide the molecule that gets the payload to the target cells, and our partners in these other spaces will provide the payload they wish to deliver."

—Pete Leone, Alvos Therapeutics Inc.

from starting a clinical trial.

The company's plan is to run side-by-side comparisons to show that linking approved and new cancer drugs to Alvos' targeting peptides will improve safety and efficacy.

Alvos' rights to the MD Anderson technology include all indications outside weight loss and obesity-related conditions. Leone said the biotech is in early discussions with two companies for candidate homing peptides that could be useful in cardiovascular diseases and in a muscle wasting disorder.

"We'll provide the molecule that gets the payload to the target cells, and our partners

in these other spaces will provide the payload they wish to deliver," he told *SciBX*. "We've also identified several candidate peptides that could be useful for delivering a therapeutic payload across the blood brain barrier and another that could potentially deliver compounds to pancreatic cells."

According to Leone, the MD Anderson group has discovered peptides that home specifically to about 30 different tissues and their corresponding receptors.

"The biggest impact of the *Science Translational Medicine* study is in demonstrating the pharmacological efficacy of our lead compound in a primate system."

—James Hulvat,
Ablaris Therapeutics Inc.

Lou, K.-J. *SciBX* 4(45); doi:10.1038/scibx.2011.1257

Published online Nov. 17, 2011

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e-mail: rpasqual@mdanderson.org
Contact: Richard L. Sidman, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Mass.
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Contact: Renata Pasqualini, University of Texas MD Anderson Cancer Center, Houston, Texas
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Contact: Wadih Arap, same affiliation as above
e-mail: warap@mdanderson.org
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COMPANIES AND INSTITUTIONS MENTIONED

Ablaris Therapeutics Inc., Pasadena, Calif.
Alvos Therapeutics Inc., Wellesley, Mass.
Arrowhead Research Corp. (NASDAQ:ARWR), Pasadena, Calif.
The University of Texas MD Anderson Cancer Center, Houston, Texas

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SciBX: Science–Business eXchange

This week in therapeutics

THE DISTILLERY brings you this week's most essential scientific findings in therapeutics, distilled by *SciBX* editors from a weekly review of more than 400 papers in 41 of the highest-impact journals in the fields of biotechnology, the life sciences and chemistry. The Distillery goes beyond the abstracts to explain the commercial relevance of featured research, including licensing status and companies working in the field, where applicable.

This week in therapeutics includes important research findings on targets and compounds, grouped first by disease class and then alphabetically by indication.

