

Xiling Shen

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Professional Preparation

| | | |
|---------------------|------------------------|------------------------------------|
| Stanford University | Electrical Engineering | B.S. 2001 |
| | Electrical Engineering | M.S. 2001 |
| | Electrical Engineering | Ph.D. 2008, advisor: Mark Horowitz |
| UC Berkeley | Bioengineering | Postdoctoral Associate, 2008-2009 |

Appointments

| | | |
|--------------|------------------------------------|---|
| 2018-present | Director | Sherry and John Woo Center for Big Data and Precision Health, Duke University |
| 2015-present | Hawkins Family Associate Professor | Biomedical Engineering, Duke University |
| 2015-present | Associate Professor | Center for Genomics, Duke University |
| 2013-2015 | Assistant Professor | Biomedical Engineering, Cornell University |
| 2009-2015 | Assistant Professor | Electrical and Computer Engineering, Cornell University |
| 2003-2004 | RF Designer | Texas Instruments |
| 2001-2003 | Design Engineer | Barcelona Design, Inc. |

Other Experience and Professional Memberships

2017 – present Scientific advisor, National Cancer Institute CB-839 clinical trial planning team
2017 – present Member, American Gastroenterological Association (AGA)
2014 – present NSF Early Career Award
2014 – present Biomedical Engineering Society (BMES)
2012 – 2015 Associate director, Cornell Stem Cell Program
2013 – present Member, International Society for Stem Cell Research (ISSCR)
2013 – present Member, American Association for Cancer Research (AACR)
2012 – present Adjunct Professor, Guangzhou Tumor Hospital
2010 – 2012 Program Committee Chair, International Workshop on Bio-Design Automation (IWBDAA)
2000 Mayfield Fellow, Technology Venture, Stanford University

Peer Reviewed Journal Publications

- **Shen, X.**, Kahn, JM., and Horowitz, MA. (2005). Compensation for Multimode Fiber Dispersion by Adaptive Optics, *Optics Letters*, 30: 2985-2987.
- **Shen, X.**, Collier, J., Shapiro, L., Dill, D., Horowitz, MA., and McAdams, HH. (2008). Architecture and Inherent Robustness of a Bacterial Cell-Cycle Control System, *Proc. Natl. Acad. Sci. USA* 105-32: 11340-11345.
- Tan, M., Kozden, JB., **Shen, X.**, Shapiro, L. and McAdams, H. (2010). An essential transcription factor, SciP, enhances robustness of Caulobacter cell cycle regulation. *Proc. Natl. Acad. Sci. USA* 107: 18985-18990.
- Sikandar, S., Dizon, D., **Shen, X.** Li, Z., Besterman, J. and Lipkin, S. (2010). The Class I Hdac Inhibitor Mgcd0103 induces cell cycle arrest and apoptosis in colon cancer initiating cells by upregulating Dickkopf-1 and non-canonical Wnt signaling. *Oncotarget*, 1: 596-605.

