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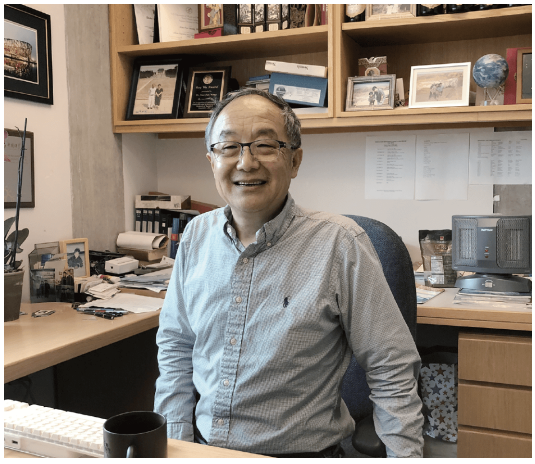
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•PROFILE•

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Profile of Dr. Xiao-Fan Wang

Dr. Xiao-Fan Wang entered Wuhan University in 1978 to receive his college education following the reform of the education system. In 1982, shortly after admitted to the graduate school of the Institute of Genetics at the Chinese Academy of Sciences (CAS), he was sent as one of the first group of Chinese students under the CUSBEA (China–United States Biochemistry Examination and Application) program to study biology in the U.S. He enrolled at the University of California, Los Angeles, and received his graduate training there with Dr. Kathryn Calame, working on the regulation of immunoglobulin gene transcription in B lymphocytes as his thesis. He received his Ph.D. in 1986 and then spent five years at Whitehead Institute for Biomedical Research and Massachusetts Institute of Technology (MIT) as a postdoctoral fellow under the guidance of Dr. Robert Weinberg, cloning two of the receptors for transforming growth factor β (TGF-β). In early 1992 he moved to Duke University Medical Center as an Assistant Professor in the Department of Pharmacology & Cancer Biology. He is currently the Donald and Elizabeth Cooke Professor of Experimental Oncology and Professor of Pharmacology and Cancer Biology at Duke University School of Medicine, and the Director of University Program in Molecular Cancer Biology.



As a world-renowned cancer biologist, Dr. Wang focuses his research primarily on elucidating the molecular mechanisms associated with tumor initiation and the tumor microenvironment. He has contributed to several important aspects of cancer research including cancer cell signaling pathways, DNA damage responses, functions of microRNAs in tumor development and metastasis, and cellular senescence program in normal and neoplastic tissues. In particular, Dr. Wang has made significant contributions in demonstrating the molecular details of the TGF-β signaling cascade and its functions in many fundamental aspects of cellular behaviors. He has published more than 100 scientific papers, many of which were published in prestigious journals including *Science*, *Nature*, *Cell*, *Cancer Cell* and *Nature Cell Biology*.

Cloning TGF-β receptor genes and exploring the molecular cascade and biological functions of TGF-β signaling pathway

The TGF-β family controls many fundamental aspects of cellular behavior and plays an important role in many pathological conditions including human cancer. Dr. Xiao-Fan Wang first cloned and characterized all the three sub-types of TGF-β receptors (TGF-β receptor I, II, and III) (Bassing et al., 1994; Lin et al., 1992; Wang et al., 1991) and thus laid the foundation for studying this signaling pathway in different cell biological processes such as cell differentiation, tumorigenesis, and metastasis.

Following these discoveries, Dr. Wang continued to make important findings in this filed by elucidating the molecular cascade and biological functions of TGF-β signaling pathway. For example, he and colleagues demonstrated that $p21^{CIP1}$ was a major downstream effector of TGF-β singling pathway to induce a cytostatic program (Datto et al., 1995). This has been verified by many laboratories in multiple model systems as one of the most important mechanisms to

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control cell proliferation by TGF-β signaling. In addition, Dr. Wang and his team illustrated how TGF-β and Wnt signaling pathways crosstalk to each other in order to fine-tune cellular responses to signaling input (Guo et al., 2008) or to regulate the proliferation and differentiation of human mesenchymal stem cells (Jian et al., 2006), expanding our understanding of how crosstalk of TGF-β and other signaling pathway cooperatively determine certain biological processes.

