1st Beijing-Manchester Cell Organization and Dynamics Symposium 2011

May 15 - 19, 2011.

Beijing, China.

Organizing Committee:

Dr. Martin Lowe
Faculty of Life Sciences
University of Manchester

Dr. Shilai Bao
Institute of Genetics and Development Biology
Chinese Academy of Sciences

Sponsored by:

Biotechnology and Biological Sciences Research Council (BBSRC)
Laboratory of Molecular and Developmental Biology, CAS

List of Sessions

Membrane trafficking	Martin Lowe (Manchester) Wei Li (IGDB, China) Philip Woodman (Manchester) Jiajia Liu (IGDB, China) Aipo Diao (NSFC，China)
Organelle function	Martin Pool (Manchester) Shilai Bao (IGDB, China) Jon Pittman (Manchester) Xun Huang (IGDB, China)
Neurons, cell death and signaling	Zhiheng Xu (IGDB, China) Mei Ding (IGDB, China) Fei Gao (Institute of Zoology,China)
Cytoskeleton	Yongqing Zhang (IGDB, China) Viki Allan (Manchester) Xiangdong Li (Institute of Zoology,China)
Plant cell wall synthesis and signaling	Yihua Zhou (IGDB, China) Simon Turner (Manchester) Thomas Nuhse (Manchester)

Program

Sunday 15th May

8:30 Arrival at airport and transfer to Olympic village garden Hotel Beijing

19：00 Welcome banquet at MEI ZHOU DONG PO RESTAURANT

Monday 16th May

Venue: Institute of Genetics and Developmental Biology, **B210 of Building No.1**

9:00-9:30 Welcome and opening remarks
Chair: Xung Huang
9:00-9:10 Welcome and the introduction of IGDB by Weicai Yang (IGDB, China)
9:10-9:25 Introduction of BBSRC program by Martin Lowe (Manchester)
9:25-9:30 All participants taking group photo

9:30-11:30 Membrane Trafficking
Chairs：Dr. Martin Lowe and Dr. Aipo Diao
9:30-10:00 **Martin Lowe** (Manchester)
Control of receptor recycling within the endocytic pathway by phosphoinositide lipids
10:00-10:30 **Wei Li** (IGDB, China)
Molecular and Cellular Mechanisms of BLOC-1 in Mediating Lysosomal Trafficking
10:30-11:00 **Philip Woodman** (Manchester)
The Cell Biology of Receptor Downregulation
11:00-11:30 **Jiajia Liu** (IGDB, China)
Molecular mechanisms of retromer-mediated retrograde vesicular transport from endosome to TGN
11:30-11:50 **Aipo Diao** (NSFC，China)

11:50-13:30 Lunch at Institute of Genetics and Developmental Biology, **B109 and B108 of Building No.1**

13:30-15:30 Organelle Function
Chairs: Dr. Martin Pool and Dr. Jiajia Liu
13:30-14:00 **Martin Pool** (Manchester)
A novel role for N-acetylation in protein sorting to the secretory pathway
14:00-14:30 **Shilai Bao** (IGDB, China)
Protein Arginine Methylation Involved in Golgi Apparatus and Cell Migration.
14:30-15:00 **Jon Pittman** (Manchester)
Cellular responses to environmental stress in plants: the regulation of vacuolar-derived Ca^{2+} signals and stress-induced lipid biosynthesis
15:00-15:30 **Xun Huang** (IGDB, China)
Tissue-autonomous function of Drosophila Seipin in preventing ectopic lipid droplet formation

15:30-16:00 Break for Tea/Coffee

16:00-17:30 Neurons, cell death and signaling
Chairs: Dr. Fei Gao and Dr. Mei Ding

16:00-16:30 **Zhiheng Xu** (IGDB, China)
Leucine-Rich Repeat Kinase 2 (LRRK2) Disturbs Mitochondrial Dynamics via Dynamin-Like Protein (DLP1) and ULK1 Complex
16:30-17:00 **Mei Ding** (IGDB, China)
Yin and Yang: the positive and negative regulators in axon outgrowth
17:00-17:30 **Fei Gao** (Institute of Zoology,China)
Wt1, a key regulator in kidney development and tumorigenesis

17:30-18:30 Free discussion + refreshments

19:00 Dinner at Beijing quanjude roast duck restaurant

Tuesday 17th May

Venue: Institute of Genetics and Developmental Biology, **B210 of Building No.1**

8:30-10:00 Cytoskeleton
Chairs: Dr. Viki Allan and Yongqing Zhang
8:30-9:00 **Yongqing Zhang** (IGDB, China)
Synaptic mechanisms of mental retardation
9:00-9:30 **Viki Allan** (Manchester)
Investigating microtubule motor function and regulation.
9:30-10:00 **Xiangdong Li** (Institute of Zoology, China)
Regulation of Unconventional Myosin-Va: an Actin-Based Molecular Motor

10:00-10:30 Break for Tea/Coffee

10:30-11:30 Plant Cell Wall Synthesis and Signaling
Chairs: Dr. Simon Turner and Yihua Zhou
10:30-11:00 **Yihua Zhou** (IGDB, China)
Study on rice brittleness mutants, a way to open the 'black box' in monocot cell wall biosynthesis
11:00-11:30 **Simon Turner** (Manchester)
Plant cell wall synthesis and vascular tissue development
11:30-12:00 **Thomas Nuhse** (Manchester)
Cell wall feedback signalling and control of cell elongation

12:00-14:00 Lunch at Institute of Genetics and Developmental Biology, **B109 and B108 of Building No.1**

14:00-16:00 Free for 1-1 discussions between CAS and Manchester investigators (to be arranged following talks)