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Autoimmune disease				
Osteoarthritis (OA)	Complement 5 (C5)	<p>Mouse and human studies suggest inhibiting C5 could help treat OA. In the synovial fluid of patients with OA, levels of C5 and other complement system proteins were greater than those in the synovial fluid of healthy controls. In three mouse models of knee OA, C5 knockout or an anti-C5 mAb decreased signs of disease and increased joint function compared with wild-type C5 expression or inactive control mAbs. Ongoing work includes investigating the mechanisms by which the complement system becomes activated in OA and testing inhibitors of the mechanisms in animal models.</p> <p>Soliris eculizumab, a humanized mAb targeting C5 from Alexion Pharmaceuticals Inc., is approved to treat hemolytic uremic syndrome and paroxysmal nocturnal hemoglobinuria (PNH).</p> <p>ARC1905, an anti-C5 aptamer from Archemix Corp. and Ophthotech Corp., is in Phase I testing to treat age-related macular degeneration (AMD).</p> <p>SciBX 4(45); doi:10.1038/scibx.2011.1258 Published online Nov. 17, 2011</p>	Patented by Stanford University; available for licensing	<p>Wang, Q. <i>et al. Nat. Med.</i>; published online Nov. 6, 2011; doi:10.1038/nm.2543</p> <p>Contact: William H. Robinson, Stanford University School of Medicine, Stanford, Calif. e-mail: wrobins@stanford.edu</p>
Rheumatoid arthritis (RA)	Integrin α_9	<p>Studies in mice suggest antagonizing integrin α_9 could help treat RA. In a mouse model of RA, an anti-integrin α_9 mAb lowered production of the proinflammatory cytokine IL-17 and the severity of RA symptoms compared with control mAbs. Next steps include producing a humanized version of the anti-integrin α_9 mAbs and testing them in nonhuman primate models of inflammatory and autoimmune diseases.</p> <p>SciBX 4(45); doi:10.1038/scibx.2011.1259 Published online Nov. 17, 2011</p>	Patent pending; available for licensing	<p>Kanayama, M. <i>et al. J. Immunol.</i>; published online Oct. 28, 2011; doi:10.4049/jimmunol.1101524</p> <p>Contact: Toshimitsu Uede, Hokkaido University, Sapporo, Japan e-mail: toshi@igm.hokudai.ac.jp</p>
Cancer				
Cancer	Angiopoietin-like 2 (ANGPTL2)	<p>Mouse studies suggest inhibiting ANGPTL2 could help treat cancer. Tissues from mice with chemically induced squamous cell carcinoma (SCC) had greater levels of the inflammatory mediator Angptl2 than tissues before chemical treatment. In mice with SCC, <i>Angptl2</i> knockout suppressed tumor formation, eliminated metastasis to the lung and decreased metastasis to the lymph nodes compared with what was seen in wild-type mice. Next steps could include developing an ANGPTL2 inhibitor.</p> <p>SciBX 4(45); doi:10.1038/scibx.2011.1260 Published online Nov. 17, 2011</p>	Patent and licensing status unavailable	<p>Aoi, J. <i>et al. Cancer Res.</i>; published online Oct. 31, 2011; doi:10.1158/0008-5472.CAN-11-1758</p> <p>Contact: Yuichi Oike, Kumamoto University, Kumamoto, Japan e-mail: oike@gpo.kumamoto-u.ac.jp</p>

This week in therapeutics (continued)

