BIOGRAPHICAL SKETCH

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NAME: Shang Su

eRA COMMONS USER NAME (credential, e.g., agency login): SHANG.SU

POSITION TITLE: Research Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Tsinghua University, Beijing, China	B.S.	07/2011	Biology
Tsinghua University, Beijing, China	Ph.D.	10.2019	Cell Biology/Cancer Biology
Van Andel Institute, Grand Rapids, MI	Post-doc	06/2020	Cancer Biology
The University of Toledo, Toledo, OH	Post-doc	06/2023	Cancer Biology

A. Personal Statement

I am a cancer biologist interested in signal transduction and protein degradation. My current research mainly focuses on deciphering the underlying mechanisms of tumor dormancy, progression, and drug resistance in prostate cancer bone metastases and developing novel agents to target vital players discovered in these biological processes. I am also engaging the targeted protein degradation techniques such as proteolysis-targeting chimera (PROTAC) in prostate cancer studies to modulate the levels of key driver proteins.

I am currently supported by:
DOD EHDA award HT9425-23-1-0015: Su (PI)
Role: PI.

&

NIH/NCI R01CA2307441: Li (PI)
Role: key personnel

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2019 - 2020 Postdoctoral researcher, Van Andel Institute, Grand Rapids, MI
2020 - 2023 Postdoctoral researcher, The University of Toledo, Toledo, OH
2023 - Research Assistant Professor, The University of Toledo, Toledo, OH

Professional Memberships

AACR (American Association for Cancer Research), Associate Member since 2019
ASBMB (American Society of Biochemistry and Molecular Biology), Affiliate Member since 2019
SBUR (Society for Basic Urologic Research), In-training Member since 2020
ACACR (Association of Chinese Americans in Cancer Research), Member since 2021
APS (American Peptide Society), Member since 2021
ASPET (American Society for Pharmacology and Experimental Therapeutics), Member since 2022
SCBA (Society of Chinese Bioscientists in America), Trainee member since 2022

Scientific services

Reviewer (20+ peer reviews)

2021 – Now, Reviewer for Chinese Journal of Cell Biology, Molecular and Cellular Endocrinology (IF 4.102) PeerJ (IF 3.061),
2022 – Now, Reviewer for BioMed Research International (IF 3.246), Cancers (IF 6.575), Cancer Letters (IF 9.756), Cells (IF 7.666), Genes and Diseases (IF 7.243), International Journal of Environmental Research and Public Health (IF 4.614), Journal of Oncology (IF 4.501), Tomography (IF 3.000)
2023 – Now, Reviewer for Current oncology (IF 3.109), Pharmaceutics (IF 6.525), Frontiers in Drug Discovery, Cell & Bioscience (IF 9.597).

Editor
2022 – Now Guest Editor for Frontiers in Drug Discovery.

Honors

2011, Level I Excellent Graduates of Tsinghua University (TOP 2% among 3000 graduates)
2014, Tsinghua Scholarship for Graduate Student, “WU Zhengyi 3-generation” Memorial Award
2016, Excellent PhD student list in School of Life Sciences, Tsinghua University
2021, Excellence Award for Outstanding Post-Doctoral Fellow in Cancer Biology at The University of Toledo

C. Contributions to Science

For a full list of my publications, please visit
https://www.ncbi.nlm.nih.gov/myncbi/shang.su.1/bibliography/public/

Drug resistance and tumor dormancy in prostate cancer bone metastases

I began to investigate the mechanisms of prostate cancer bone metastasis since I joined Dr. Xiaohong Li’s group. Prostate cancer (PCa) is the most frequently diagnosed cancer and the second leading cause of cancer-related deaths in men in the United States. Up to 90% of patients with advanced-stage PCa develop bone metastases, but only 10% are diagnosed with bone metastases at the time of initial diagnosis. Primary PCa cells can disseminate early and remain dormant in distant organs before reactivation, causing metastasis and recurrence. For those established bone metastases, currently FDA-approved drugs can best elongate patients’ survival for 6 months and all the patients eventually develop drug resistance. Therefore, we aim to deeply understand the biology of prostate cancer bone metastases, specifically for the tumor dormancy at the early dissemination phase and drug resistance in the later overt metastases.