16:00-17:00 Round table meeting to discuss future CAS-Manchester strategy for collaboration
Discuss visit of CAS members to Manchester
Chairs: Dr. Martin Lowe and Dr. Shilai Bao
17:00-17:30 Summary remark
Dr. Martin Lowe (Manchester)
Dr. Yongqing Zhang (IGDB, China)

19:00 Dinner at MEI ZHOU DONG PO RESTAURANT

Cultural Tour

Wednesday 18th May,

8:00	**Departure at Olympic village garden Hotel and Great Walls Sightseeing**
	Lunch from the travel agency
	The Summer Palace Sightseeing
17:30	**transfer to Olympic village garden Hotel**
19:00	**Dinner at MEI ZHOU DONG PO RESTAURANT**

Thursday 19th May,

8:30	**Departure at Olympic village garden Hotel and Forbidden City Sightseeing**
	Lunch from the travel agency
Thereafter	**Sightseeing in Old Beijing a hutong tour**
Thereafter	**freetime (selecting play site according to the personal interest)**
	Individuals will be responsible for own return and dinner

Friday 20th May,

9：30 **Departure and transfer to airport**

Note: For each invited talk, 25 min presentation plus 5 min discussion.

Presentation Abstracts and Details of speakers

Dr. Martin Lowe, Principle Investigator

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ABSTRACT

Membrane Traffic in the Secretory and Endocytic Pathways

Our research is focussed on membrane traffic and how defects in this fundamental process lead to disease. We have main areas of interest, namely the structural and functional organization of the Golgi apparatus, and the regulation of membrane traffic in the endocytic pathway by phosphoinositide lipids.

The Golgi apparatus lies at the heart of the secretory pathway and plays a major role in the modification, sorting and trafficking of protein and lipid cargo molecules. Key players in Golgi structure and trafficking are the golgin family of coiled-coil proteins found on the cytoplasmic surface of the Golgi membrane. These elongated proteins are attached to the Golgi at one end and are thought to tether membranes over relatively long distances to promote both Golgi assembly and transport vesicle fusion. We have concentrated on two golgins, namely GM130 and GMAP210, which both associate with the cis or entry side of the Golgi apparatus. Functional studies in mammalian tissue culture cells point to a role for both proteins in promoting tethering of incoming carriers that in turn is required to maintain Golgi organization and ensure efficient trafficking of cargo. We have also recently identified ZFPL1 as an interactor of both golgins, and we believe it acts as a novel regulator of golgin-mediated tethering. We are currently using a variety of approaches to dissect the mechanisms by which these proteins function.

Phosphoinositide lipids are key regulators of many cellular processes including intracellular signaling, cytoskeletal dynamics and membrane traffic. Seven different phosphoinositides exist in cells, each generated by specific kinases and phosphatases that phosphorylate or dephosphorylate the 3-, 4-, and 5- positions of the inositol ring. The tight temporal and spatial regulation of phosphoinositides is important to maintain cellular homeostasis, and therefore the kinases and phosphatases that generate these lipids are key cellular regulators.We are particularly interested in two 5-phosphatases that are located on endosomes, called INPP5B and OCRL1. Mutation of OCRL1 causes the rare X-linked disorders known as Lowe syndrome and Dent'sdisease 2, which are characterised by defects in the kidney and in the case of Lowe syndrome there is also perturbation of the central nervous system and eyes. Data form our lab and others suggestsINPP5B and OCRL1 regulate membrane trafficwithin the endocytic pathway, most likely in the recycling of cargo from endosomes back to the trans-Golgi network and plasma membrane. We are currently using both mammalian tissue culture cells and zebrafish embryos to investigate the molecular mechanisms involved, and how loss of function of OCRL1 leads to pathological changes that occur in Lowe syndrome and Dent's disease.

Dr. Wei Li, Principle Investigator and Laboratory Head

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Dr. Li was trained in Medical Sciences (M.D., 1985, Gannan Medical College), Biochemistry (M.S., Tongji Medical University, 1991), Medical Genetics (1997, Ph.D., Sun Yat-Sen University of Medical Sciences) and Bioinformatics (2004, M.S., University at Buffalo). He did his postdoctoral training in the Department of Molecular and Cellular Biology, Roswell Park Cancer Institute (Buffalo, USA) from 1998 to 2004. He and his colleagues have cloned nine genes involving in vesicle trafficking and organelle development. He has published over 30 peer-reviewed papers in international journals including *Nature Genetics, PNAS, Blood, JCB*. His laboratory is mainly focused on the molecular and cellular mechanism in regulating lysosomal trafficking and the biogenesis of lysosome-related organelles by using mouse mutants of Hermansky-Pudlak syndrome.

ABSTRACT

Molecular and Cellular Mechanisms of BLOC-1 in Mediating Lysosomal Trafficking

Lysosomal trafficking is being regarded as an important process after endosomal sorting. This trafficking pathway has been involved in the biogenesis of lysosome-related organelles (LROs), modulation of signaling pathways and regulation of secretory lysosomes. It is known that several lysosomal trafficking complexes including AP-3, HOPS, ESCRTs, BLOCs participate in this process by mediating the binding of cargo proteins and motor proteins during trafficking. Disruption of any of these protein complexes may result in multiple LRO defects such as in the patients with Hermansky-Pudlak syndrome (HPS). In addition, the aberrant lysosomal degradation of signaling molecules affects the signaling transduction. In the neuronal cells, synaptic vesicle (SV) shares common features with lysosome-related organelles (LROs), such as containing lysosome associated membrane proteins (LAMPs) and lower luminal pH. Lysosomal trafficking is involved in the presynaptic SV biogenesis and exocytosis, as well as postsynaptic receptor degradation and signaling. I will discuss the current understanding of the components and functions of the biogenesis of lysosome-related organelles complex-1 (BLOC-1) and related disease caused by the traffic jam.