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Cancer	EGF-like-domain multiple 7 (EGFL7)	<p>Studies in mice suggest inhibiting EGFL7 could help treat cancer. In mice with xenograft breast cancer cells overexpressing Egfl7, tumor growth and metastasis were greater than those in mice that had cancer cells with normal Egfl7 expression. Next steps could include developing Egfl7 inhibitors and testing the molecules <i>in vivo</i>.</p> <p>RG7414, an anti-EGFL7 antibody from Roche, is in Phase I trials to treat solid tumors.</p> <p>SciBX 4(45); doi:10.1038/scibx.2011.1261 Published online Nov. 17, 2011</p>	Patent application filed; available for licensing	<p>Delfortrie, S. <i>et al. Cancer Res.</i>; published online Oct. 28, 2011; doi:10.1158/0008-5472.CAN-11-1301</p> <p>Contact: Fabrice Soncin, Centre National de la Recherche Scientifique (CNRS), Lille, France e-mail: fabrice.soncin@ibl.fr</p>
Cancer	Proteasome	<p><i>In vitro</i> and mouse studies identified a small molecule proteasome inhibitor that could help treat cancer. <i>In vitro</i>, the small molecule b-AP15 bound to the regulatory 19S subunit of the proteasome and blocked its deubiquitinating activity. In four xenograft mouse models of solid tumors, b-AP15 decreased tumor growth compared with vehicle control. In a mouse model of acute myelogenous leukemia (AML), b-AP15 induced remission in 8 of 10 mice, whereas vehicle did not induce remission. Next steps include lead optimization.</p> <p>Takeda Pharmaceutical Co. Ltd. and Johnson & Johnson market Velcade bortezomib, a proteasome inhibitor, to treat multiple myeloma (MM) and mantle cell lymphoma (MCL).</p> <p>Carfilzomib, a proteasome inhibitor from Onyx Pharmaceuticals Inc. and Ono Pharmaceutical Co. Ltd., is in Phase III testing to treat MM and Phase II trials to treat solid tumors.</p> <p>SciBX 4(45); doi:10.1038/scibx.2011.1262 Published online Nov. 17, 2011</p>	Patent application filed; licensed to Vivolux AB	<p>D'Arcy, P. <i>et al. Nat. Med.</i>; published online Nov. 6, 2011; doi:10.1038/nm.2536</p> <p>Contact: Stig Linder, Karolinska Institute, Stockholm, Sweden e-mail: stig.linder@ki.se</p>
Cancer	Pyruvate kinase M2 isozyme (PKM2)	<p>Mouse and cell culture studies suggest PKM2 activators could block an antioxidant mechanism to help treat cancer. In human lung cancer cell lines, a small molecule PKM2 activator increased oxidative stress-induced cell death compared with vehicle. Next steps could include testing PKM2 activators in models of cancer with high levels of oxidative stress.</p> <p>Agios Pharmaceuticals Inc. has a discovery program targeting PKM2 to treat cancer.</p> <p>Dynamix Pharmaceuticals Ltd.'s DNX-3000, a fructose bisphosphate mimetic that activates PKM2, is in preclinical development to treat cancer.</p> <p>SciBX 4(45); doi:10.1038/scibx.2011.1263 Published online Nov. 17, 2011</p>	Patent and licensing status unavailable	<p>Anastasiou, D. <i>et al. Science</i>; published online Nov. 3, 2011; doi:10.1126/science.1211485</p> <p>Contact: Lewis C. Cantley, Beth Israel Deaconess Medical Center, Boston, Mass. e-mail: lewis_cantley@hms.harvard.edu</p>

