• Information Update •

Program of International Research Coordination Networks on Dimensions of Biodiversity Announced

The National Natural Science Foundation of China (NSFC) and the National Science Foundation (NSF) seek to encourage the development of international research coordination networks. Such networks would support interactions among Chinese and US scientists to develop new research directions or to advance new fields of research. Groups of investigators in China and the US may be supported to communicate and coordinate their research, training, and educational activities across disciplinary, organizational, institutional and geographic boundaries. NSFC will award up to 750 000 RMB to each approved project for a period of 5 years. The due date for Chinese applicants is April 5, 2011.

* * * *

• Research Results •

Relations found between human memories and similar neural patterns

In a project funded by NSFC, Professor Xue Gui of Beijing Normal University and his research team discovered that memories stick to similar neural patterns. A paper published on *Science* in September 2010 reported this discovery. This paper was jointly written by Xue Gui and his colleague Q. Dong in Beijing and US collaborators G. Xue, Z. Lu at University of Southern California, C. Chen at University of California, Irvine, J. A. Mumford and R. A. Poldrack at University of Texas, Austin.

According to the article on *Science*, when someone is studying something or trying to keep it in mind, they generate various patterns of neural activity. Professor Xue Gui and his collaborators found out that similar patterns of neural activity during this memory-encoding period actually indicate a greater likelihood that the individual will recall that memory at a later date. Patterns of neural activity that appear different are less likely to be remembered, they say.

It is reported by *Science* that in order to make this discovery, Xue Gui and his colleagues monitored the brains of healthy human volunteers with fMRI while they performed a set of experiments. In one experiment, for example, the volunteers attempted to memorize 120 different faces of people, each one presented to them four separate times. After an hour, the volunteers were shown 240 faces-half of them learned and half of them new-and asked to identify which ones they had already seen in the previous task.

The research results answered a long-standing debate among the psychology community by demonstrating that memories are more likely to stick in an individual's mind when the same neural representations are reactivated, rather than when the patterns of activation appear variable.

The title of the article published on *Science* is "Greater Neural Pattern Similarity Across Repetitions is Associated with Better Memory".

Double Star Program Received the IAA Laurels for Team Achievement Award

In the award ceremony in Prague on September 26, 2010, the International Academy of Astronautics (IAA) awarded the Laurels for Team Achievement Award to the Double Star/Cluster Team. Prof. Liu Zhenxing, Member of CAS and the principal scientist of the Double Star program, attended the ceremony.

The Laurels Team Achievement Award is an honorable award in the international astronautic community. It is one of the two major awards given by IAA every year, the other for individual recipients. The team award was established in 2000 with the first laurels given to the Russian Mir Space Station team. The following awardees include the Space Shuttle team, SOHO, Hubble Space Telescope, Sprit (MER-A) and Opportunity (MER-B) teams.

The Double Star Program was a significant space science project complemented by China National Space Administration in collaboration with ESA Cluster Program. The program consisted of two satellites, TC-1 and TC-2. They were launched into space in December 2003 and in July 2004 respectively. TC-1 functioned on its orbit for 46 months while TC-2 for 51 months, much longer than their designed life spans of 18 months and 12 months.

The Double Star Program was China's first satellite program designed and operated for scientific research purpose. On June 7, 2002, the *Science* magazine published a report about the Double Star Program on its "News Focus" section in issue 296.

The two satellites of Double Star Program fly in equatorial and polar obits near the earth. The Cluster Program consists of four satellites of the same kind flying in a higher altitude polar orbit which formed a quadrangle. The distances among the Cluster satellites can be adjusted in the range from hundreds to thousands kilometers. The six satellites together enable the first coordinated six-point measurements of the Earth magnetosphere.

The launch of TC-2 and the implementation of the Double Star Program together were selected as one of the "China's Top Ten Achievements in Science in 2004" by Members of CAS and CAE.

The Double Star Program was the first major China-ESA space science collaboration. China National Space Administration was responsible for the design and launch of two satellites. CAS was responsible for ground data reception and application research. ESA provided 7 testing instruments from the Cluster Program and developed the Neutral Particle Imager on TC-2 in a joint effort with Chinese scientists. In addition, ESA provided a ground station for data reception and science operation for the European instruments.