Prof. Philip Woodman, Principle Investigator

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ABSTRACT

The Cell Biology of Receptor Downregulation

Activated mitogenic receptors such as EGFR are removed from the cell surface and targeted to the endosome. This compartment serves two purposes. Firstly, it appears to form a specialised signalling platform from which receptors initiate signalling pathways that are distinct from those initiated at the plasma membrane. Secondly, the endosome acts as a decision point to determine the duration of signalling, since receptors are either sorted to the lysosome for degradation or are recycled back to the plasma membrane. Our recent research has focussed on the role of ESCRT complexes in sorting activated EGFR within the endosome in order to target it for lysosomal degradation. Our work is now beginning to focus on how this sorting event might be integrated with the control of EGFR signalling.

Dr. Jia-Jia Liu, Principle Investigator

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ABSTRACT

Molecular mechanisms of retromer-mediated retrograde vesicular transport from endosome to TGN

The retromer is a protein complex that mediates retrograde transport of transmembrane cargoes from endosomes to the *trans*-Golgi network (TGN). It is comprised of a cargo-selection subcomplex of Vps26, Vps29 and Vps35 and a membrane-binding coat subcomplex of sorting nexins (SNXs). Previous studies identified SNX1/2 as one of the components of the SNX subcomplex. How the retromer-associated cargoes are recognized and transported by molecular motors are largely unknown. In this study, we found that SNX6, another component of the SNX subcomplex, interacts with the $p150^{Glued}$ subunit of the dynein/dynactin motor complex. We present evidence that recruitment of the motor complex to the membrane-associated retromer requires the SNX6-$p150^{Glued}$ interaction. Disruption of the SNX6-$p150^{Glued}$ interaction causes failure of formation and detachment of the tubulovesicular sorting structures from endosomes and results in block of CI-MPR retrieval from endosomes to the TGN. These observations indicate that in addition to SNX1/2, SNX6 in association with the dynein/dynactin complex drive the formation and movement of tubular retrograde intermediates. In addition, we have investigated the mechanism underlying release of retromer-associated cargo at TGN. We show that PI4P, the Golgi-enriched phospholipid, plays a critical role in regulation of the motor-cargo interaction between $p150^{Glued}$ and SNX6.

RESEARCH FOCUS

Our laboratory is mainly interested in molecular mechanisms of retrograde vesicular transport and related human diseases, focusing on 1) mechanisms of membrane trafficking and protein sorting. 2) mechanisms of membrane trafficking-dependent temprospatial control of signaling pathways which are crucial for differentiation, development and survival of neurons.

Ongoing projects:

1. *Motor-cargo interaction in retrograde vesicular transport*

The dynein/dynactin motor complex propels cargoes along microtubule tracks from cell periphery to the cell center. Cargo adaptors are molecules responsible for tethering the motor complex to membranous cargoes. We identified several dynein/dynactin interacting proteins through yeast two-hybrid screen and we are in the process of investigating their roles in retrograde transport and membrane trafficking.

2. *Mechanisms of BDNF endocytic trafficking and signaling in CNS neurons.*

A wide variety of cargoes including signaling endosomes of neurotrophin-receptor complex and other endocytic vesicles, nerve injury signals, apoptotic signals, development signals such as neuron migration and axon guidance cues, and organelles such as mitochondria need to be transported retrogradely in a neuron. How are signaling pathways coupled with vesicular transport to regulate development and survival of neurons? Currently we are studying functions of two neuronal proteins involved in BDNF-TrkB endocytic trafficking and dendrite development. We will further investigate their biological roles in retrograde transport and neurodevelopment using knockout mouse models.

Dr. Martin Pool, Principle Investigator

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ABSTRACT

Regulating the fate of newly synthesized proteins

Cellular proteins are synthesized by large macromolecular machines, termed ribosomes. The fate of a newly made protein is frequently determined while the protein is still being synthesized by the ribosome. For example, N-terminal processing (methionine excision and N-acetylation) and folding of cytosolic proteins frequently occurs co-translationally. Similarly, proteins that are targeted to cellular organelles or the secretory pathway typically possess localisation signals at their N-termini, which are already recognised during ongoing protein synthesis. These are major cellular events and if these processes go wrong, it can frequently lead to disease states.

We are interested in understanding how the factors and enzymes that perform these various folding, processing and targeting functions are recruited to the ribosome-nascent chain complex to ensure the right factor interacts with the correct nascent chain at the correct time.

We employ a combination of biochemical, structural and genetic approaches using yeast and mammalian systems to answer these questions.

Our work has defined ribosomal protein L23 as a highly conserved universal docking platform for nascent-chain interacting factors on the ribosome. Whereby it optimally positions such factors directly to where the nascent chain emerges from the ribosome.

Recently, we have investigated the competition between N-terminal processing and targeting factors and uncovered protein N-acetylation as a novel determinant in the co-translational sorting of proteins within the cell.

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Research Interests:

Golgi Apparatus Biogenesis The Golgi apparatus plays a central role in the post-translational modification, sorting, and transport of proteins. Maintenance of the Golgi structure and function depends on Golgi matrix proteins. The Golgi apparatus function in development and disease pathogenesis, however, remains largely unknown. My laboratory is mainly interested in elucidating the molecular mechanism of PRMT5 complex components in regulating Golgi structure and function. Our previous studies find that PRMT5 localizes to GA and physically interacts with golgin GM130. Both PRMT5 and GM130 arginine methylation are critical for Golgi structure. We are generating knockout mice to investigate into the significance of the Golgi apparatus in development and disease pathogenesis.

