BIOGRAPHICAL SKETCH

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NAME: Kang, Yibin

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

POSITION TITLE: Warner-Lambert/Parke-Davis Professor of Molecular Biology

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)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Fudan University, Shanghai, China	B.S.	09/1991	06/1995	Genetics
Duke University, Durham, NC	Ph.D.	09/1995	05/2000	Genetics
Memorial Sloan Kettering Cancer Center, NYC	Postdoctoral	06/2000	09/2004	Cancer Biology & Genetics

A. Personal Statement

I am the Associate Director of Consortium Research and Co-Director of the Genomic Editing Shared Resource at Rutgers Cancer Institute of New Jersey. I have the expertise, leadership, training, expertise and motivation to successfully carry out the proposed research project. The goal of my research program is to reduce and eventually eliminate the morbidity and mortality from metastatic breast cancer, and my entire research program has been exclusively devoted to this goal in the past 20 years. My research program has encompassed a wide spectrum of breast cancer metastasis research, from mammary gland cell fate regulation to epithelial-mesenchymal transition (EMT) and early invasion, to metastatic colonization in distant organs and treatment resistance. I have made major contributions to the study of regulation of mammary gland stem cells (MaSCs) and the role of breast cancer stem cells (BCSC) in breast cancer initiation and metastasis. We identify Elf5, ΔNp53 and miR-199a as key regulators of MaSC and BCSCs, and our research identified macrophages as a key component of the MaSC niche through the coupling of Notch and Wnt signaling. My laboratory has also made major contributions to the study of organ-tropic metastasis to bone and other organs. We developed a functional genomic approach to comprehensively identify bone metastasis genes, established novel imaging approaches to analyze the cellular and molecular dynamics of bone metastasis, and illustrated the functional mechanism of miRNAs, matrix metalloproteases, EGFR, E-selectin, CCL-2, hypoxia, TGF-β signaling, Jagged1-Notch and Wnt signaling in bone metastasis. Our group also played a significant leading role in the identification and functional analysis of the novel breast cancer progression gene Metadherin (MTDH). I have published more than 190 research articles, including many in leading journals such as Cell, Science, Cancer Cell, Nature Medicine, Nature Cancer and Nature Cell Biology. I have also severed in several leadership positions in the breast cancer research community, including the President of the Metastasis Research Society (2016-2018) and the Chair of the Steering Committee of the AACR Tumor Microenvironment (TME) Working Group (2018-2019).

I have major responsibilities in the teaching of cancer biology and the training of the next generation of cancer researchers at Princeton University. I teach “Molecular Basis of Cancer” (MOL523) and serve as a member of our graduate committee. Most pre- and post-doctoral trainees in my lab have received highly competitive fellowships for cancer research from NIH, DOD, ACS, Susan Komen, HHMI and NJCCR. Among the graduate students and postdoctoral fellows who have completed their training in my lab, over 95% of them remain in career paths related to cancer research, including many who have obtained tenured or tenure-track faculty positions in breast cancer research in leading institutions, such as the University of Pennsylvania (3), Danar Farber Cancer Institute/Harvard, Jackson Laboratory Cancer Center, University of Notre Dame, Karmanos Cancer Center/Wayne State University, Tsinghua University and Shanghai Institute of Health Sciences.

Ongoing and recently completed projects that I would like to highlight include:

Breast Cancer Research Foundation BCRF-21-082
Kang (PI)
10/1/21-9/30/22
The Role of Metadherin in Immune Evasion of Metastatic Breast Cancer

Breast Cancer Research Foundation BCRF-20-082
Kang (PI)
10/01/20-09/30/21
Targeting Metadherin to reduce the initiation and metastasis of breast cancer

The Susan G. Komen Breast Cancer Foundation SAC190067
Kang (PI)
06/10/19-06/09/22
Targeting of a key enzyme in breast cancer metastasis and chemoresistance

NIH 1R01CA212410-05
Kang (PI)
01/2017-12/2021
Jagged 1 – Dependent Tumor-stromal Interactions in Bone Metastasis

