Abstracts

The Fourth Annual Joint Scientific Symposium of NIH/FDA CAA and Washington DC Chapter of SCBA

ADVANCES IN BIOLOGICAL SCIENCES

The NIH (National Institute of Health)/FDA (Food and Drug Administration of USA) CAA (Chinese American Association) and the Washington DC Chapter of SCBA (Society of Chinese Bioscientists in America) have successfully organized three symposia in the last three years. The fourth symposium will be held on the NIH campus (Bldg. 31, Rm 6C10) on August 9, 1997.

Like the previous symposia, this symposium will cover a broad spectrum in biomedical research. We are honored to have the experts at the forefront of various biomedical areas to present their work. Although the topics covered at this symposium only reflect a small fraction of biomedical research carried out by Chinese scientists, we hope that this gathering will serve as a starting point for further in-depth discussions and productive collaborations among Chinese Scientists.

From different angles, the speakers will discuss their efforts in solving major problems facing today's scientists in biomedical research. Most of the studies are focused on cell membrane signaling, gene regulation, and cell division. Five talks will be devoted to the role of signal transduction in the regulation of cellular functions. One of them is about a novel IkB binding protein, VVP, which releases and thus activates NFkB. Two presentations will focus on the effects of signal transduction on cytoskeletal changes by studying cortactin and tensin. The other two speakers will be related to the regulatory role of neurotrophins and bone morphogenic proteins during organ development. In addition, interesting advances in metal binding proteins and their roles in mediating cell functions will also be discussed.

The ultimate effect of signals from cell surface is to regulate specific genes. One example is the control of transcription factors by HSP-70 via the change in the activity of protein kinase C and protein phosphatase. One speaker will specifically present data on the regulation of TATA binding protein by transcriptional activators.

The expression of various genes often results in the change in cell fate, i.e., cell division or apoptosis. Uncontrolled cell division or inadequate cell death often leads to tumorigenesis. One study employs a plant system, where cell migration is limited while cell division is the main driving force for organogenesis. The speaker will discuss the function of TSO1 gene in the cell division in flowers. Two other presentations will focus on cancer development. One will be about the structure of the GST enzyme and its relation with drug resistance in tumors. The other speaker will present a novel finding about the mycoplasma mediated tumorigenesis process.

Cellular homeostasis of multicellular organisms is tightly controlled by the fine balance between cell division and apoptosis. The relationship between cell division and apoptosis will be discussed by examining the role of c-myc in the regulation of Fas and Fas ligand during activation-induced T-cell apoptosis. Another presentation will report studies on the role of protease in cell death in a bacteria system.

Our efforts in biomedical research will improve our life through biotechnology. One example is a talk on promoting antigenecity of antigens by GM-CSF via enhancing antigen presentation. Such a strategy can potentially be employed in vaccine development.

Dr. Juliann G. Kiang and Dr. Yunbo Shi were instrumental in the organization of this meeting. We would like to express our gratitude to Dr. M. K. Jeang, Cardiovascular Center, University of Texas of Health Sciences Center at Houston, and the Science Division of Taipei Economic and Cultural Representative Office in US as well as a number companies for their generous support of the meeting. We specially thank Dr. K.-T. Jeang, a former president of NIH/FDA CAA, for his advice in organizing this meeting.

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S1. TS01 AND ITS ROLE IN CELL DIVISION AND ORGAN MORPHOGENESIS IN ARABIDOPSIS FLOWERS

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One of the fundamental differences between animals and plants is that plant cells are surrounded by a rigid wall, preventing cell migration. The lack of mobility of plant cells leads to the requirement for well organized and regulated cell divisions with specific cell division orientations to achieve directional growth. Such control of division planes may ensure properly organized meristems and thus proper organ initiation and morphogenesis.

In addition, plant cell division is unique in several aspects: the presence of a preprophase band (PPB), the absence of an obvious microtubule-organizing center (MTOC), and a mechanism for cytokinesis involving vesicle fusion. However, little is known about the genes and the control mechanisms underlying its cell division process.

TS01 was identified in a genetic screen by mutations that disrupt meristem organization and floral organ morphogenesis. Mutations in ts01 cause callus-like tissues to form instead of normal flowers. Other parts of the plants develop normally. Scanning Electron Microscopy (SEM) analysis showed that ts01 flowers produce 4 to 6 morphologically abnormal sepals and then produce callus-like cells in the center. These callus-like cells do not differentiate further, resulting in complete sterility. Using Confocal Laser Scanning Microscopy (CLSM), we observed that ts01 floral meristems often have disorganized cell layers. Using Transmitted Electron Microscopy (TEM), we observed that ts01 floral meristem cells have partially formed cell walls, and that the nuclear membranes frequently invaginate. In addition, the nuclei of ts01 flowers are irregular in size and shape. Microspectrofluorometric measurements indicated polyploidy greater than 16C in some cells of ts01 mutant floral meristems, whereas the wild type floral meristems exhibited DNA contents of 2C and 4C. These observations suggest that the primary defect of ts01 likely resides in mitosis and cytokinesis. To further define the specific function of TS01, a map-based cloning approach is being employed to isolate the TS01 gene. TS01 has been mapped to chromosome 3 on a single YAC. In addition, the cytoskeleton organization in the ts01 mutant cells are being examined using anti-tubulin antibody and GFP-tagged tubulin. Our finding that TS01 is essential for cell division in floral tissues but not in vegetative tissues suggests that the cell division machinery may be different in these two types of tissues.

S2. From Growth Factors to The Cytoskeleton

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Fibroblast growth factor requires a continual stimulation of Balb/c 3T3 cells during the transition from G0 to S phase, and initiates a series of proteins that are profoundly phosphorylated at tyrosine residues. One of those proteins has been identified as cortactin, a unique protein characterized by six and half 37-amino-acid repeats in the NH2-terminus and a SH3 domain at its carboxyl end. Cortactin was also found as a prominent substrate for Src tyrosine kinases. The human cortactin gene, also called EMS1, is frequently amplified with cyclin-D1 and overexpressed in human malignancies. Our goal is to define the physiological and pathological roles of cortactin. Using histochemical analysis, we have shown that cortactin is highly expressed in megakaryocytes and platelets in circulating blood. Furthermore, expression of cortactin is upregulated during the maturation of megakaryocytes in response to various extracellular signals including hematopoietic factors IL-3, thrombopoietin, IL-11 and phorbol ester on a megakaryoblast cell line CMK. In adherent cells, cortactin primarily localizes within peripheral cell structures such as lamellipodia, pseudopodia and membrane ruffles, which are enriched for cytoskeletal proteins. We have recently shown that cortactin can promote sedimentation of F-actin under conditions where F-actin is otherwise not able to be precipitated. Electron microscopic analysis after negative staining further revealed that actin filaments in the presence of cortactin are crosslinked into bundles of various degrees of thickness. Hence, cortactin is also an F-actin crosslinking protein. We also demonstrate that the optimal F-actin crosslinking activity of cortactin requires a physiological pH in a range from 7.3 to 7.5. Furthermore, Src phosphorylates cortactin exclusively at tyrosine residues in vitro, resulting in a dramatic reduction of its F-actin crosslinking activity in a manner depending on levels of tyrosine phosphorylation. In addition, Src inhibits moderately the F-actin binding activity of cortactin. Our study presents a strong evidence that Src can directly regulate the activity of its substrate toward the cytoskeleton, and implies a role of cortactin as an F-actin modulator in tyrosine kinase-regulated cytoskeleton reorganization.