Epigenetics Acute lymphoblastic leukemia (ALL) is the most common malignancy diagnosed in children, representing nearly one third of all pediatric cancers. The ALL is caused by the defects of differentiation processes from hematopietic stem cell to mature lymphocytes. Many proteins have been found to be involved in lymphocytes differentiation and ALL pathogenesis. In addition to Golgi localization, PRMT5 also localizes to nucleus and catalyzes histone H4R3 symmetric dimethylation. Our preliminary results have shown that PRMT5 localization and Golgi structure in ALL are different from normal lymphocytes. We are going to investigate into Golgi apparatus and histone modifications in regulating the lymphocyte differentiation and the ALL pathogenesis.

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ABSTRACT

Cellular responses to environmental stress in plants: the regulation of vacuolar-derived Ca^{2+} signals and stress-induced lipid biosynthesis

Plants are frequently exposed to abiotic stresses and have sophisticated mechanisms to respond and appropriately adapt to these stresses. My lab is interested in understanding the cellular and molecular mechanisms that mediate these responses using two model systems, the plant *Arabidopsis thaliana* and the unicellular green microalgae *Chlamydomonas reinhardtii.* This presentation will give an overview of two of the current research areas that are active in the lab: the role of vacuolar Ca^{2+} transporters in generating Ca^{2+} signals in response to stress and the analysis of metabolic changes, particularly carbohydrate and lipid changes in stressed algae. Changes in cytosolic Ca^{2+} concentration within a cell are an early response to environmental stress but the mechanisms responsible for shaping Ca^{2+} signals are poorly understood. In plant cells, cation/H^+ exchangers (CAX) are one of the key Ca^{2+} transport pathways that mediate Ca^{2+} export from the cytosol by the high-capacity transport of Ca^{2+} into the vacuole. Analysis of *Arabidopsis cax* mutant phenotypes suggest that these transporters are involved in specific abiotic stress responses including low temperature, salinity and oxidative stress. Furthermore, CAX transporters are regulated in response to these stresses. These vacuolar Ca^{2+} transporters appear to be central components in controlling cytosolic Ca^{2+} signal dynamics under specific stress conditions. We have also begun to use *Chlamydomonas* as a single-celled model to study stress-induced Ca^{2+} signaling. *Chlamydomonas* mutants for Ca^{2+} transporter genes have been generated to allow the Ca^{2+} signaling functions of these transporters to be examined. While the generation of Ca^{2+} signals is an early stress response in algae, metabolic changes such as the accumulation of starch and lipid are a longer term response. Following nutrient deficiency stress, lipid bodies form within the cytosol and accumulate triacylglycerol. To gain further understanding into the mechanisms of stress-induced lipid induction in *Chlamydomonas*, a combination of metabolic profiling and gene expression analysis in conjunction with gene over-expression is being performed. This work is providing fundamental insights into the mechanisms of lipid biosynthesis in this organism and is also of applied interest such as for the generation of biofuels from algae.

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ABSTRACT

Tissue-autonomous function of *DrosophilaSeipin* in preventing ectopic lipid droplet formation

Obesity is characterized by accumulation of excess body fat while lipodystrophy is characterized by loss or absence of body fat. Despite their opposite phenotypes, these two conditions both cause ectopic lipid storage in non-adipose tissues, leading to lipotoxicity which has health-threatening consequences. The exact mechanisms underlying ectopic lipid storage remain elusive. Here we report the analysis of a Drosophila model of the most severe form of human lipodystrophy, Berardinelli-Seip Congenital Lipodystrophy 2, which is caused by mutations in the BSCL2/Seipin gene. Our data suggest that dSeipin may participate in phosphatidic acid metabolism and subsequently down-regulate lipogenesis to prevent ectopic lipid droplet formation in a tissue-autonomous manner.

RESEARCH FOCUS

The main interest of our lab is to understand the cell biology and developmental biology of lipid metabolism. In particular, we are studying the regulation of lipid metabolism under normal conditions and under disease conditions. We use Drosophila to study the regulation of lipid metabolism in both adipose tissue and non-adipose tissues. We are mainly focusing on the following questions. How is lipid storage (lipid droplet formation) regulated in adipose tissue and non-adipose tissues? How is lipid trafficking regulated? What are the molecular and physiological mechanisms of lipid metabolic related disorders? And what are the developmental consequences when lipid metabolism is defective? Apart from these, a small part of the lab investigates the fundamental mechanisms of neural development in both C.elegans and Drosophila.

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ABSTRACT

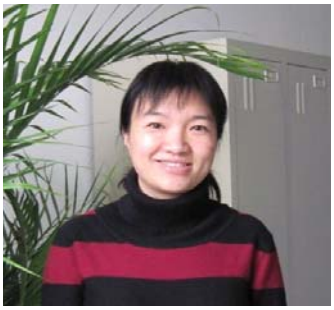
Leucine-Rich Repeat Kinase 2 (LRRK2) Disturbs Mitochondrial Dynamics via Dynamin-Like Protein (DLP1) and ULK1 Complex

Mutations in LRRK2 are the leading causes of inherited Parkinson's disease (PD) identified so far. The underlying mechanism whereby missense alterations in LRRK2 initiate neurodegeneration remains largely unclear. Mitochondrial dysfunction has been recognized to contribute to the pathogenesis of both sporadic and familial PD. The pathogenic gain-of-function mutant form of LRRK2, LRRK2 G2019S, is associated with elevated kinase activity and PD. Here we show that LRRK2 G2019S can cause defects in the morphology and dynamics of mitochondria in cortical neurons and DLP1 plays an essential role in LRRK2-induced mitochondrial fission. In support of this, expression of LRRK2 leads to the translocation of DLP1 from the cytosol to the mitochondria and knockdown of DLP1 expression inhibits LRRK2 induced mitochondrial fission. More interestingly, co-expression of LRRK2 and DLP1 induces mitochondrial clearance (mitophagy). We provide evidence here that expression of LRRK2 can induce autophagy via a ULK1 complex.

Taken together, our results provide insights into the pathobiology of LRRK2 and suggest that LRRK2 G2019S may induce neuronal dysfunction or cell death via perturbation of normal mitochondrial fission/fusion dynamics.