This week in therapeutics (continued)

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Gastric cancer	Focal adhesion kinase (FAK); Src	<p>Cell culture studies suggest the <i>Enterolobium contortisiliquum</i>-derived trypsin inhibitor EcTI could help treat gastric cancer. In human gastric cancer cell lines, EcTI inhibited Src-FAK signaling and decreased migration and invasion compared with vehicle. Next steps include evaluating the cytotoxicity of EcTI.</p> <p>Sprycel dasatinib, a small molecule inhibitor of BCR-ABL tyrosine kinase and Src from Bristol-Myers Squibb Co. and Otsuka Pharmaceutical Co. Ltd. is marketed to treat acute lymphoblastic leukemia (ALL) and chronic myelogenous leukemia (CML).</p> <p>Bosutinib, a dual inhibitor of BCR-ABL tyrosine kinase and Src kinase from Pfizer Inc., is under review for CML.</p> <p>At least five other companies have compounds targeting Src or FAK in Phase I trials or earlier to treat cancer.</p> <p>SciBX 4(45); doi:10.1038/scibx.2011.1264 Published online Nov. 17, 2011</p>	Patented; available for licensing	<p>de Paula, C.A.A. <i>et al. J. Biol. Chem.</i>; published online Oct. 28, 2011; doi:10.1074/jbc.M111.263996</p> <p>Contact: Maria Luiza V. Oliva, Federal University of Sao Paulo, Sao Paulo, Brazil e-mail: olivaml.bioq@epm.br</p>
Pancreatic cancer	Transforming growth factor- β (TGFB; TGF β) pathway; hedgehog pathway	<p>A study in mice suggests combined inhibition of the hedgehog and TGFβ pathways could increase the efficacy of pancreatic cancer chemotherapy.</p> <p>In xenograft mice with pancreatic cancer cells, a combination of small molecule inhibitors of both pathways plus the chemotherapeutic gemcitabine decreased tumor growth and levels of cancer stem cells compared with gemcitabine alone. Next steps include screening for inhibitors that target receptors upstream of TGFβ.</p> <p>SciBX 4(45); doi:10.1038/scibx.2011.1265 Published online Nov. 17, 2011</p>	Patent application filed; available for licensing	<p>Lonardo, E. <i>et al. Cell Stem Cell</i>; published online Nov. 4, 2011; doi:10.1016/j.stem.2011.10.001</p> <p>Contact: Christopher Heeschen, Spanish National Cancer Research Centre (CNIO), Madrid, Spain e-mail: christopher.heeschen@cnio.es</p>
Prostate cancer	Thrombospondin-1 (TSP-1; THBS1)	<p><i>In vitro</i>, mouse and human studies suggest that inhibiting the antiangiogenic protein TSP-1 could help treat castration-resistant prostate cancer (CRPC). In patient samples, high TSP-1 mRNA levels in tumor tissue were associated with recurrence. In mice bearing xenograft CRPC tumors, small interfering RNA against TSP-1 decreased tumor growth compared with untargeted siRNA. Ongoing work includes investigating the association between early expression of TSP-1 and tumor progression in animal models and patients.</p> <p>Tasquinimod (ABR-215050), a second-generation linomide that agonizes TSP-1 from Active Biotech AB, is in Phase III testing to treat metastatic CRPC.</p> <p>SciBX 4(45); doi:10.1038/scibx.2011.1266 Published online Nov. 17, 2011</p>	Patented by the Centre National de la Recherche Scientifique (CNRS) and SeleXel; available for licensing or partnering	<p>Firlej, V. <i>et al. Cancer Res.</i>; published online Oct. 28, 2011; doi:10.1158/0008-5472.CAN-11-0833</p> <p>Contact: Florence Cabon, Institut National de la Santé et de la Recherche Médicale (INSERM), Toulouse, France e-mail: florence.cabon@inserm.fr</p>
Renal cancer	Colony-stimulating factor 1 receptor (CSF1R; C-FMS; CD115)	<p>Studies in patient samples and in mice suggest inhibiting CSF1R could help treat renal cell carcinoma (RCC). In renal biopsy samples, CSF1R expression was greater in RCC tissue than in normal kidney tissue. In a mouse model of RCC, a CSF1R inhibitor decreased macrophage infiltration and tumor growth compared with vehicle control. Next steps include testing the safety of CSF1R inhibition and comparing its effectiveness with that of other cancer therapies.</p> <p>PLX5622, a small molecule CSF1R inhibitor from Daiichi Sankyo Co. Ltd., is in Phase I testing to treat rheumatoid arthritis (RA).</p> <p>SciBX 4(45); doi:10.1038/scibx.2011.1267 Published online Nov. 17, 2011</p>	Unpatented; licensing status unavailable	<p>Menke, J. <i>et al. Cancer Res.</i>; published online Nov. 3, 2011; doi:10.1158/0008-5472.CAN-11-1232</p> <p>Contact: Julia Menke, Johannes Gutenberg University Mainz, Mainz, Germany e-mail: menkj005@gmx.de</p>

This week in therapeutics (continued)