Elucidating important tumor-cell-intrinsic and tumor-stroma-interacting mechanisms during tumorigenesis and metastasis

Dr. Xiao-Fan Wang has made significant contributions to a variety of fields in cancer biology. For example, DNA damage is commonly considered as the root cause of cancer via the induction of genomic instability. Thus, it is important to understand the cellular machinery regulating DNA damage responses in order to identify genes imposing high cancer risks. In 2001, Dr. Wang and his colleagues demonstrated that Rad17 protein could be directly phosphorylated by checkpoint kinases ATM and ATR, and this is a critical event during checkpoint signaling in DNA-damaged cells (Bao et al., 2001). In 2004, they identified another protein, serine-threonine phosphatase 5 or PP5, playing an essential role in the activation and check-point signaling functions of ATM (Ali et al., 2004). In addition, senescence is a cellular stress response characterized by persistent cell growth arrest under various stress conditions, including oncogene activation or tumor suppressor loss, which functions as a critical barrier that must be overcome to allow the progression from a pre-cancerous or pre-invasive lesion to a malignant tumor. Until recent time, the detailed mechanisms controlling the senescence program remain largely elusive. Dr. Wang and his team identified several important regulators for cellular senescence, including trefoil factor 1 (Radiloff et al., 2011), EGF signaling (Alexander et al., 2015), and IMMP2L signaling (Yuan et al., 2018).

Metastasis is the most life-threatening risk for cancer patients, with more than 90% of cancer-associated deaths being caused by metastatic disease rather than by the corresponding primary tumors. Studying the molecular mechanisms enabling benign tumor cells to develop invasive, malignant phenotypes is another major field for the Wang laboratory. In 2004, they reported that secreted protein Periostin facilitated colon cancer metastasis by suppressing apoptosis of tumor cells and augmenting the survival of endothelial cells to promote angiogenesis (Bao et al., 2004). In 2008, they found another extracellular matrix protein βig-h3/TGFBI, which promotes tumor cell extravasation into the circulation system and thus facilitates metastasis (Ma et al., 2008). In addition, Dr. Wang and colleagues have reported novel functions of several microRNA genes that regulate tumor progression and metastasis via shaping tumor microenvironment (Yang et al., 2012; Zhang et al., 2013) or adapting to hypoxia (Hu et al., 2016; Wang et al., 2014). These findings have been widely recognized in the field and many of the publications were highly cited.

Dr. Xiao-Fan Wang has led many research projects supported by NIH/NCI. During his career, he has trained more than 30 Ph.D. students and more than 20 postdoctoral fellows. From 2006 to 2019, he served as an Associated Editor for *the Journal of Biological Chemistry*, as the first Asian to serve such a position since the establishment of this historic journal for more than 100 years. In 2012–2014, he served as the president of Society of Chinese Biologists in America (SCBA) as the first mainland-born scholar to hold this position. From 2013, he served as an Associated Editor for Science China Life Sciences.

In addition to his academic achievements, Dr. Xiao-Fan Wang has taken great efforts to promote the development of China's science and technology and higher education. From 2008 to 2013, he chaired the International Advisory Committee of Bureau of Biological Sciences and Technology at CAS and helped to establish international evaluation system for many CAS institutes in the biological domain. He has also been invited by many universities, including Tsinghua University, Peking University, Fudan University, Shanghai Jiao Tong University, and Zhejiang University, to organize international committees and conduct assessment of their schools of life sciences and medicine. From 2011 to 2017, he served as a member of the Committee for National Major Scientific Research Projects at Ministry of Science and Technology, contributing to the improvement of the evaluation process for scientific funding in China. As a world-renowned scientist, Dr. Wang continues to help improve the international influence of Chinese scholars. In the past few years, he has recommended more than 30 Chinese scholars into the Editorial Board of *the Journal of Biological Chemistry* and more than 20 Chinese scholars to become Fellows of American Association for the Advancement of Science (AAAS).

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