Curriculum Vitae

Junjie Chen

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Education

1984-88 Fudan University, Shanghai, P.R. China. B.S., Genetics and Genetic Engineering,

1988-89 Enrolled in the Master's Program at the Institute of Plant Physiology, Academia SINICA, Shanghai, P.R. China.

1989-93 University of Vermont, Burlington, Vermont. Ph.D., Cell and Molecular Biology Program, December, 1993.

Research and Professional Experience

1988-89 Research Assistant in the Laboratory of Molecular Genetics (Dr. S.J. Shen), Institute of Plant Physiology, Academia Sinica.

1990-93 Teaching Assistant in Microbiology and Molecular Genetics, University of Vermont.

1989-93 Predoctoral Research, Laboratory of Dr. David S. Pederson, University of Vermont. Thesis title: Chromatin Structure and Regulation of the HSP26 Gene in the Yeast *Saccharomyces cerevisiae*.

1994-96 Postdoctoral Fellow with Dr. Anindya Dutta, Department of Pathology, Brigham and Women's Hospital, Harvard Medical School. Worked on the Tumor Suppressor protein p53, the cell cycle regulatory protein p21 and control of DNA replication.

1996-1999 Postdoctoral Fellow with Dr. David M. Livingston, Department of Cancer Biology, Dana Farber Cancer Institute, Harvard Medical School.

1999-2003 Senior Associate Consultant, Department of Oncology, Mayo Clinic.

2000- Assistant Professor of Biochemistry and Molecular Medicine, Mayo Medical School, Mayo Foundation.

2001- Assistant Professor of Molecular Pharmacology and Experimental Therapeutics, Mayo Medical School, Mayo Foundation.

2003- Consultant, Department of Oncology, Mayo Clinic.

The role of BRCT domains in DNA damage responses

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Summary:

The C-terminal domain (BRCT) of the Breast Cancer Gene 1 (BRCA1) protein is an evolutionarily conserved module that exists in a large number of proteins from prokaryotes to eukaryotes. While most BRCT domain-containing proteins participate in DNA damage checkpoint or DNA repair pathways, or both, the function of the BRCT domain is not fully understood. We show that the BRCA1 BRCT domain directly interacts with phospho-proteins, suggesting that BRCT domain is a phospho-protein binding motif. In agree with this hypothesis, we show that multiple additional BRCT domains also preferentially bind phospho-peptides rather than non-phosphorylated control peptides. These data imply that the BRCT domain is a general phospho-protein binding domain involved in cell cycle control.

Breast cancer tumor suppressor BRCA1 participates in the maintenance of genomic integrity by regulating multiple cellular events including DNA damage/repair and apoptosis. The molecular mechanism underlying this multi-functional nature of BRCA1 is not fully understood. Recent studies suggest that the key functions of BRCA1 are in the control of DNA damage-induced cell cycle checkpoints. BRCA1 is involved in both the S/M (also called G2 accumulation) and G2/M checkpoint controls following ionizing radiation. We now demonstrate that two distinct phosphorylation-dependent BRCA1-containing complexes carry out these checkpoint functions. While the BRCA1/BACH1 complex is required for the S/M checkpoint, the BRCA1/CtIP complex is essential for the G2/M checkpoint control following DNA damage. Interestingly, BRCA1 BRCT domains recognize a similar phosphorylated motif existed on both BACH1 and CtIP. BACH1 and CtIP are phosphorylated and associate with BRCA1 at different cell cycle stages, which may explain their involvement in two distinct cell cycle checkpoints controlled by BRCA1. Taken together, these data suggest that different phospho-dependent BRCA1 BRCT domain partners may carry out various functions of BRCA1 in the cell.