RESEARCH FOCUS

Signal Transduction in Tumorigenesis, Brain Development and Neurodegenerative Diseases.



Dr. Mei Ding, Principle Investigator

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ABSTRACT

Yin and Yang: the positive and negative regulators in axon outgrowth

How do individual nerve fibers find their way along specific paths in a complex environment such as the developing central nervous system? A principal mechanism in axon guidance is the binding of a receptor protein on the axon surface to a guidance molecule. However, it remains a mystery exactly how a limited number of guidance molecules can pilot the growth of billions of neurons.Through an unbiased genetic screen, we uncovered CWN-2, a member of the Wnt ligands, as the main guidance cue for RME neurite anterior-posterior (A-P) outgrowth. In *cwn-2* mutant, RME neurons lose A-P neurites. CWN-2 is expressed in the anterior part of the worm, especially higher in posterior pharynx and could act as an attractive cue for neurite outgrowth. The activity of CWN-2 can be partially substituted by expressing other Wnts (MOM-2, CWN-1 or EGL-20) locally, suggesting that specific spatial distribution plays a key role in the function specificity of Wnts. In addition, we found that CFZ-2， MIG-1 and CAM-1 receptors, and DSH-1 down stream effector also function in guiding axon outgrowth. Genetic evidence indicates that CAM-1 acts cell-autonomously within RME neurons and its function dependents on cysteine-rich and kinase domains. Compared to *cam-1* mutants, *cfz-2* or *mig-1* only displays weak phenotypes and *mig-1;cfz-2* double mutants exhibit much stronger phenotype resembling *cam-1* mutants. This suggests that CAM-1 may act as the main receptor for CWN-2/Wnt, while CFZ-2 and MIG-1 could be co-receptors with CAM-1. Through a yeast two-hybrid screen, we identified DSH-1 as a binding partner for CAM-1, indicating that CAM-1 may facilitate CWN-2/Wnt signaling by its physical association with DSH-1. To address how axon outgrowth is terminated and how the termination signal interacts with Wnt pathway, we further searched mutants with longer RME processes. From an unbiased screen, we recovered an *xd49* mutant, which displays longer RME process phenotype. We also identified two additional genes that could negatively regulate RME neurite outgrowth. Currently, we are taking genetics and biochemistry approaches to address how Wnt pathway interact with this newly identified axon termination signal and how Wnt activity could be attenuated on time to fine tune the proper length of axon. Detailed analysis will be reported in this meeting.

RESEARCH FOCUS

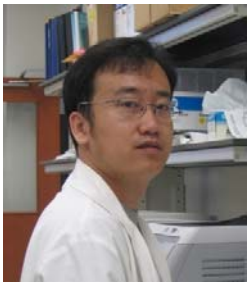
We are studying the development of neural circuits by characterizing pathways for synapse specificity, synaptogenesis and neuronal differentiation.

How is the target specificity established?

The intricate patterns of synaptic connections in a nervous system underlie nearly all aspects of neuronal function, but we know little about how each neuron distinguishes the correct synaptic target from the many other non-target cells. We have identified that ubiquitin-mediated protein degradation contributes to precise synaptic connectivity through selective synapse elimination. Currently, we are continuing on understanding how the hierarchy of synaptic choice is established using genetics, cell biology and biochemistry approaches.

How does a neuron form synapses with its partners?

Synapses are the means that neurons use to communicate with others. At the presynaptic terminal, neurons develop elaborate subcellular structures to facilitate the accumulation and release of synaptic vesicles. Although much of the progress has been made in understanding neurotransmitter release, how the cyto-architecture of a presynaptic terminal is built is less well understood. Using a combination of fluorescent protein markers that label different presynaptic components, we are going to isolate mutants that display abnormal synaptic morphology. With multi-label technique, we shall be able to analyze the dynamic spatial changes among various presynaptic proteins in great details.



Dr. Fei Gao, Principle Investigator

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ABSTRACT

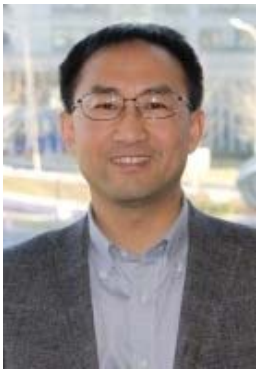
Wt1, a key regulator in kidney development and tumorigenesis

The Wilms' tumor (WT) suppressor gene, *WT1*, encodes a zinc finger nuclear transcriptional factor that is normally expressed during development in induced renal mesenchyme and later in the crescent- and S-shaped bodies of the developing glomerulus. *WT1* was originally identified as playing an etiologic role in the development of WT and was subsequently identified as being mutated in patients with Denys-Drash syndrome (DDS), which consists of a triad of phenotypes: WT predisposition, male pseudohermaphrodism, and early-onset (<3 year of age) renal failure. Ironically, understanding the roles of Wt1 in kidney development and Wilms' tumor development has progressed slowly, primarily due to the embryonic lethality of Wt1 knockout mice model. We have now developed a Wt1 conditional knockout mice strain and inactivated Wt1 in kidney during early embryonic stage results in the defects of glomeruli differentiation, no mature glomeruli was found in the mutant kidney, however, no kidney tumor was noted. Suggesting that Wt1 is important for renal mesenchyme differentiation, but single mutation is not sufficient to induce kidney tumor development. To further explore the etiology of WT, Wt1 was inactivated and Igf2 was up-regulated in kidney simultaneously, these alterations were observed in some human tumors. We found that >60% of mice developed kidney tumors in 20 weeks of age. Our data indicate that loss of Wt1 function and up-regulation of Igf2 act cooperatively, are rate-limiting for tumor development, and act to impair normal cellular differentiation in nephrogenesis and to abrogate normal growth control, respectively. This model provides powerful tools to further understand cancer etiology and progression and to explore treatment options.

