Mutations in a gene called XRCC2 cause increased breast cancer risk, according to a study in the American Journal of Human Genetics. The study looked at families with a history of the disease but do not have mutations in currently known breast cancer susceptibility genes.

“We have added to the list of genes that harbour mutations causing breast cancer,” said Dr. Sean Tavtigian. “This knowledge will improve breast cancer diagnostics and add years to patients’ lives. More important, relatives who have not been affected by the disease but carry the mutations will benefit even more. They can find out they are at risk before they have cancer and take action to reduce their risk or catch the cancer early.”

XRCC2 may also provide a new target for chemo. “A type of drug called a PARP inhibitor appears to kill tumor cells that have gene mutations in a particular DNA repair pathway. XRCC2 is in this pathway, as are BRCA1 and BRCA2. It’s reasonably likely that a breast cancer patient who has a mutation in XRCC2 will respond well to treatment with PARP inhibitors,” said Tavtigian.

Many breast cancer cases appear in families with a weak history of the disease. Only about 30% of the familial risk for breast cancer can be explained by a combination of mutations to & common sequence variation in the known breast cancer susceptibility genes. “So far most of the clinical diagnostic effort has been directed toward the very strong family history set of breast cancer cases and their close relatives,” he says. “Our research looks at a population with a weaker family history, and as it turns out, a very rare gene mutation.”

The researchers used a technology called exome capture massively parallel sequencing, which shows the exact order of the nucleotides in all of the protein coding genes in the human genome. The ability of technology to analyze DNA of all of the genes in the genome in a single experiment, makes it an amazingly powerful tool for genetic research.

“We focused on the genes involved in a particular type of DNA repair, because most known breast cancer genes have been found there. That analysis allowed us to identify XRCC2 as a breast cancer susceptibility gene in individuals with a family history of breast cancer,” says Tavtigian. “From the exome sequencing data, we found two different types of XRCC2 mutations that occur in breast cancer patients.”

He explains that one type of mutation causes the gene to create an incomplete version of the protein. The resulting protein is usually dysfunctional. The other type occurs when a single amino acid in the protein is changed. “It’s a subtle change to the protein, but the resulting change in function could range anywhere from innocuous to even worse dysfunction than the incomplete protein causes.”

For more information on this research, click [here](#).
N C I  F U N D I N G  A N N O U C E M E N T S

PAR-12-140, Role of the Microflora in the Etiology of Gastro-Intestinal Cancer (R01) – July 2, 2012
PAR-12-095, Basic Cancer Research in Cancer Health Disparities (U01) – June 20, 2012
PA-12-108, Assays for High Throughput Screening (HTS) to Discover Chemical Probes in the Molecular Libraries Probe Production Centers Network (MLPCN) (X01) – August 15, 2012
PAR-12-039, Small Grants Program for Cancer Epidemiology (R03) – July 17, 2012
PA-12-136, Translational Research at the Aging/Cancer Interface (TRACI) (R01) – June 5, 2012
PA-11-152, The Role of Microbial Metabolites in Cancer Prevention and Etiology (U01) – November 15, 2012
PA-11-297, Pilot studies in Pancreatic Cancer (R21)– June 16, 2012
PA-11-158, Biomarkers of Infection-Associated Cancers (R01) – June 5, 2012
PA-11-073, Mitochondria in Cancer Epidemiology, Detection, Diagnosis and Prognosis (R01) – June 5, 2012

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

A D V I S O R Y  C O M M I T T E E  M A R C H  M E E T I N G S

On March 20, ODAC met to discuss sNDA 022465/S-010, trade name Votrient (pazopanib hydrochloride) tablets, application submitted by GlaxoSmithKline. The proposed indication is for treatment of patients with advanced soft tissue sarcoma who have received prior chemotherapy.

The committee also discussed NDA 022576, with the proposed trade name Taltorvic (ridaforolimus) tablets, application submitted by Merck. The proposed indication is for treatment of adult & pediatric patients with metastatic soft tissue sarcoma or bone sarcoma as a maintenance therapy.

On March 21, the committee discussed NDA 202497, proposed trade name Marqibo (vincristine sulfate liposomes injection), application submitted by Talon Therapeutics. The proposed indication is for the treatment of adult patients with Philadelphia Chromosome-negative acute lymphoblastic leukemia in 2nd or greater relapse or whose disease has progressed following 2 or more treatment lines of anti-leukemia therapy.

On March 20, ODAC met to discuss supplemental biologics license application 125320/28 for XGEVA (denosumab) injection, application submitted by Amgen Inc. The proposed indication for this product is for the treatment of men with castrate-resistant prostate cancer at high risk of developing bone metastases, or spread of cancer to the bones. (For minutes, click here.)

On March 21, the committee discussed supplemental new drug application (sNDA) 21790/010 for Dacogen (decitabine) for injection, application submitted by Eisai Inc. The proposed indication for this product is for the treatment of acute myelogenous leukemia in adults 65 years of age or older who are not considered candidates for induction chemotherapy. (For minutes, click here.)