From 2003 to 2009, NSFC provided strong support to the Double Star Program, including a major program and a major international cooperation project.

Prof. Piao's Review Paper Published in *Nature*

Prof. Piao Shilong from the College of Urban and Environmental Sciences, Peking University was invited to publish a review paper in the September 2 issue of *Nature*. The paper, titled "The Impacts of Climate Change on Water Resources and Agriculture in China", introduces the progress of researches on the impact of climate change on China's agriculture and water resources.

Although China's economy developed rapidly in the past 30 years, as the most populous country in the world, China has to feed 22% of the world's population with only 7% of the world's arable land. It is a great challenge for China to maintain a sustainable development of agriculture and water resources. For this reason, the impact of climate change on China's water resources and agriculture output becomes a major concern for Chinese scientists and the international community. Based on in-depth analysis of relevant Chinese and foreign researches, Prof. Piao and his research partners looked into the trend of China's climate change and its impact in the past 50 years, and made a prediction for the coming 100 years. They further analyzed uncertainties in various researches and clarified the key issues in future researches on global climate change. In the paper, Prof. Piao pointed out that, in the recent 5 decades, China's climate has experienced a clear warming trend. Precipitation in south and north China has shown great distinctions with increasing rainfall in the south and more droughts in the north except the northwest. In addition, most glaciers in the western part of China have been melting down at an increasing speed. However, the complexity and highly coupling features in climate change make it hard to obtain an explicit assessment of the impact of climate change on the country's water resources and agriculture. Future researches must improve regional climate simulations, especially precipitation simulation, and develop a better understanding of the managed and unmanaged responses of crops to changes in climate, diseases, pests and atmospheric constituents.

Prof. Piao's specialty is the study on the responses and feedbacks of terrestrial ecosystem to global climate change. He is one of the lead authors in the Working Group I for the IPCC Fifth Assessment Report, responsible for the chapter on carbon cycles. Since 2008, Prof. Piao has successively published three papers as the first author in *Nature*. His article on the impact of rising CO2 concentration and land use changes on global river runoff was published in the journal of *PNAS* in 2007.

Prof. Piao's research was funded by NSFC.

Arsenic Trioxide Controls the Fate of the PML-RARα Oncoprotein by Directly Binding PML

In a project funded by NSFC, Professor Zhang Xiaowei of Rui Jin Hospital affiliated to Shanghai Jiao Tong University School of Medicine and his research team discovered that the fate of the PML-RARα oncoprotein is controlled by arsenic trioxide through direct binding of PML. A short report article published on *Science* in April 2010 reported this discovery.

This report was co-authored by a group of 21 researchers in China and France including Dr. Chen Zhu.

Arsenic, an ancient drug used in traditional Chinese medicine, has attracted worldwide interest because it shows substantial anticancer activity in patients with acute promyelocytic leukemia (APL), the report says.

According to the report, arsenic trioxide (As2O3) exerts its therapeutic effect by promoting degradation of an oncogenic protein that drives the growth of APL cells, PML-RARα (a fusion protein containing sequences from the PML zinc finger protein and retinoic acid receptor alpha). PML and PML-RARα degradation is triggered by their SUMOylation, but the mechanism by which As2O3 induces this posttranslational modification is unclear.

Research findings show that arsenic binds directly to cysteine residues in zinc fingers located within the RBCC domain of PML-RARα and PML. Arsenic binding induces PML oligomerization, which increases its interaction with the small ubiquitin-like protein modifier (SUMO)-conjugating enzyme UBC9, resulting in enhanced SUMOylation and degradation.

The identification of PML as a direct target of As2O3 provides new insights into the drug's mechanism of action and its specificity for APL, they say.

Setdb2 restricts dorsal organizer territory and regulates left-right asymmetry through suppressing *fgf8* activity

Summarizing research work partly funded by NSFC, Dr. Chen Zhu of State Key Laboratory of Medical Genomics, Shanghai Institute of Hematology, RuiJin Hospital, Shanghai Jiao Tong University and his research team reported on *PNAS* in February 2010 their research findings on dorsal organizer.