RESEARCH FOCUS

Gametogenesis is a very complicated process including PGC specification, sex differentiation, gonad development, spermatogensis and folliculogenesis. Reproductive disorder or other related diseases will happen if any step was dysregulated, therefore, understanding the molecular mechanism of this process will provide useful information for clinical treatment or birth control. In our lab, we are mainly focusing on exploring the roles of tumor suppressing gene, Wt1, in sex differentiation, testis development, and spermatogensesis using gene knockout mice models.
Research directions in our lab including:

1. Sex determination;
2. Gonad development and spermatogenesis;.
3. Primordial follicle initiation and folliculogenesis;.
4. Primordial germ cells (PGC) self renewal and migration;



Dr. Yongqing Zhang, Principle Investigator and Vice Director of IGDB

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Research Area:

Developmental Neurobiology and Genetic Modeling of Neurological Diseases

Main Interests:

To understand how the brain functions using Drosophila melanogaster as a model system. The molecular and cellular features of vertebrate nervous system are extremely similar in Drosophila. Thus, studies on Drosophila will help reveal the mechanisms of human brain functions.

Research Projects:

1). Taking an interdisciplinary approach including molecular, cell, developmental and genetic methods to study nervous system development, structure and function, using Drosophila peripheral neuromuscular junction synapses and central mushroom body neurons as model systems.

2). Study the molecular and cellular bases of major neurological diseases including Fragile X mental retardation in order to develop an intervention and/or a cure for the diseases, using Drosophila melanogaster as a model organism. These studies will also help advance our understanding of normal development and function of nervous system.

Prof. Viki Allan, Principle Investigator

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ABSTRACT

Investigating microtubule motor function and regulation.

We work on the microtubule motors cytoplasmic dynein and kinesins 1-3. Kinesins 1-3 move towards the dynamic plus ends of microtubules, which are usually located at the cell periphery, while cytoplasmic dynein moves towards microtubule minus ends at the cell centre. A significant part of the work on dynein is a collaboration with Philip Woodman.

My main focus is the roles these motors play in the secretory and endocytic pathways. They establish the position and organisation of each organelle, and facilitate membrane traffic between them. The overall questions I am asking are:

- how do motors contribute to organelle function and membrane trafficking?
- how is motor activity regulated?
- is motor regulation integrated with organelle activities such as protein sorting?
- which motor, or motor isoform, moves each cargo, and is there redundancy?
- how do motors associate with their cargoes?

In addition to using standard biochemical, cell and molecular biological approaches, we use a range of specialist imaging techniques to study motor protein function:

1. Reconstitution of motor protein function in vitro. We use Xenopus laevis egg extracts to reconstitute membrane movement and have studied the role of kinesins in ER and ERGIC movement, and characterised the cell cycle regulation of membrane movement. In addition, we analyse the activity of purified motor proteins.
2. Use of semi-intact cells to study membrane movement. We use digitonin to permeabilise the plasma membrane of cells transfected with organelle-targeted GFP. Using fluorescence microscopy, we observe membranes moving when cytosol is added back to the cells.
3. Live cell imaging. We image the movement of organelles such early endosomes (with Philip Woodman and Martin Lowe) or the ER, identified using specific FP-tagged markers. In collaboration with Philip Woodman and Tom Waigh in Physics and Astronomy, University of Manchester, we are using automated particle tracking to analyse the motile properties of endosomes on a global scale.

In addition to showing how we use the above techniques, I will talk briefly about our recent work on the function of the light intermediate chains of dynein (LICs). Using RNAi, we have tested whether the two LICs move different cargoes. We find that LICs act redundantly for organelle movement, but may have some distinct roles in mitosis. Although depletion of both LICs inhibits membrane movement in vivo, purified dynein lacking LICs exhibits normal motor activity in vitro. Since membrane binding of dynein is not affected by the loss of LICs, this suggests that LICs are required for controlling dynein function on native cargoes.

Dr. Xiangdong Li, Principle Investigator

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ABSTRACT

Regulation of Unconventional Myosin-Va: an Actin-Based Molecular Motor

Unconventional myosin-Va is a well-known processive motor involved in transport of organelles along actin filaments. A tail-inhibition model is generally accepted for the regulation of myosin-Va: the inhibited myosin-Va is in a folded conformation such that the tail interacts with the head and inhibits its motor activity, and high Ca2+ or cargo-binding interrupts the head-tail interaction thus relieving the inhibition. Our studies indicate that the C-terminal globular tail domain (GTD) is the inhibitory domain which directly inhibits the motor activity of the head. However the mechanism of GTD inhibition is still not clear, as the structural information of inhibited Myosin-Va is not available. We recently assigned the GTD-binding site in a pocket of the head, formed by the N-terminal domain, converter, and the calmodulin in IQ1. We proposed that the binding of the GTD to the head prevents the movement of the converter/lever arm of the motor domain during ATP hydrolysis cycle, thus inhibiting the chemical cycle. The activation of myosin-Va by Ca2+ can be readily explained by our model: Ca2+ binds to the calmodulin in IQ1 and its conformational change prevents the interaction between the GTD and the head. Consistently, we found that the GTD inhibition of the truncated myosin-Va with only motor domain and IQ1 is still regulated by Ca2+. We further identified the C-terminal Ca2+-binding sites in calmodulin as the key determinant of Ca2+ regulation of myosin-Va.