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Cardiovascular disease				
Angina; myocardial infarction (MI); heart failure	Aldehyde dehydrogenase 2 family mitochondrial (ALDH2)	Rat studies suggest an ALDH2 activator plus nitroglycerin could help treat cardiac indications more safely than nitroglycerin alone. Continuous use of nitroglycerin leads to inactivation of ALDH2 and nitroglycerin tolerance. In rats with induced MI, those that had received sustained delivery of nitroglycerine plus an ALDH2 activator had smaller infarct size and greater cardiac function than rats that had received sustained delivery of nitroglycerine alone. Next steps could include testing ALDH2-activating compounds in patients typically given nitroglycerin. Aldea Pharmaceuticals Inc. is working to optimize their lead ALDH2 activator, dubbed Alda1. SciBX 4(45); doi:10.1038/scibx.2011.1268 Published online Nov. 17, 2011	Patented; available for licensing through Aldea Pharmaceuticals	Sun, L. <i>et al. Sci. Transl. Med.</i> ; published online Nov. 2, 2011; doi:10.1126/scitranslmed.3002067 Contact: Daria Mochly-Rosen, Stanford University School of Medicine, Stanford, Calif. e-mail: mochly@stanford.edu Contact: Lihan Sun, same affiliation as above e-mail: lsun1219@gmail.com Contact: Julio Cesar Batista Ferreira, same affiliation as above e-mail: juliof@stanford.edu
Endocrine/metabolic disease				
Obesity	Prohibitin 1 (PHB; PHB1)	Nonhuman primate studies suggest a PHB1-binding peptidomimetic called adipotide could help treat obesity. In obese primates, daily adipotide injections lowered body weight, abdominal circumference and total body fat percentage compared with saline injections ($p < 0.0001$). Adipotide also improved insulin resistance compared with saline ($p = 0.006$). Next steps include evaluating adipotide in a Phase I trial. The Ablaris Therapeutics Inc. subsidiary of Arrowhead Research Corp. is running preclinical studies of adipotide in weight loss- and obesity-related metabolic conditions (<i>see MD Anderson's private screening, page 7</i>). SciBX 4(45); doi:10.1038/scibx.2011.1269 Published online Nov. 17, 2011	Patents issued and pending; licensed to Ablaris Therapeutics	Barnhart, K.F. <i>et al. Sci. Transl. Med.</i> ; published online Nov. 9, 2011; doi:10.1126/scitranslmed.3002621 Contact: Renata Pasqualini, The University of Texas MD Anderson Cancer Center, Houston, Texas e-mail: rpasqual@mdanderson.org Contact: Wadih Arap, same affiliation as above e-mail: warap@mdanderson.org
Hematology				
Bleeding; hemophilia	Factor IX	Mouse studies identified two human recombinant full-length factor IX variants that could be better than wild-type factor IX at treating bleeding disorders such as hemophilia. In two mouse models of bleeding disorders, vector-induced expression of either recombinant factor IX variant decreased clotting times and blood loss compared with expression of wild-type factor IX. Next steps include evaluating the effects of delivering the factor IX variants without using gene transfer approaches. BeneFIX, a recombinant coagulation factor IX from Pfizer Inc., is marketed to treat hemophilia. IB1001, a recombinant coagulation factor IX from Inspiration Biopharmaceuticals Inc., is under review for the same indication. At least five other companies have compounds targeting or based on factor IX in Phase III trials or earlier to treat hemophilia. SciBX 4(45); doi:10.1038/scibx.2011.1270 Published online Nov. 17, 2011	Patent application filed covering use in bleeding disorders; licensed to an undisclosed company; some applications still available for licensing	Milanov, P. <i>et al. Blood</i> ; published online Oct. 26, 2011; doi:10.1182/blood-2011-05-353672 Contact: Jörg Schütrumpf, Johann Wolfgang Goethe University, Hessen, Germany e-mail: j.schuettrumpf@blutspende.de

This week in therapeutics (continued)