We discovered that enzalutamide could trigger the degradation of TGFBR2 in osteoblasts which in turn led to the resistance of prostate cancer bone metastases to enzalutamide. The enzalutamide-induced TGFBR2 loss was fulfilled by endocytosis-mediated by another membrane protein PTH1R and PTH1R blockade could rescue the TGFBR2 decrease in osteoblasts and restore enzalutamide response in prostate cancer cells We also observed via a subcutaneous xenograft model that surgical removal of primary prostate tumors resulted in enriched disseminated tumor cells in the bones and osteoblasts induced these bones into dormancy via physical contact and a focal-adhesion-kinase-mediated signaling pathway. Blocking focal adhesion kinase via a clinically tested small molecule induces prostate cancer cells into dormancy and could act as a promising approach to prevent/delay bone metastatic relapse/onset by inducing disseminated tumor cells into dormancy.

1. **Su S**[#], Cao J[#], Meng X[#], Liu R, Vander Ark A, Woodford E, Zhang R, Stiver I, Zhang X, Madaj Z, Bowman M, Wu Y, Chen B, Yu H, Li X. Enzalutamide-induced PTH1R-mediated TGFBR2 decrease in osteoblasts contributes to resistance in prostate cancer bone metastases. Cancer Letters, 2021, 525: 170-178. (#, co-first author)
2. **Su S**, Li X. Dive into Single, Seek out Multiple: Probing Cancer Metastases via Single-Cell Sequencing and Imaging Techniques. Cancers, 2021, 13, 1067.
3. Zhao Y, **Su S**, Li X. Parathyroid Hormone-Related Protein/Parathyroid Hormone Receptor 1 Signaling in Cancer and Metastasis. Cancers. 2023,15(7).

4. Liu R[#], **Su S**[#], Xing J[#], Liu K, Zhao Y, Stangis M, Jacho DP, Yildirim-Ayan ED, Chen B, Li X. Tumor removal limits prostate cancer cell dissemination in bone and osteoblasts induce cancer cell dormancy through focal adhesion kinase. Preprint on BioRxiv, under review in Oncogene. (#, co-first author)

Targeted protein degradation

I developed my expertise in the field of targeted protein degradation under the supervision of Dr. Yu Rao and Dr. Wei Wu. We designed and characterized a series of proteolysis-targeting chimera (PROTAC) molecules against vital therapeutic target proteins in cancers, including CDK4/6, HDAC6, and PARP1. We also developed a fluorescence-based tool to monitor the degradation induced by PROTAC molecules in live cells. I am currently funded by DoD with a project integrating PROTAC and CRISPR technique to develop novel systematic approach for regulator binder protein screen.

1. **Su S**[#], Yang Z[#], Gao H, Yang H, Zhu S, An Z, Wang J, Li Q, Chandarlapaty S, Deng H, Wu W and Rao Y. Potent and Preferential Degradation of CDK6 via Proteolysis Targeting Chimera. Journal of Medicinal Chemistry, 2019, 62 (16), 7575-7582. (#, co-first author)
2**.** An Z, Lv W, **Su S**, Wu W and Rao Y. Developing potent PROTACs tools for selective degradation of HDAC6 protein. Protein & Cell, 2019, 10(8): 606-609.
3**.** Zhao Q, Lan T, **Su S**, Rao Y. Induction of Apoptosis in MDA-MB-231 Breast Cancer Cells by a PARP1-Targeting PROTAC Small Molecule. Chemical Communications, 2019, 55 (3), 369-372.

Cell cycle regulation of Wnt signaling

I am also interested in the periodical perturbation or fluctuation of cellular signals in cancer cells. I got trained in the signal transduction studies on cell cycle and Wnt signaling at Dr. Wei Wu's lab.. We observed that the central signaling molecule beta-catenin binds to its transcription factor TCF7L2 (also known as TCF4) in a cell-cycle-dependent manner: peak at G2/M phase and diminish upon G1 entry. We demonstrated that this phase-specific beta-catenin-TFC complex formation drives the expressions of genes that protect cells from apoptosis/anoikis and help cells cross the M/G1 border.

1**.** Ding Y[#], **Su S**[#], Tang W, Zhang X, Chen S, Zhu G, Liang J, Wei W, Guo Y, Liu L, Chen Y-G and Wu W. Enrichment of the β-catenin–TCF complex at the S and G2 phases ensures cell survival and cell cycle progression. Journal of Cell Science, 2014, 127: 4833-4845. (#, co-first author)
2**. Su S**, Wu W. Regulation of target gene transcription by Wnt/β-catenin signaling. SCIENTIA SINICA Vitae, 2014, 44: 1029–1042. (Invited review in Chinese).