Department of Defense Breast Cancer Program Breakthrough Award
Kang (PI)
9/30/16 – 9/29/20
Functional Mechanism and Targeting of Metadherin in Breast Cancer

Citations:

1. Sethi N and **Kang Y**. (2011) Unraveling the complexity and dynamics of metastasis: from molecular understanding to targeted therapeutics. ***Nature Reviews Cancer***, 11(10):735-748. PMID: 21941285
2. Wan L, Pantel K, and **Kang Y**. (2013) Tumor metastasis: translating new biological insights into better anti-cancer therapeutics. ***Nature Medicine***, 19:1450-1464. PMID: 24202397
3. Celià-Terrassa T and **Kang Y**. (2018) Metastatic niche in the control of metastatic seeding, outgrowth, plasticity and immune regulation. ***Nature Cell Biology***, 20(8):868-877.
4. Esposito M, Ganesan S and Kang Y. (2021) Finding efficacy in 'incurable' cancers: emerging strategies for treating metastasis. ***Nature Cancer***, 2:258-270.

B. Positions, Scientific Appointments and Honors

Main Appointments

2021-present	Member, Ludwig Institute for Cancer Research, Princeton Branch
2012-present	Warner-Lambert/Parke-Davis Professor of Molecular Biology (endowed), Department of Molecular Biology, Princeton University, Princeton, NJ
2004 -present	Member, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ
2012	Professor, Department of Molecular Biology, Princeton University, Princeton, NJ
2010-2012	Associate Professor (tenured), Department of Molecular Biology, Princeton University, Princeton, NJ
2004-2009	Assistant Professor, Department of Molecular Biology, Princeton University, Princeton, NJ

Other Positions and Scientific Appointments

2018-2022	President, Chinese Biological Investigator Society
2021-present	Scientific Advisory Board Member, Vibrant Pharma Limited, Guangzhou, China

2019-present	Scientific Advisory Board Member, Cytocares, Inc, Shanghai, China
2019-present	Co-founder and Chair of Scientific Advisory Board, KayoThera, Inc. USA
2015-present	Co-founder and Chair of Scientific Advisory Board, Firebrand Therapeutics, Inc. USA
2018-2019	Chair, AACR Tumor Microenvironment (TME) Working Group
2017-present	Associate Director for Consortium Research, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ
2017-present	Grant Review Panel, University Grant Council of Hong Kong
2016-2018	President, Metastasis Research Society
2014-present	Research Task Force member, Metastatic Breast Cancer Alliance
2012-present	Steering Committee, Cancer Institute of New Jersey-Princeton University Consortium
2010-present	Director, Genome Editing Shared Resource, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ
2010-2014	National Institute of Health, Tumor Microenvironment (TME) Study Section
2010-2014	American Cancer Society, Tumor Biology and Genomics (TBG) Study Section
2006-present	Department of Defense Breast Cancer Program review or integration panels
2000-2004	Postdoctoral Research Associate at Dr. Joan Massagué's Laboratory, Cancer Biology and Genetics Program and Howard Hughes Medical Institute, Memorial Sloan-Kettering Cancer Center, New York, NY
1996-2000	Graduate Research Assistant at Dr. Bryan R. Cullen's Laboratory, Department of Genetics and Howard Hughes Medical Institute, Duke University Medical Center, Durham, NC

Honors

2019	American Cancer Society Research Professor
2016	Komen Scholar
2016	Inaugural inductee, Duke Graduate School Few-Glasson Alumni Society
2016	AAAS Fellow
2014	Fidler Innovation Award, Metastasis Research Society
2014	Fuller Albright Award, American Society for Bone and Mineral Research
2014	AACR Outstanding Investigator Award in Breast Cancer Research
2013	Distinguished Young Investigator Award, Chinese Biological Investigator Society
2013	The Axios Award of the AHEPA 5th District Cancer Research Foundation
2012	The 36th AACR Award for Outstanding Achievement in Cancer Research
2011	The Vilcek Prize for Creative Promise in Biomedical Science
2006	Era of Hope Scholar Award, Department of Defense Breast Cancer Research Program
2005	The Padget Foundation Young Investigator Award
2005	American Cancer Society Research Scholar Award
2004	AIMM-ASBMR John Haddad Young Investigator Award
2004	Memorial Sloan-Kettering Cancer Center Annual Postdoctoral Research Award
2001-2004	Irvington Institute Postdoctoral Fellowship for Immunological Research