- Shin, YJ., Hency, B., Lipkin, S., and **Shen, X.** (2011). Frequency domain analysis reveals external periodic fluctuations can generate sustained p53 oscillation. *PLOS One*, 6:1-13. PMID: 21829536.
- Chen, H. J., Edwards, R., Tucci, S., Bu, P., Milsom, J., Lee, S., Edelmann, W., Gumus, Z. H., **Shen, X.*** and Lipkin, S. (2012). Chemokine 25-induced signaling suppresses colon cancer invasion and metastasis. *The Journal of Clinical Investigation*, 122:3184-96 * Equal corresponding author.
- Shin, YJ., Sayed AH. and **Shen, X.** (2012). Adaptive Models for Gene Networks. *PLOS One*, 7:1-6. E31657
- Li, J., Bu, P., Chen, K. and **Shen, X.** (2013) Spatial perturbation with synthetic protein scaffold reveals robustness of asymmetric cell division. *Journal of Biomedical Science and Engineering*, 6, 134-143.
- Shin, YJ., Sayed AH. and **Shen, X.** (2012). Using an adaptive gene network model for self-organizing multicellular behavior. *IEEE Eng Med Biol.* 2012:5449-53
- Bu, P., Chen, K.Y., Chen, H. J., Wang, L., Walters, J., Shin, Y.J., Goerger, J.P., Sun, J., Witherspoon, M., Rakhilin, N., Li, Yang, H., Milsom, J., Lee, S., Zipfel, W., Jin, M.M., Gümüő, Z.H., Lipkin, S.M., and **Shen, X.** (2013). A microRNA miR-34a Regulated Bimodal Switch targets Notch in Colon Cancer Stem Cells. *Cell Stem Cell*, 12, 602-615.
- Bu, P., Chen, K.Y., Lipkin, S.M., and **Shen, X.** (2013). Asymmetric division: a marker for cancer stem cells in early stage tumors? *Oncotarget*, 4, 948.
- Shin, YJ., Chen, KY., Hency, B., Lipkin, S., Sayed AH. and **Shen, X.** (2013) Post-translational regulation enables robust p53 regulation. *BMC Systems Biology*, 7:83.
- Johnson, C., Warmoes, MO., **Shen, X.**, Locasale, JW. Epigenetics and cancer metabolism. (2013) *Cancer letters*, 0304-3835.
- Chen, K-Y., Liu, X., Bu, P., Lin, C.S., Rakhilin, N., Locasale, J.W., **Shen, X.** (2014) A Metabolic Signature of Colon Cancer Initiating Cells. *IEEE Eng Med Biol.*, 4759-4762 doi: 10.1109/EMBC.2014.6944688.
- Chen, K-Y., Joe, D. J., Shealy J. B., Land B. R., and **Shen, X.** (2014) A Bio-inspired spatial patterning circuit., *IEEE Eng. Med Biol.*, 2014 Aug;2014:86-9. doi:10.1109/EMBC.2014.6943535.
- Bu, P, Wang, L, Chen, K.Y., Sun J, Rakhilin, N., Closa, A., Tung, K. L., Xu, Y., Cummings, B., Hsu, D., Lipkin, S.M., Moreno, V., Gümüő, Z.H., and **Shen, X.** (2015) miR-1269 promotes metastasis and forms a positive feedback loop with TGF- β . *Nature Communications*, 6:6879. doi: 10.1038/ncomms7879.
- Chen, H. J., Sun, J., Huang, Z., Hou, H., Arcilla, M., Rakhilin, N., Joe, D., Choi, J., Gadamsetty, P., Milsom, J., Nandakumar, G., Longman, R., Zhou, X. K., Edwards, R., Chen J., Chen K. Y., Bu, P., Wang, L., Xu, Y., Munroe, R., Abratte, C., Miller, A. D., Gümüő, Z. H., Shuler, M., Nishimura, N., Edelmann, W., **Shen, X.***, and Lipkin, S., M. (2015) Comprehensive models of human primary and metastatic colorectal tumors in immunodeficient and immunocompetent mice by chemokine targeting. *Nature Biotechnology*, 33,656–660 doi:10.1038/nbt.3239 * Equal corresponding author.
- Li J, Ai Y, Wang L, Bu P, Sharkey CC, Wu Q, Wun B, Roy S, **Shen X**, King MR. (2016) Targeted drug delivery to circulating tumor cells via platelet membrane-functionalized particles. *Biomaterials*. 76:52-65. doi: 10.1016/j.biomaterials.2015.10.046.Shengyi
- Cao Y, Rakhilin N, Gordon PH, **Shen X**, Kan EC. (2016) A real-time spike classification method based on dynamic time warping for extracellular enteric neural recording with large waveform variability. *J Neurosci Methods*. 2015 Dec 21. pii: S0165-0270(15)00446-X. doi: 10.1016/j.jneumeth.2015.12.006.