According to their paper, dorsal organizer formation is one of the most critical steps in early embryonic development. Several genes and signaling pathways that positively regulate the dorsal organizer development have been identified; however, little is known about the factor(s) that negatively regulates the organizer formation. Here, we show that Setdb2, a SET domain-containing protein possessing potential histone H3K9 methyltransferase activity, restricts dorsal organizer development and regulates left-right asymmetry by suppressing fibroblast growth factor 8 (fgf8) expressions. Knockdown of Setdb2 results in a massive expansion of dorsal organizer markers floating head (flh), goosecoid (gsc), and chordin (chd), as well as a significant increase of fgf8, but not fgf4 mRNAs. Consequently, disrupted midline patterning and resultant randomization of left-right asymmetry are observed in Setdb2-deficient embryos. These characteristic changes induced by Setdb2 deficiency can be nearly corrected by either over expression of a dominant-negative fgf receptor or knockdown of fgf8, suggesting an essential role for Setdb2-Fgf8 signaling in restricting dorsal organizer territory and regulating left-right asymmetry. These results provide unique evidence that a SET domain-containing protein potentially involved in the epigenetic control negatively regulates dorsal organizer formation during early embryonic development.

Their research work was also supported in part by the National Basic Research Program of China, the Science and Technology Commission of Shanghai Municipality, the National High Tech Program for Biotechnology, the Chinese National Key Basic Research Project, the Key Discipline program of Shanghai Municipal Education Commission, in addition to the Grant for Innovation Group of the National Natural Science Foundation of China, and the Shanghai Municipal Commission for Science and Technology.

Short-range scattering in quantum dots

In a project funded by NSFC, Professor Li Guodong and colleagues at the National Center for Nanoscience and Technology in Beijing made a new breakthrough in understanding the way electrons travel around quantum dots. This might lead to promising new fabrication methods of novel quantum devices, as they reported in *Journal of Applied Physics*, published by the American Institute of Physics in October 2010.

According to their report, Professor Li and his research team carried out an experiment using self-assembled quantum dots and a two-dimensional electron gas, and then fit the data to a model to find out the type of scattering exhibited.

To study these effects, they placed an AlGaAs/GaAs two-dimensional electron gas (2DEG) near embedded GaSb/GaAs type-II quantum dots at a temperature of 4.2 K.

"The type-II GaSb quantum dots only confine the holes and not the electrons," says coauthor Chao Jiang, "so they are free to interact with the 2DEG."

Measurements at various voltages in the coupled system showed that the scattering mechanism is short-range, an idea verified by a simple model with a constant scattering potential.

"For the first time, we have clarified that the mechanism of electron scattering in this type of quantum dot system is short-range," says Chao. "The result is particularly significant for the future designing of very efficient quantum-dot-based devices."

The title of the article published on the *Journal of Applied Physics* is "Short Range Scattering Mechanism of Type-II GaSb/GaAs Quantum Dots on the Transport Properties of Two-dimensional Electron Gas", co-authored by Chao Jiang, Guodong Li, Hong Yin (National Center for Nanoscience and Technology, China), Qinsheng Zhu (Chinese Academy of Science) and Hiroyuki Sakaki (Toyota Technological Institute).

Single-molecule magnets may find their use in microelectronics

In a project funded by NSFC, Xue Haibin and his colleagues at Shanxi University have made progress in understanding the single-molecule magnet, which combines the classical macroscale properties of a magnet with the quantum properties of a nanoscale entity. Their findings were reported in the *Journal of Applied Physics* in October 2010 for research on the statistics of how electrons move through a single-molecule magnet to better understand the magnet's inner level structure.

According to a report by EurekAlert, in the world of the very small, understanding the single-molecule magnet inner level structure is an important step toward the development of revolutionary ways to store and process information, as well as quantum computation. The results are important to the field of molecular spintronics, which combines molecular electronics with the field of spintronics—the manipulation of spin and charge.