C. Contributions to Science

1. One of my major contributions to the study of cancer metastasis is the elucidation of molecular pathways that mediate tumor-stromal interactions in organ-tropic metastasis of breast cancer. A large part of my research program is devoted to identifying molecular mediators used by tumor cells to engage various stromal cell types in the bone microenvironment to promote the initiation and progression of osteolytic bone metastasis. We developed a live imaging system to provide the direct in vivo evidence that TGF-β is released from bone destruction to stimulate bone metastasis. We also established a new "vicious cycle" of bone metastasis by showing that bone-derived TGF-β stimulates the expression of Jagged1 in tumor cells, which then engages Notch signaling in osteoblasts and osteoclasts to activate osteoclast differentiation and promote tumor growth through a positive feedback via IL-6 signaling. In collaboration with Amgen, we developed a therapeutic antibody against Jagged1, and showed its strong synergy with chemotherapy against bone metastasis, as it also block the tumor-protective effect of osteoblast-derived Jagged1 induced by chemotherapy. We also developed a unique mouse model of dormant bone metastasis and used it to identify VCAM1 as a crucial driver of the transition of dormant disseminated tumor cells to aggressive overt macrometastasis. Our research also identified a number of osteoclast miRNAs as biomarkers and functional

mediators of osteolytic bone metastasis. Most recently, we revealed a critical role of the E-selectin-dependent vascular niche for the initial seeding of bone metastasis and a novel function of Dact1-dependent biomolecular condensates in the modulation of TGF-β and Wnt signaling in bone metastasis. This series of studies not only significantly broadened our basic understanding of breast cancer bone metastasis, but also established several new avenues to develop new therapeutic agents for metastatic disease.

a. Ell B, Mercatali L, Ibrahim T, Campbell N, Schwarzenbach H, Pantel K, Amadori D, and **Kang Y**. (2013) Tumor-induced miRNA changes in osteoclast as mediators and biomarkers of osteolytic bone metastasis. ***Cancer Cell***, 24:542-56. PMCID: PMC3832956.
b. Zheng H, Bae Y, Kasimir-bauer S, Tang R, Chen J, Ren G, Yuan M, Esposito M, Li W, Wei Y, Shen M, Zhang L, Tupitsyn N, Pantel K, King C, Sun J, Moriguchi J, Jun HT, Coxon A, Lee B and **Kang Y**. (2017) Therapeutic antibody targeting tumor- and osteoblastic niche-derived Jagged1 sensitizes bone metastasis to chemotherapy. ***Cancer Cell***, 11;32(6):731-747. PMCID: PMC5729937.
c. Esposito M, Mondal N, Greco T, Wei Y, Spadazzi C, Song CL, Zheng H, Cheung C, Magnani JL, Lin S-H, Cristea IM, Sackstein R and **Kang Y**. (2019) Endosteal niche E-selectin induces mesenchymal-epithelial transition and Wnt activation in cancer cells to promote bone metastasis. ***Nature Cell Biology***, 21(5):627-639.
d. Esposito M, Fang C, Cook KC, Park N, Wei Y, Spadazzi C, Bracha D, Slabodkin H, Gunaratna R, Laevsky G, DeCoste CJ, Brangwynne CP, Cristea IM, **Kang Y**. (2020) TGF-β-induced Dact1 biomolecular condensates repress Wnt signaling via multivalent protein-protein interactions. ***Nature Cell Bio***., 23(3):257-267.