- Joe, DJ, Hwang, J, Johnson, C, Cha, H-Y, Lee, J-W, **Shen, X.**, Spencer, MG, Tiwari, S, and Kim, M. "Surface Functionalized Graphene Biosensor on Sapphire for Cancer Cell Detection." *Journal of nanoscience and nanotechnology* 16, no. 1 (2016): 144-151.
- Rothschild, D. E., Srinivasan, T., Aponte-Santiago, A., L., **Shen, X.**, and Allen, I. C. "The Ex Vivo Culture and Pattern Recognition Receptor Stimulation of Mouse Intestinal Organoids." *J. Vis. Exp.*, no. 111 (2016).
- Bu, P., Wang, L., Chen, K.Y., Srinivasan, T., Murthy, P.K.L, Varanko, A.K., Chen, H.J., Ai, Y., King, S., Lipkin, S.M., **Shen, X.** (2016) A miR-34a-Numb feed-forward loop triggered by inflammation regulates asymmetric stem cell division in intestine and colon cancer. *Cell Stem Cell*, 18(2), 189-202. doi: 10.1016/j.stem.2016.01.006
- Srinivasan, T., Walters, J., Bu, P., Than, E.B., Tung, K.L., Chen K.Y., Panarelli, N., Milsom, J., Augenlicht, L., Lipkin, S.M., and **Shen, X.** (2016) NOTCH Signaling Regulates Asymmetric Cell Fate of Fast- and Slow-Cycling Colon Cancer Initiating Cells. *Cancer Research*, 10.1158/0008-5472.CAN-15-3198.
- Srinivasan, T, Bich, ET., Bu, P., Tung, K-L., Chen, K-Y., Augenlicht, L., Lipkin, S.M., and **Shen, X.** (2016) Notch signalling regulates asymmetric division and inter-conversion between lgr5 and bmi1 expressing intestinal stem cells. *Scientific Reports*, 6(26069). doi: 10.1038/srep26069.
- Wang, L., Bu, P., Ai, Y., Srinivasan, T., Chen, H.J., Xiang, K., Lipkin, S.M., **Shen, X.** (2016) A Long Non-Coding RNA Targets MicroRNA miR-34a to Regulate Colon Cancer Stem Cell Asymmetric Division. *eLife* 2016;10.7554/eLife.14620
- Rakhilin, N., Barth, B., Choi, J., Muñoz, N.L, Kulkarni, S., Jones, J., Small, D., Cheng, Y-U., Cao, Y., LaVinka, C., Kan, E., Dong, X., Spencer, M., Pasricha, P., Nishimura, N., **Shen, X.** (2016) Simultaneous Optical and Electrical In Vivo Analysis of the Enteric Nervous System. *Nature Communication*, 7:11800. doi: 10.1038/ncomms11800.
- Chen, H.J., Wei, Z., Sun J., Bhattacharya, A., Savage, D.J., Serda, R., Mackeyev, Y., Curley, S.A., Bu, P., Wang, L., Chen, S., Cohen-Gould, L., Huang, E., **Shen, X.**, Lipkin, S., Copeland, N. G., Jenkins, N. A., Shuler, M.L. (2016) A recellularized human colon model identifies cancer driver genes. *Nature Biotechnology*. 34, 845-851 doi: 10.1038/nbt.3586.
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- Wang, L, Bu, P, and **Shen, X.** "Asymmetric division: An antitumor player?" *Molecular & cellular oncology* 3, no. 4 (2016).
- Petritsch, C, and **Shen, X.** "Chapter 11: Asymmetric Division of Cancer Stem Cells." In *Cancer Stem Cells*, 1st Edition. Academic Press, ISBN : 9780128038925., 2016.
- Chen, K.Y., Srinivasan, T., Tung, K.L., Belmonte, J.M., Choi, J., Rakhilin, N., King, S., Varanko, A.K., Wang, L., Witherspoon, M., Nishimura, N., Glazier, J., Lipkin, S.M., Bu, P., and **Shen, X.** (2017) A Notch positive feedback in the intestinal stem cell niche is essential for stem cell self-renewal. *Molecular Systems Biology*, 13(4): p. 927.
- Kulkarnia, S., Miccib, M., Lesera, J., Shinc, C., Tangd, S-C., Fua, Y-Y., Liua, L., Lia, Q., Sahaa, M., Lia, C., Enikolopove, G., Beckerg, L., Rakhilinh, N., Anderson, M., **Shen, X.**, Dong, X., Bogunovic, M., and Pasrichaa, P. (2017) Adult enteric nervous system in health is maintained by a dynamic balance