RESEARCH FOCUS

We are interested in the function and regulation of myosin motor protein. Myosin is the major component of thick filament in muscle. The contraction of muscle is caused by the slide between thin filaments and thick filaments. Besides being a key component of muscle, myosins exist in nearly all types of eukaryotic cells. With the completion of a number of eukaryotic genomic projects, it became apparent that the myosin superfamily is much larger and more diverse than previously predicted. Based on structural similarities , the myosin superfamily is organized in over 30 classes, including conventional myosins (muscle myosin and non-muscle myosin II) and unconventional myosins. The human genome contains 39 different myosin genes belonging to 12 of these classes. Although the functions of conventional myosins in muscle contraction and cell division have been intensively studied, little is known about the unconventional myosin. Mutations in unconventional myosins cause a number of genetic diseases in human and mammals. The association of myosins with these genetic diseases highlights the importance of understanding the cellular roles of myosins. We will investigate the precise function and regulation mechanism of each family of unconventional myosins by using various modern technologies including Molecular biology, biochemistry, structural biology, biophysics, and cell biology.

Dr. Yihua Zhou, Principle Investigator

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ABSTRACT

Study on rice brittleness mutants, a way to open the 'black box' in monocot cell wall biosynthesis

Rice is a model organism for studying the mechanism of cell wall biosynthesis and remolding in Gramineae. Mechanical strength is an important agronomy trait of rice plants (*Oryza sativa* L.) that affects crop lodging and gain yield. As a prominent physical property of cell walls, mechanical strength reflects upon the structure of different wall polymers and how they interact. Studies on the mechanisms that regulate the mechanical strength therefore depend on uncovering the functions of corresponding genes in cell wall biosynthesis and remodeling. Our group focuses on the studies of systematical isolation of *brittle culm* (*bc*) mutants and functional characterization of their corresponding genes. Till now, we have reported five *bc* mutants. The identified genes cover several pathways of cell wall biosynthesis, including cellulose biosynthesis and deposition, membrane trafficking, and matrix polysaccharides formation. All of those have revealed many secrets in monocot cell wall biosynthesis and remodeling, which are helpful for harnessing the waste rice straws for biofuel production.

RESEARCH FOCUS

Functional characterization of genes involved in monocot cell wall biosynthesis

Plant cell wall is the most abundant renewable resource on this planet. It plays important roles in plant growth and development, and is used as industrial raw material to meet our society's fiber, material and energy demands. My laboratory is mainly interested in the molecular mechanism of monocot cell wall formation and remodeling, focusing on functional characterization of genes involved in these processes. We use forward genetic approach to systematically screen rice brittle culm mutants (bc) and functionally characterize the genes involved in cell wall biosynthesis; we also use reverse genetic approach to identify the roles of some important gene families related to cell wall metabolism. All those allow us progressively understanding the complicated mechanism of cell wall biosynthesis in rice.

Mechanical support is an important agronomic trait, which is highly correlated with crop yield and stress resistance. My laboratory is also interested in the mechanisms that affect rice lodge. Based on the established analytic platform of cell wall polysaccharides, we explore the correlation of cell wall discrepancy and lodge behaviors in different rice varieties. The related mechanisms are beneficial for breeding rice varieties with improved mechanical properties.

Prof. Simon Turner, Principle Investigator

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ABSTRACT

Plant cell wall synthesis and vascular tissue development

A focus of my laboratory has been on the biosynthesis of the plant secondary cell wall principally in the model plant Arabidopsis. In particular, we are interested in the synthesis of the very abundant plant cell wall polymers cellulose and xylan. We have used both forward and reverse genetics to identify irregular xylem mutants that have allowed us to identify many of the genes involved in the biosynthesis of these important plant cell polymers. Although cellulose is the most abundant biopolymer identifying the large membrane-bound complex that synthesizes cellulose remains elusive, however identification of components of this complex remains one of our major priorities. In addition to identifying the genes involved in the biosynthesis of the cell wall, we are also interested in various aspects of the cell biology. In particular, how microtubules contribute to localization and guide the movement of the cellulose synthase complex in the plasma membrane and how cell wall components are targeted to and integrated into the cell wall.

The orientation of cellulose microfibril deposition is determined by the orientation of the underlying microtubule array. In the transition from dividing cells to expanding cells the cortical microtubule array must reorganize from a net-like orientation to a highly ordered array in which the majority of the microtubules of our parallel to one another. We have identified an essential role for the microtubule severing enzyme katanin in this process. Katanin mutants are unable to switch from netlike to ordered arrays. We are currently looking at what other proteins regulate this process.
We are also interested in two areas of plant cell growths. In particular, what regulates the orientation and write off plant cell division. We have used plant vascular development as a convenient model for this process since the vascular tissue arises by a series of very orders cell divisions. By identifying mutants with altered vascular development. We have identified an LLR receptor kinase and its peptide ligand that are involved in regulating both the rate and the orientation of vascular cell divisions.

Dr. Thomas Nuhse, Principle Investigator

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ABSTRACT

Cell wall feedback signalling and control of cell elongation

Cell expansion in plants requires rearrangement and *de novo* production of cell wall polysaccharides. To ensure these processes are in sync with the increase in cell size and surface area, information about wall structure and stability has to be fed back into the cytoplasm. We know that a dedicated pathway for cell wall integrity signalling exists in plants but - unlike its well-established counterpart in yeast – it is poorly understood.

We use primary root tips of Arabidopsis as a model system with extreme demand for cell wall remodelling and therefore vulnerability to perturbation or damage. Interference with cell wall assembly or biosynthesis rapidly slows down elongation via a signalling pathway that requires ACC biosynthesis but surprisingly not ethylene perception. This unusual “ACC shortcut” that controls elongation is however a downstream element shared by other stress signals. To identify sensors and signalling components upstream of this general pathway, we analyse candidate genes rapidly induced by cell wall stress in root tips. We have also begun to use quantitative phosphoproteomics to identify changes in protein phosphorylation triggered by cell wall stress. The ultimate aim is to understand the homoeostatic mechanisms for cell wall stability during normal growth, and to explore how plant responses to biotechnological manipulation of cell wall composition can be controlled.