2. Another major contribution of my research is in the study of the molecular regulatory circuitry of epithelial-mesenchymal transition (EMT), and key step in metastatic progression. The major contribution of my laboratory to the field is the revelation of the complex regulatory network of epithelial-mesenchymal plasticity upstream and downstream of EMT transcriptional factors, such as Snail1/2 and Zeb1/2. We are one of the first laboratories to identify miR-200 family miRNAs as potent inhibitors of EMT and revealed their paradoxical role in promoting metastatic colonization inhibiting the secretion of metastasis suppressive proteins such as Tinagl1. We also showed that alveolar luminal cell fate regulator Elf5 is a negative regulatory of EMT and metastasis by suppressing the expression of Snail2. Furthermore, our recent genome-wide E3 ligase screening identified FBXO11 as a post-translational regulator of Snail in a PKD1-phosphorylation-dependent manner. These findings significantly enrich our molecular understanding of the regulatory network of EMT and its physiological and clinical relevance in normal development and cancer metastasis. Most recently, using mathematical modeling and experimental validation, we demonstrated that the metastasis-promoting function of EMT is dependent on the dynamics of the EMT process, which may help resolve one of the major controversies in the field.

a. Korpal M, Ell BJ, Buffa FM, Ibrahim T, Terrasa AC, Mercatali L, Khan Z, Blanco MA, Goodarzi H, Hua Y, Wei Y, Hu G, Garcia B, Ragoussis J, Amadori D, Harris AL, and **Kang Y**. (2011) Direct targeting of Sec23a by miR-200s influences cancer cell secretome and promotes metastatic colonization. ***Nature Medicine***, 17:1101–1108. (Cover Article) PMCID: PMC3169707.
b. Zheng H, Shen M, Cha Y-L, Li W, Wei Y, Blanco MA, Ren G, Zhou T, Storz P, Wang H-Y, and **Kang Y**. (2014) PKD1 phosphorylation-dependent degradation of SNAIL by SCF-FBXO11 regulates epithelial-mesenchymal transition and metastasis. ***Cancer Cell***, 26:358-373. PMCID: PMC4159622.
c. Celià-Terrassa T, Bastian C, Liu D, Ell B, Aiello NM, Wei Y, Zamalloa J, Blanco AM, Hang X, Kunisky D, Li W, Williams ED, Rabitz H, and **Kang Y**. (2018) Hysteresis control of epithelial-mesenchymal transition dynamics conveys a distinct program with enhanced metastatic ability. ***Nature Communications***, 9(1):5005. PMCID: PMC6258667.
d. Shen M, Jiang Y-Z, Wei Y, Ell B, Sheng X, Esposito EM, Kang J, Hang X, Zheng H, Rowicki M, Zhang L, Shih WJ, Celià-Terrassa T, Liu Y, Cristea I, Shao Z-M, **Kang Y**. (2019) Tinagl1 suppresses triple-negative breast cancer progression and metastasis by simultaneously inhibiting integrin/FAK and EGFR signaling. ***Cancer Cell***, 35(1):64-80.

3. We have also pioneered the study of cell lineage regulators in breast cancer initiation and metastasis, thus linking together the early and late phases of breast cancer progression. Although it was initially thought that metastatic capacity is acquired late during tumor progression, mounting evidence suggests that different

cellular origins and early transformation events may set the resulting tumors on distinct paths towards either aggressive metastasis or slow progression. My laboratory has made significant progress in identifying the shared and distinctive regulatory mechanisms between normal and cancerous stem cells in the mammary epithelium. We showed that reduced expression of luminal cell fate determinant Elf5 promotes EMT and lung metastasis. On the other hand, mammary stem cell regulators ΔNp63 and miR-199a promote tumor initiating cell function in basal-like breast cancer by activating Fzd7 expression and Wnt signaling and suppressing interferon response, respectively. More recently, we reported macrophages as a key stromal niche component for mammary gland stem cells through Dll1-mediated coupling of Wnt and Notch signaling.