"The single-molecule magnet can be regarded as a magnetic quantum dot with a more complex level structure," says co-author Yi-Hang Nie, "which makes it a good candidate for molecular spintronics devices."

How electrons move through single-molecule magnets is not well understood. "The current-voltage characteristics of such a system are not known well enough for practical application," says co-author Hai Bin Xue. "Our results go significantly beyond earlier studies of magnetic molecules in general, for which the current noise has been studied very little. The predictions permit experimental tests in the near future."

The title of the article published on the *Journal of Applied Physics* is "Tunable electron counting statistics in a single-molecule magnet," coauthored by Hai-Bin Xue, Y.-H. Nie, Z.-J. Li, and J.-Q. Liang

β-Arrestin1 Regulates Zebrafish Hematopoiesis through Binding to YY1 and Relieving Polycomb Group Repression

In a project funded by NSFC, Professor Yue Rui of Laboratory of Molecular Cell Biology, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences and his research team reported on *Cell* in October 2009 their research on regulation of β-Arrestin1 for zebrafish hematopoiesis.

According to the article, β-Arrestin1 is a multifunctional protein critically involved in signal transduction. Recently, it is also identified as a nuclear transcriptional regulator, but the underlying mechanisms and physiological significance remain to be explored. Here, we identified β-arrestin1 as an evolutionarily conserved protein essential for zebrafish development. Zebrafish embryos depleted of β-arrestin1 displayed severe posterior defects and especially failed to undergo hematopoiesis. In addition, the expression of cdx4, a critical regulator of embryonic blood formation, and its downstream hox genes were downregulated by depletion of β-arrestin1, while injection of cdx4, hoxa9a or hoxb4a mRNA rescued the hematopoietic defects. Further mechanistic studies revealed that β-arrestin1 bound to and sequestered the polycomb group (PcG) recruiter YY1, and relieved PcG-mediated repression of cdx4-hox pathway, thus regulating hematopoietic lineage specification. Taken together, this study demonstrated a critical role of β-arrestin1 during zebrafish primitive hematopoiesis, as well as an important regulator of PcG proteins and cdx4-hox pathway.

Studies shown gene present and absent complementation may contribute to the heterosis of maize

Partly funded by NSFC, a group of researchers in China Agricultural University and BGI in China, together with international collaborators from Iowa State University, University of Minnesota and University of Copenhagen completed studies on a whole genome map of single nucleotide polymorphism, insertion/deletion variation and the gene content variation among elite maize lines in China. The results, published online in *Nature Genetics*, provide a valuable resource for genetic studies and molecular breeding of this important crop.

This research team resequenced a group of six elite commercial maize inbred lines, some of which are the parents from popular heterotic groups. The study obtained 1.26 billion 75-bp paired reads which were aligned to the maize reference genome using SOAP software v2.18, and uncovered 1,272,134SNPs and 30,178indel polymorphisms (IDPs), providing a collection of markers with high-density through the genome. 101 chromosomal intervals with low-sequence-diversity were identified in the maize genome, containing a number of candidate genes related with maize improvement during selection.

The team also investigated the situation of presence/absence variations (PAVs) in maize lines by mapping the sequences of Mo17 and other inbred lines to the reference genome of B73. Different numbers of PAVs were identified for each heterotic group. Using SOAP de novo to assemble reads absent in B73 but present in other maize lines, the team found many putative genes missing in the current version of B73 reference genome.

Based on the discoveries that SNPs and IDPs have potential disabling effect on gene function and that different sets of PAVs present in different heterotic groups, the team hypothesized that the complementation effect of presence/absence variations and other deleterious mutations could have contributed on heterosis.

"The maize genome is large and complex while with abundant genetic resources in population. With the development of next generation sequencing technology, it has become feasible to resequence entire large genomes and thereby to carry out genome-wide surveys of genetic variation. The complement of more maize genomics data resource will have great contribution to the maize research community, said Dr. Xu Xun, the project investigator of BGI in China.

"The study will provide additional clues to the molecular basis of heterosis and will be helpful to researchers to identify quantitative trait loci that are important for crop improvement, the team wrote.