A D V I S O R Y  C O M M I T T E E  F E B R U A R Y  M E E T I N G S

On February 8, ODAC met to discuss supplemental February 8-9
March 20-21
June 20-21
July 24-25
September 12-13
November 6-7
December 4-5
On December 23, 2011, President Obama signed into law the Consolidated Appropriations Act, which appropriated funds for various federal agencies, including the National Institutes of Health (NIH). Included in NIH’s $30.690 billion budget authority was an appropriation of $576.5 million for the newly-authorized National Center for Advancing Translational Sciences (NCATS). The goal of the Center is to work in partnership with the public and private sectors to develop innovative ways to overcome obstacles in the translational science pipeline.

NCATS unifies certain existing NIH programs to accomplish these goals, including the Clinical and Translational Science Awards, the Office of Rare Diseases and Research, the Therapeutics for Rare and Neglected Diseases (TRND) program, the Bridging Interventional Development Gaps program, and the NIH Chemical Genomics Center. NCATS will also develop the Cures Acceleration Network (CAN), which was authorized in 2010 and recently appropriated $10 million in new funds to help bridge the “valley of death” between basic and clinical research.

**MUC-1 Tumor Antigen Agonist Epitopes for Enhancing T-cell Responses to Human Tumors**

The C-terminus region of MUC-1 (MUC-1C) has been shown to be an oncogene & has been associated with a more aggressive phenotype in several different cancers. Scientists at NIH have identified 7 new agonist epitopes of MUC-1 tumor associated antigen. Peptides reflecting these agonist epitopes have been shown to enhance the generation of human tumor cells, which have a greater ability to kill human tumor cells endogenously expressing the native MUC-1 epitope. The technology encompasses the use of these agonist epitopes in peptide- & protein-based vaccines, with dendritic cells or other antigen presenting cells, or encoding sequences in DNA, viral, bacterial, yeast, or other types of vectors, or to stimulate T-cells in vitro for adoptive immunotherapy protocols.

**Novel Diagnostic, Prognostic and Therapeutic Biomarker for Hepatocellular Carcinoma**

Scientists at NCI have discovered that Stearol-CoA desaturase-1 (SCD-1) is associated with hepatocellular carcinoma (HCC). Utilizing a microarray to analyze HCC patient samples, the investigators found SCD-1 is elevated in liver tumor tissues and it is a marker for a highly aggressive form of HCC, hepatic stem cell-like HCC subtype (HpSC HCC). The investigators found SCD-1 is significantly elevated in HpSC tumors in comparison to less aggressive HCC tumors and it is associated with poor patient survival. In vitro studies demonstrate SCD-1 inhibition and/or addition of saturated palmitic acid reduces HpSC HCC characteristics.

To view full descriptions of these technologies and to find others available for licensing, please click here.

**P A T I E N T  O R G A N I Z A T I O N  E V E N T S**

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<tr>
<th>American Society of Clinical Oncology</th>
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<tr>
<td>Annual Meeting</td>
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Click here for more details.
BIO supports two pieces of legislation that would reform and modernize the FDA to speed life-saving treatments and breakthrough medicines to patients living with debilitating diseases. BIO CEO Jim Greenwood issued statements praising both the TREAT Act and the FAST Act. BIO has also testified on the Hill in support of the proposed reforms.

**S. 2113 – Transforming the Regulatory Environment to Accelerate Access to Treatments (TREAT) Act**
This bill would reform the FDA by advancing regulatory science and innovation, elevating FDA and empowering operational excellence, and enabling modernized patient-centric clinical development. Specific proposed reforms include updating FDA’s mission statement, enhancing the agency’s access to external scientific experts, and strengthening the Accelerated Approval pathway.
- **Sponsor:** Sen. Kay Hagan (NC)
- **Status:** Referred to the Senate HELP Committee

**H.R. 4132 – Faster Access to Specialized Treatments (FAST) Act**
This bill would reform the Accelerated Approval pathway at the FDA to expedite the approval of drugs for serious of life-threatening diseases or conditions while maintaining important safety standards.
- **Sponsors:** Rep. Cliff Stearns (FL-6) and Rep. Edolphus Towns (NY-10)
- **Status:** Referred to the House Committee on Energy and Commerce

### OncoLOGY-FOCUSed Legislation

**H.R. 1394 – Lung Cancer Mortality Reduction Act**
This bill would require the Secretary of HHS to implement a program to achieve a 50% reduction in the mortality rate of lung cancer by 2020 and require the CDC to establish a Lung Cancer Early Detection Program.
- **Sponsor:** Rep. Donna Christensen (VI)
- **Status:** Referred to the House Committee on Energy and Commerce

**H.R. 733 – Pancreatic Cancer Research and Education Act**
This bill would require the Secretary of HHS to establish and implement a Pancreatic Cancer Initiative to assist in coordinating activities to address the high mortality rate associated with pancreatic cancer.
- **Sponsor:** Rep. Anna G. Eshoo (CA-14)
- **Status:** Referred to the House Committee on Energy and Commerce