Travel Information:

- We will shuttle guests to the airport

Conference Information:

- **Beijing**

As the capital of China, Beijing is one of the world\'s truly imposing cities, with a 3,000-year history and 11 million people. Covering 16,808 square kilometers in area, it is the political, cultural and economic center of the People's Republic.

The long history leaves Beijing abundance of historical and cultural heritage that representstreasures from the city\'s civilizations.Today, the old city walls have been replaced by ring roads, and many of the old residential districts of alleys and courtyard houses have been turned into high-rise hotels, office buildings, and department stores. Beijing, a dynamic city where the old and new intermingle, remains a magnet for visitors from inside and outside China. Also, you can find all kinds of Beijing snacks and flavor food from all of the citiesof China. Beijing thrives today as the political and cultural capital of China as well as a center of international activity and an important socialist base.

As Beijing has been confirmed home city of Olympics 2008, the spirit of "green Olympics, scientific Olympics and humanized Olympic" brings more and more changes to Beijing, promote the development of sports and Olympics in China as well as in the world, and strengthen the friendly communications between Chinese and foreign people.

- **The Chinese Academy of Sciences (CAS)**

Chinese Academy of Sciences (CAS) is a leading academic institution and comprehensive research and development center in natural science, technological science and high-tech innovation in China. It was founded in Beijing on 1st November 1949 on the basis of the former Academia Sinica (Central Academy of Sciences) and Peiping Academy of Sciences. Current president of CAS is Prof. Bai Chunli.

In the early days, the CAS was mandated as the key force of the new China’s scientific research system, undertaking missions of defining scientific research orientations, restructuring its research institutions, encouraging and helping overseas Chinese scientists to return home, training and properly allocating professionals, outlining strategies for the nation’s future scientific and technological development while contributing to the national economic and social development. Since China adopted the reform and opening-up policy in the late 1970’s, the CAS has been devoting itself into the reform and innovation for social and economic development, as a major driving force in the reform of the national scientific and technological system and the rejuvenation of the country’s hi-tech industry, just in the wake of the world’s science and technology development. The CAS, at present facing a new era of development, is now targeting at the national strategic needs and world frontiers of science, striving to accomplish world-class science and to continuously make fundamental, strategic and forward-looking contributions to national economic construction, national security and social sustainable development by strengthening original scientific innovation, innovation of key technologies and system integration.

As the nation’s highest academic institution in natural sciences and its supreme scientific and technological advisory body, and national comprehensive research and development center in natural sciences and high technologies, it consists of the Academic Divisions and various subordinate institutions.

The Academic Divisions are composed of all CAS members. The life-long honor of CAS member is the highest academic title set up in science and technology in China. The CAS membership system includes members, emeritus members and foreign members. It has now 692 CAS members in total. At present, there are six academic divisions, functioning as the national scientific think-tank, providing advisory and appraisal services on issues stemming from the national economy, social development and S&T progress.

Today’s CAS has 12 branch offices, 103 institutes with legal entity, more than 100 national key laboratories and national engineering research centers, and about 1,000 field stations throughout the country. Its staff even surpassed 50,000.

- **The Institute of Genetics and Developmental Biology**

The Institute of Genetics and Developmental Biology (IGDB) of the Chinese Academy of Sciences (CAS) was founded in 2001 by a merger of three former institutes of CAS, the Institute of Genetics (founded in 1959), the Institute of Developmental Biology (founded in 1980) and the Shijiazhuang Institute of Agricultural Modernization (founded in 1978). The mission of the institute is to address fundamental questions in genetics and developmental biology and to develop new technologies for the uses in health care and agriculture sciences as well as to meet the nation's strategic needs in science and technology.

IGDB has a strong and young scientific community. Among 541 employees, 365 persons are directly involved in research activities. The faculty includes 2 Fellows of CAS and fifty-nine Principal Investigators. Among them, 36 faculty members are the recipients of the CAS Young Talented Award, also known as One Hundred Talent Program, the highest honor in CAS for young starters, and 25 of them have also received the National Natural Science Foundation of China (NSFC) Award for young investigators, the highest honor for young scientists in the nation. Three research teams in the institute have received the Fund for Creative Research Groups from the NSFC, while other two teams have been supported by the CAS International Partnership Program for Creative Research Teams. There are a total of 509 graduate students, and among them 346 students are doing their PhD.

Scientists in the institute use both plant and animal models to address fundamental questions in life sciences, such as genetic control of growth and development, gene expression, signal transduction, structural and functional genomics, biotech and molecular breeding, bioinformatics and systems biology. As China owns the biggest agricultural market in the world, our researchers in the Institute have also made significant efforts on water saving agriculture and agronomic studies, focusing on the improvement of crop productivity and quality as well as bio-safety.

There are five highly interactive centers in the institute: Genome Biology, Molecular Agro-biology, Developmental Biology, Molecular Systems Biology and Agro-Resources Research. The institute has four key labs: the State Key Lab of Plant Genomics, the State Key Lab of Plant Cell and Chromosome Engineering, the Key Lab of Molecular and Developmental Biology of Chinese Academy of Sciences and the Hebei Key Lab of Water-Saving Agriculture. In addition, the National Plant Gene Research Center (Beijing) is affiliated with the institute.

Hotel Accommodation and Meeting Site

- **Accommodation :**Olympic Village Garden hotel, Building A1, No 1 Lin Cui East Road, Chao yang District, Beijing P.R. China , VIP hotline: +86 10 8437333
- **Meeting Site:** Institute of Genetics and Developmental Biology, CAS, No.1 West Beichen Road, Chaoyang District, Beijing, China

Official Language

The official language for the meeting will be English. It will be used for all presentations, discussions and printed materials.

Contact Information

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