Low frequency genetic variation may determine complex diseases

In an international project jointly funded by NSFC, researchers in BGI-Shenzhen, China, together with international collaborators from UC Berkeley, University of Copenhagen and some other European institutions conducted research on the re-sequencing and analysis of 200 human exomes, established the largest data set for human exomes published so far and revealed an excess of low frequency deleterious nonsynonymous genetic mutations. Their findings were reported in a paper in *Nature Genetics* on October 4, 2010.

According to a report by EurekAlert, the team used Nimble Gen 2.1M exon capture array to targeted capture 18 654 coding genes of human genome and sequenced 200 individuals from Denmark. A large number of unknown SNPs were found and most of them appeared with low frequency. This study has developed the largest scale and the highest resolution genetic map of human exomes so far. Moreover, the massive data and in-depth analysis demonstrated that the excess of low frequency genetic mutations may cause the variations of protein amino acid sequences which would influence human health and under natural selection regulation.

Recently, a number of scientific researches indicated that association studies of complex diseases, following theoretical strategy, has identified numerous candidate genes in various experiments, but the results can only explain a limited fraction of the heritability of complex diseases. This missing heritability is also a major problem in complex disease genetics research. This study for the first time confirmed that genetic mutations associated with human health and disease susceptibility are generally at low frequency and are associated with multiple loci. Previous association studies using genotyping microarray can only detect common genetic variation and overlooks low frequency genetic mutations which may related with complex diseases, thus causing missing heritability.

This study not only shows the drawback of current disease research approach but also raise the revolutionary approach to apply genome sequencing technology instead of genotyping in association studies of disease. As a milestone, it will change the research methods of complex diseases and lead to the developments of human health and medical research.

This study is a part of the collaborative Sino-Danish Diabetes-associated Genes and Variations Study (LuCAMP). LuCAMP aims to detect novel rare and common genetic variations related with metabolic disorders through the exome sequencing of 1000 patients and 1000 controls.

Previously, a paper in *Science* (Science. 2010 July; 329(5987): 75-78) reported sequencing the exomes of 50 Tibetan individuals and found evidence for high altitude adaption of Tibetan populations. It shows that next generation sequencing is getting more applications and will have great potential in genomics research, drug discovery and personalized medical treatment.

Cation-π interaction playing vital roles in the regulation of integrin affinity, signaling, and biological functions

In a project funded by NSFC, Dr. Pan Youdong and his colleagues at the Laboratory of Molecular Cell Biology in Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, and his collaborator Timothy A. Springer of The Immune Disease Institute, Children's Hospital Boston in the US revealed their findings of important roles of Cation-π interaction in the regulation of integrin affinity, signaling, and biological functions in a paper published on *PNAS* in October 2010.

According to the paper, main findings of their research focus on the role of integrin α4β7. Integrin α4β7 mediates rolling and firm adhesion of leucocytes, two of the critical steps in leukocyte migration and tissue specific homing. Affinity of α4β7 for ligand is dynamically regulated by three interlinked metal ion-binding sites in β7-subunit I domain. In this study, we found that Phe185 (F185), a highly conserved aromatic residue in β7-subunit, links the specificity-determining loop and the synergistic metal ion-binding site (SyMBS) through cation-π interaction. Mutations of F185 that disrupted the SyMBS cation-F185 interaction led to deficient firm cell adhesion mediated by high affinity α4β7, and only slightly affected rolling adhesion mediated by low affinity α4β7. Disruption of SyMBS cation-F185 interaction induced partial extension of integrin ectodomain and separation of cytoplasmic tails, and impaired α4β7-mediated bidirectional signaling. In addition, loss of SyMBS cation-F185 interaction increased paxillin expression and promoted paxillin-integrin binding, leading to deficient cell spreading. Furthermore, integrin α4β7-mediated cell migration was decreased by the abolishment of SyMBS cation-F185 interaction. Thus, these findings reveal a cation-π interaction playing vital roles in the regulation of integrin affinity, signaling, and biological functions.

The title of the article published on *PNAS* is "Cation-π interaction regulates ligand-binding affinity and signaling of integrin α4β7".