a. Chakrabarti R, Hwang J, Blanco MA, Wei Y, Lukačišin M, Romano R, Smalley K, Liu S, Yang Q, Ibrahim T, Mercatali L, Amadori D, Haffty BG, Sinha S and **Kang Y** (2012) Elf5 inhibits epithelial mesenchymal transition in mammary gland development and breast cancer metastasis by transcriptionally repressing Snail2/Slug. ***Nature Cell Bio***., 14(11):1212-22. PMCID: PMC3500637.
b. Chakrabarti R, Wei Y, Hwang J, Hang X, Blanco MA, Choudhury A, Tiede B, Romano R-A, DeCoste C, Mercatali L, Ibrahim T, Amadori D, Kannan N, Eaves CJ, Sinha S, and **Kang Y**. (2014) ΔNp63 promotes stem cell activity in mammary gland development and basal-like breast cancer by enhancing Fzd7 expression and Wnt signaling. ***Nature Cell Bio***, 16(10):1004-15. PMCID: PMC4183725.
c. Celià-Terrassa T, Liu D, Choudhury A, Hang X, Wei Y, Zamalloa J,2, Alfaro-Aco R, Chakrabarti R, Jiang Y-Z, Koh B, Smith H, DeCoste C, Li J-J, Shao Z-M and **Kang Y**. (2017) Normal and cancer stem cells of the mammary gland evade interferon-induced differentiation and senescence through the miR-199a-LCOR Axis. ***Nature Cell Bio***., 19: 711–723. PMCID: PMC5481166.
d. Chakrabarti R, Choudhury A, Peng J, Hwang J, Hang X, Wei Y, Grady JJ, DeCoste C, Gao J, Van Es J, Aifantis I, Clevers H, and **Kang Y**. (2018) Dll1-mediated macrophageal niche for mammary gland stem cells. ***Science***, 360(6396). pii: eaan4153. doi: 10.1126/science.aan4153. PMID: 29773667

4. My laboratory pioneered the identification and functional analysis of a novel breast cancer metastasis gene called Metahderin (MTDH). We first identified MTDH as a dual functioning gene in promoting breast cancer metastasis and chemoresistance through genomic analysis of clinical breast cancer datasets. Using genetically modified mouse models, we showed that MTDH is crucial for sustaining the survival of tumor initiation cells (TICs) through its physical interaction with SND1, but is dispensable for normal development. These results not only identified MTDH as a cancer stem cell-specific survival factor, but also indicated MTDH as an important link between tumor-initiating properties with metastatic traits. MTDH forms an RNA-binding complex with SND1 to 1) promote the survival of tumor-initiating cells under stress and 2) suppress tumor antigen presentation and anti-tumor immune response. We have also developed a small molecule inhibitor of MTDH-SND1 interaction that shows strong synergy with immunotherapy and chemotherapy in suppressing metastatic progression.

a. Hu G, Chong RA, Yang Q, Wei Y, Blanco MA, Li F, Reiss M, Au JL-S, Haffty B, and **Kang Y**. (2009) MTDH activation by 8q22 genomic gain promotes chemoresistance and metastasis of poor-prognosis breast cancer. ***Cancer Cell***, 15(1):9-20. (Cover Article)
b. Wan L, Lu X, Yuan S, Wei Y, Guo F, Shen M, Yuan M, Chakrabarti R, Hua YSmith HA, Blanco MA, Chekmareva M, Wu H, Zheng A, Bronson RT, Haffty BG, Xing Y, and **Kang Y** (2014) MTDH-SND1 interaction is essential for the expansion and activity of tumor-initiating cells in diverse oncogene- and carcinogen-induced mammary tumors. ***Cancer Cell***, 26(1):92-105.
c. Shen M, Wei Y, Kim K, Wan L, Jiang Y-Z, Hang X, Raba M, Remiszewski S, Rowicki M, Zhang L, Lu X, Yuan M, Smith HA, Zheng A, Lin H, Bertino J, Jin JF, Xing Y, Shao Z-M, and **Kang Y**. (2022) Small-molecule inhibitors that disrupt the MTDH–SND1 complex suppress breast cancer progression and metastasis. ***Nature Cancer***, 3(1):43-59.
d. Shen M, Smith HA, Wei Y, Jiang Y-Z, Zhao S, Wang N, Rowicki M, Tang Y, Hang X, Wan L, Shao Z-M, **Kang Y**. (2022) Pharmacological disruption of the MTDH–SND1 complex enhances tumor antigen presentation and synergizes with anti-PD-1 therapy in metastatic breast cancer. ***Nature Cancer***, 3(1):60-74.

Complete List of Published Work in MyBibliography (180 Publications):
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