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Hematology	Hepcidin antimicrobial peptide (HAMP); solute carrier family 40 iron-regulated transporter member 1 (SLC40A1; SLC11A3)	<i>In vitro</i> and mouse studies suggest HAMP mimics could help treat hereditary hemochromatosis (HHC) and other iron-overload diseases. <i>In vitro</i> and computational studies identified small HAMP peptides and peptidomimetics (minihepcidins) as HAMP agonists. In a Hamp-deficient mouse model of HHC, one minihepcidin prevented iron overload in the liver compared with vehicle. Future studies could include testing the minihepcidins in mouse models of β thalassemia.	Patent and licensing status unavailable	Preza, G.C. <i>et al. J. Clin. Invest.</i> ; published online Nov. 1, 2011; doi:10.1172/JCI57693 Contact: Elizabeta Nemeth, University of California, Los Angeles, Calif. e-mail: enemeth@mednet.ucla.edu
SciBX 4(45); doi:10.1038/scibx.2011.1271 Published online Nov. 17, 2011				
Infectious disease				
Cytomegalovirus (CMV)	Bone marrow stromal cell antigen 2 (BST2; CD317)	<i>In vitro</i> studies suggest inhibiting BST2 could help treat CMV infection. In BST2-expressing human fibroblasts and endothelial cells, CMV entry and infection were greater than those in non-BST2-expressing controls. In primary BST2-expressing human peripheral blood monocytes, BST2 knockdown lowered CMV entry and infection compared with wild-type BST2 expression. Planned work includes testing BST2 inhibition in a macaque model of CMV infection.	Unpatented; available for partnering	Viswanathan, K. <i>et al. PLoS Pathog.</i> ; published online Nov. 3, 2011; doi:10.1371/journal.ppat.1002332 Contact: Klaus Früh, Oregon Health & Science University, Beaverton, Ore. e-mail: Fruehk@ohsu.edu
SciBX 4(45); doi:10.1038/scibx.2011.1272 Published online Nov. 17, 2011				
Influenza virus	Fc fragment of IgG receptor transporter- α (FCGRT; FCRN); influenza A virus hemagglutinin (HA)	<i>In vitro</i> and mouse studies identified an intracellular transport mechanism required for antibody-mediated influenza protection. In influenza virus-infected canine kidney cells expressing rat Fcrn, an anti-HA antibody inhibited viral fusion with intracellular envelope proteins and decreased viral load 100-fold compared with IgG control. Wild-type mice receiving an anti-HA antibody were protected against lethal influenza infection, whereas Fcrn knockout mice were not. Next steps include testing whether the mechanism applies to other infectious pathogens. Vaxart Inc.'s ND1, a vaccine expressing influenza A HA, is in Phase I testing. VaxInnate Corp.'s VAX125, an influenza vaccine linking HA to flagellin, is in Phase II testing.	IP disclosure filed with the University of Maryland Office of Technology Commercialization; available for licensing	Bai, Y. <i>et al. Proc. Natl. Acad. Sci. USA</i> ; published online Oct. 31, 2011; doi:10.1073/pnas.1115348108 Contact: Xiaoping Zhu, University of Maryland, College Park, Md. e-mail: xzhu1@umd.edu Contact: Pamela J. Björkman, California Institute of Technology, Pasadena, Calif. e-mail: bjorkman@caltech.edu
SciBX 4(45); doi:10.1038/scibx.2011.1273 Published online Nov. 17, 2011				
SARS-associated coronavirus	Cyclophilin	<i>In vitro</i> studies suggest cyclosporine A derivatives could help treat coronaviruses such as SARS. In a binding assay, human cyclophilins bound the coronavirus nonstructural protein 1 and helped upregulate the calcineurin pathway, which is involved in SARS pathogenesis. In a human cell line infected with the SARS coronavirus, cyclosporine A inhibited cyclophilin and blocked viral replication compared with no treatment. Next steps could include developing cyclosporine A analogs. At least four companies have cyclophilin inhibitors in clinical and preclinical testing for infectious diseases.	Findings unpatented; unavailable for licensing	Pfefferle, S. <i>et al. PLoS Pathog.</i> ; published online Oct. 27, 2011; doi:10.1371/journal.ppat.1002331 Contact: Albrecht von Brunn, Ludwig Maximilian University of Munich, Munich, Germany e-mail: vonbrunn@mvp.uni-muenchen.de Contact: Christian Drosten, University of Bonn, Bonn, Germany e-mail: drosten@virology-bonn.de Contact: Jürgen Haas, The University of Edinburgh, Edinburgh, U.K. e-mail: juergen.haas@ed.ac.uk
SciBX 4(45); doi:10.1038/scibx.2011.1274 Published online Nov. 17, 2011				

This week in therapeutics (continued)