**H.R. 912 – Colorectal Cancer Prevention, Early Detection, and Treatment Act**
This bill would allow the Secretary of HHS to make grants to states to carry out programs to increase quality colorectal cancer screening. Gives priority to low-income individuals who lack adequate coverage,
- **Sponsor:** Rep. Kay Granger (TX-12)
- **Status:** Referred to the House Committee on Energy and Commerce

**H.R. 1970 – National Childhood Brain Tumor Prevention Network Act**
This bill would require a National Childhood Brain Tumor Prevention Network to provide grants and coordinate research with respect to the causes of and risk factors associated with childhood brain tumors.
- **Sponsor:** Rep Barbara Lee (CA-9)
- **Status:** Referred to House Committee on Energy and Commerce

**H.R. 1988 – Qualifying Therapeutic Discovery Project Tax Credit Extension Act**
This bill would extend the Therapeutic Discovery Project through the year 2017 and fund it at $1 billion per year. Qualifying investments in years 2011 through 2015 would qualify for the credit or grant.
- **Sponsors:** Rep. Susan Davis (CA-53) and Rep. Allyson Schwartz (PA-13)
- **Status:** Referred to the House Committee on Energy and Commerce
At this hearing, the Health Subcommittee heard from a variety of industries that are regulated by the FDA and depending on the User Fee Acts being reauthorized. For the biopharmaceutical industry, the committee focused on the FDA Accelerated Approval process. BIO Board Member John Maraganore testified on the importance of the Accelerated Approval pathway and in support of the FAST Act, which would enhance Accelerated Approval at FDA.

This hearing focused on the newly-established National Center for Advancing Translational Sciences (NCATS) at NIH. NIH Director Collins and NCATS Acting Director Insel testified on the process of getting NCATS up and running and the expectations they have for the Center. Industry representatives, including BIO Board Member Scott Koenig, testified on the importance of NCATS and the key role it will play in advancing translational research.

The Technology and Innovation Subcommittee held this hearing to better understand how federal policies and regulations affect competition, innovation, and job growth. BIO Board Chairman Ron Cohen testified on several steps that Congress has already taken to spur innovation, including SBIR, TDP, and patent reform. He also spoke in favor of reforms to the Accelerated Approval pathway at FDA.

The Senate Banking Committee held this hearing to discuss several proposals on how to ease capital formation for emerging companies. The bills under consideration included an on-ramp to the public market for emerging growth companies and reforms to SEC Regulation A, SEC Regulation D, and the SEC private shareholder limit. OncoMed Pharmaceuticals CFO Will Waddill testified on how these policies would affect growing biotech companies and stimulate innovation and job growth. The legislation that BIO supported at the hearing was later combined into one bill and passed as the JOBS Act.

The Senate HELP Committee held this hearing to discuss the upcoming reauthorization of PDUFA and how FDA and its regulated industries can speed treatments and therapies to patients. Sara Radcliffe, Executive Vice President of Health, testified on behalf of BIO; she was joined by other industry representatives as well as Janet Woodcock (CDER) and Jeffrey Shuren (CDRH) from the FDA.
PRESIDENT OBAMA SIGNS SBIR REAUTHORIZATION

On December 31, 2011, President Obama signed into law the National Defense Authorization Act, which reauthorized the SBIR program through 2017. Included in the reauthorization was an end to the eligibility ban on venture-backed companies. Now, venture-backed companies will be able to compete for 25% of SBIR funds at NIH, NSF, and the Department of Energy and 15% of funds at all other agencies. Additionally, research agencies with SBIR programs will increase the set aside from 2.5% to 3.2% by 2017. BIO is in the process of reaching out to SBA, which will propose rules on affiliation in the upcoming months.

CONGRESS PASSES THE JOBS ACT

In late March, Congress passed the Jumpstart Our Business Startups (JOBS) Act to ease capital formation for growing startup companies. The legislation includes an “on-ramp” to the public market for “emerging growth companies,” which will give them a five-year transition period before having to comply with certain regulatory burdens, including Sarbanes-Oxley (SOX) Section 404(b). The bill will also allow companies to conduct direct public offerings of up to $50 million under SEC Regulation A, eliminate the ban on general solicitation in Rule 506 of SEC Regulation D, and raise the shareholder limit that requires private companies to register with the SEC. The JOBS Act passed both houses of Congress with broad bipartisan support and President Obama has indicated that he will sign it into law.

BIO ADVOCATES FOR TDP EXTENSION AND EXPANSION

BIO has been advocating Congress for an extension and expansion of the Therapeutic Discovery Project (TDP) tax credit program. The TDP was enacted in 2010 and awarded $1 billion in tax credits and grants to breakthrough biotechnology companies with fewer than 250 employees. To support extension and expansion of this important program, BIO produced three video vignettes which give policymakers a view of what TDP has done for biotech companies already. The videos highlight companies that received awards through the program and emphasize the positive effect that the funding had on job creation, the development of treatments, and U.S. competitiveness. To view these videos, please click here, here, and here.