Soybean diversity map may provide important basis for breeding

In an international project jointly funded by NSFC, a research team composed of scientists from the Chinese University of Hong Kong, BGI-Shenzhen, the Chinese Ministry of Agriculture, the Chinese Academy of Agricultural Sciences and University of Copenhagen, reported a large-scale analysis of the patterns of genome-wide genetic variation in soybeans. The results, published online in *Nature Genetics* on 14th November 2010, provide a valuable resource for the genomic and genetic analysis of soybeans and facilitate future breeding and quantitative trait analysis.

According to a report by EurekAlert, using the next generation sequencing platform, the team re-sequenced the genomes of 17 wild and 14 cultivated soybeans and obtained 900 million 45bp or 76bp paired-end reads which were aligned to the soybean reference genome using SOAP2. From the analysis, the researchers identified a total of 6,318,109 single nucleotide polymorphisms (SNPs), which is the first genome-wide variation map of soybean. Using the program SOAPdenovo, they assembled the wild and cultivated soybeans and identified 186,177 present and absent variations (PAVs), including genes which might be lost in cultivated soybean during domestication. This research established the first comprehensive re-sequencing data of wild and cultivated soybean genomes as well of Fabaceae family members.

The researchers identified two unique features of the soybean genome that are distinct from other crop plants: they have exceptionally high linkage disequilibrium (LD) and a high ratio of average nonsynonymous versus synonymous nucleotide changes (Nonsyn/Syn), which indicates that marker-assisted breeding would be less challenging than map-based cloning for soybean improvement.

The researchers found higher genomic diversity in the wild soybeans than in the cultivated soybeans, indicating that human selection had a strong impact on the genetic diversity in the cultivated soybeans. The team also discovered an unexpected observation that wild soybeans have less low frequency SNPs as compared to cultivated soybean, which would be explained by the reduced population size of wild soybean as a result of the shrinking habitat. The team also reported linkage disequilibrium block location and distribution and identified a set of 205,614 tag SNPs that may be useful for QTL mapping and association studies.

"The study lays the foundation for future large scale population studies, marker-assisted breeding application and gene function identification in soybeans. It provides great benefits to the international soybean research community and breeding groups," said Dr Xun Xu, Project Investigator at BGI.

The project investigator at CUHK, Dr. Hon-Ming Lam said: "This research has generated a huge amount of genomic data to expedite future soybean researches. It also provides important information to facilitate soybean breeding program. It is the first time a large scale soybean genome project can be completed solely by Chinese scientists in the home of soybean, China. It is also an exemplar of deep collaborations between research institutes in Hong Kong and Mainland that will lead to significant breakthrough in science."

Mutations related to Alzheimer's and rare skin disease

In a project funded by NSFC, Dr. Wang Baoxi of Peking Union Medical College Hospital in Beijing and his collaborators in China conducted research on Mutations related to Alzheimer's and rare skin disease. Their findings are reported on *EurekAlert*, an online science news reporting service provided by AAAS in the US.

According to the report, genetic mutations in a rare skin disease offer new insights into a signaling pathway that is a drug target for Alzheimer's disease, according to new research. Acne inversa is a chronic inflammatory disease of the hair follicles, whose key features include draining sinuses, painful skin abscesses and disfiguring scars. The German philosopher Karl Marx is thought to have suffered from this skin condition, the authors say in this Brevium. To investigate the genetic mechanisms underlying this condition, Dr. Wang Baoxi and colleagues analyzed genome sequences from six Han Chinese families with features of acne inversa. They identified several mutations that appear to cause the condition by deactivating an enzyme called gamma-secretase. Mutations in two of these gamma-secretase genes are known to cause an early-onset form of Alzheimer's disease as well as non-Alzheimer dementias. Interestingly, preliminary analyses of patients with acne inversa revealed no evidence of Alzheimer's disease. If further studies show that the mutations cause the two diseases through distinct mechanisms, that could have important implications for how gamma secretase operates in Alzheimer's disease and how Alzheimer's drugs should be targeting this enzyme.