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Staphylococcus	<i>S. aureus</i> pyruvate kinase	<i>In vitro</i> studies suggest bisindole alkaloids could help treat methicillin-resistant <i>S. aureus</i> (MRSA). Screening a library of extracts from marine invertebrates identified bisindole alkaloids as inhibitors of MRSA pyruvate kinase. <i>In vitro</i> , the inhibitors were active against methicillin-sensitive and -resistant strains of <i>S. aureus</i> with MICs of 6–12 µg/mL. Next steps could include optimizing the potency of the compounds. SciBX 4(45); doi:10.1038/scibx.2011.1275 Published online Nov. 17, 2011	Patent and licensing status unavailable	Zoraghi, R. <i>et al. J. Biol. Chem.</i> ; published online Oct. 26, 2011; doi:10.1074/jbc.M111.289033 Contact: Neil E. Reiner, The University of British Columbia, Vancouver, British Columbia, Canada e-mail: ethan@interchange.ubc.ca
Inflammation				
Inflammation	IL-17; IL-17 receptor (IL17R; IL17RA); IL-25 (IL-17E)	Cell culture and mouse studies suggest that a cell-permeable decoy peptide that binds IL17RA could help treat inflammation. In cell culture, the peptide bound IL17RA and inhibited IL-17 and IL-25 signaling compared with vehicle. In mice, the peptide reduced IL-17- and IL-25-induced pulmonary inflammation compared with a scrambled control peptide. Next steps could include testing the peptide in additional models of inflammatory disease. Secukinumab, a human mAb targeting IL-17 from Novartis AG, is in Phase III and Phase II testing for multiple autoimmune diseases. At least 10 other companies have IL-17-targeting compounds in Phase II trials or earlier to treat autoimmune diseases and inflammation. SciBX 4(45); doi:10.1038/scibx.2011.1276 Published online Nov. 17, 2011	Patent and licensing status unavailable	Liu, C. <i>et al. Sci. Signal.</i> ; published online Nov. 1, 2011; doi:10.1126/scisignal.2001843 Contact: Xiaoxia Li, Cleveland Clinic, Cleveland, Ohio e-mail: lix@ccf.org
Neurology				
Nerve damage	PTEN (MMAC1; TEP1); suppressor of cytokine signaling 3 (SOCS3)	Mouse studies suggest combined inhibition of PTEN and SOCS3 could help promote regeneration following nerve damage. In a mouse model of optic nerve injury, co-deletion of <i>Pten</i> and <i>Socs3</i> increased axon regeneration compared with deletion of either gene alone ($p < 0.001$). Next steps include developing strategies to promote functional integration of the regenerating axons and developing compounds that inhibit PTEN and SOCS3 signaling. SciBX 4(45); doi:10.1038/scibx.2011.1277 Published online Nov. 17, 2011	Patent application filed covering use in promoting neuronal survival and regeneration; licensing status undisclosed	Sun, F. <i>et al. Nature</i> ; published online Nov. 6, 2011; doi:10.1038/nature10594 Contact: Zhigang He, Children's Hospital Boston, Mass. e-mail: zhigang.he@childrens.harvard.edu
Transplantation				
Transplantation	Intercellular adhesion molecule-1 (ICAM-1; CD54)	<i>In vitro</i> , mouse and nonhuman primate studies suggest an anti-ICAM-1 antibody could help prevent transplant rejection. In diabetic, humanized mice, an anti-ICAM-1 antibody induced T cell tolerance toward the porcine islet antigens and prevented rejection of porcine islet xenografts compared with IgG control. In a nonhuman primate model of diabetes, the anti-ICAM-1 antibody induced T cell tolerance to porcine islet xenografts and prolonged graft survival when given in combination with regulators of B cell activation. Next steps could include additional studies to understand the mechanism of action. At least three companies have inhibitors of ICAM-1 in preclinical to Phase II testing to treat cancer and inflammatory indications. SciBX 4(45); doi:10.1038/scibx.2011.1278 Published online Nov. 17, 2011	Patent and licensing status unavailable	Jung, K.C. <i>et al. J. Exp. Med.</i> ; published online Oct. 24, 2011; doi:10.1084/jem.20111242 Contact: Seong Hoe Park, Seoul National University, Seoul, South Korea e-mail: pshoe@snu.ac.kr

This week in techniques

THE DISTILLERY brings you this week's most essential scientific findings in techniques, distilled by *SciBX* editors from a weekly review of more than 400 papers in 41 of the highest-impact journals in the fields of biotechnology, the life sciences and chemistry. The Distillery goes beyond the abstracts to explain the commercial relevance of featured research, including licensing status and companies working in the field, where applicable.

This week in techniques includes findings about research tools, disease models and manufacturing processes that have the potential to enable or improve all stages of drug discovery and development.

Approach	Summary	Licensing status	Publication and contact information
Chemistry			
Gram-scale preparation of paclitaxel precursors for synthesis of taxane analogs	Gram-scale synthesis of two paclitaxel precursor molecules could enable discovery of biologically active taxanes. An 8-step reaction sequence produced gram-scale quantities of the paclitaxel precursor taxadienone with an overall yield of 20%. An additional 3-step reaction sequence produced gram-scale quantities of taxadiene from taxadienone with an overall yield of 52%. Planned work includes the synthesis of paclitaxel and other taxanes from taxadienone. SciBX 4(45); doi:10.1038/scibx.2011.1279 Published online Nov. 17, 2011	Unpatented; unlicensed	Mendoza, A. <i>et al. Nat. Chem.</i> ; published online Nov. 6, 2011; doi:10.1038/nchem.1196 Contact: Phil Baran, The Scripps Research Institute, La Jolla, Calif. e-mail: pbaran@scripps.edu
Drug platforms			
Target-specific, near-infrared photoimmunotherapy to treat cancer	Mouse studies suggest near-infrared photoimmunotherapy could be used to treat cancer. A near-infrared dye was conjugated to the epidermal growth factor receptor 1 (EGFR1; HER1; ERBB1)-targeting mAb Vectibix panitumumab or to the HER2 (EGFR2; ERBB2; neu)-targeting mAb Herceptin trastuzumab. In mice with HER1- and HER2-positive tumors, the resulting dye-mAb conjugates plus near-infrared irradiation decreased tumor volume compared with conjugates delivered without irradiation. Next steps include toxicology studies and GMP production of the conjugates. Vectibix panitumumab is marketed by Amgen Inc. and Takeda Pharmaceutical Co. Ltd. to treat metastatic colorectal cancer. Herceptin trastuzumab is marketed by Roche's Genentech Inc. unit to treat breast and gastric cancers. SciBX 4(45); doi:10.1038/scibx.2011.1280 Published online Nov. 17, 2011	Patent application filed; unlicensed	Mitsunaga, M. <i>et al. Nat. Med.</i> ; published online Nov. 6, 2011; doi:10.1038/nm.2554 Contact: Hisataka Kobayashi, National Institutes of Health, Bethesda, Md. e-mail: kobayash@mail.nih.gov
Instrumentation			
Intra-arterial catheter for <i>in vivo</i> microstructural and molecular imaging	Tissue sample and rabbit studies suggest an intra-arterial catheter capable of molecular imaging could improve diagnosis and prognosis of cardiovascular diseases such as atherosclerosis. The catheter was designed to collect 2D and 3D imaging data. In a cadaver implanted with a coronary artery stent, the catheter produced images of the vasculature. In a rabbit model of atherosclerosis, the catheter imaged atherosclerotic plaques. Next steps could include evaluating the catheter for imaging vasculature in large animal models. SciBX 4(45); doi:10.1038/scibx.2011.1281 Published online Nov. 17, 2011	Patent application filed; available for licensing	Yoo, H. <i>et al. Nat. Med.</i> ; published online Nov. 6, 2011; doi:10.1038/nm.2555 Contact: Guillermo J. Tearney, Massachusetts General Hospital, Boston, Mass. e-mail: gtearney@partners.org

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