between neuronal apoptosis and neurogenesis. *Proc. Natl. Acad. Sci. USA*. April 18, 2017, doi: 10.1073/pnas.1619406114

- Barth, B.B., Henriquez, C.S., Grill, W.M., **Shen, X.** (2017) Optimal electrical stimulation of gut motility guided by an in silico model. *Journal of Neural Engineering*. 17 Aug 2017.
- Klose, C., Mahlakoiv, T., Rankin, L., Moeller, J., Flamar, A-L., Kabata, H., Monticelli, L.A., Moriyama, S. Putzel, G.G., Rakhilin, N., **Shen, X.**, Kostenis, Ev., Konig, G.M., and Artis, D. (2017) The neuropeptide neuromedin U stimulates innate lymphoid cells and type 2 inflammation. *Nature*, 549(7671):282-286 06 Sep 2017.
- Barth, B., **Shen, X.** (2018) Computational motility models of neurogastroenterology and neuromodulation, *Brain Research*, 1693(Pt B):174-179. doi: 10.1016/j.brainres.2018.02.038.
- Barth, B.B.; Huang, H.-I.; Hammer, G.E.; **Shen, X.** (2018) Opportunities and Challenges for Single-Unit Recordings from Enteric Neurons in Awake Animals. *Micromachines* 9, 428.
- Xu Y., Wang, L., Zimmerman, M.D., Chen, K-Y., Huang, L., Fu, D-J., Kaya, F, Rakhilin, N., Nazarova, E.V., Bu, P., Dartois, V., Russell, D.G., **Shen, X.** (2018) Matrix Metalloproteinase inhibitors enhance the efficacy of frontline drugs against Mycobacterium tuberculosis. *PLoS Pathogen*, 14(4): e1006974.
- Murthy, P.K.L., Srinivasan, T., Bochter, M.S., Varanko, A., Xi, R., Tung, K.L., Fatih, S., Xu, K., Maletic-Savatic, M., Cole, S.E., and **Shen, X.** (2018) Spatially Specific Fringe Modulation of Notch Ligands Supports Intestinal Homeostasis. *eLife*, 2018;7:e35710 doi: [10.7554/eLife.35710](https://doi.org/10.7554/eLife.35710).
- Bu, P., Chen, K.Y., Xiang, K., Johnson, C., Crown, S., Rakhilin, N., Ai, Y., Wang, L., Xi, R., Astapova I., Han, Y., Li, J., Barth, B.B., Lu, M., Gao, Z., Zhang, L., Herman, M., Hsu, D., Zhang, G-F., **Shen, X.** (2018) Aldolase b mediated fructose metabolism drives metabolic reprogramming of colon cancer liver metastasis. *Cell Metabolism*, 27 (6), 1249–1262, June 5, 2018. doi: <https://doi.org/10.1016/j.cmet.2018.04.003>.
- J Choi, N Rakhilin, P Gadamsetty, DJ Joe, T Tabrizian, SM Lipkin, DM Huffman, **X Shen**, N Nishimura (2018), “Intestinal crypts recover rapidly from focal damage with coordinated motion of stem cells that is impaired by aging,” *Scientific Reports*, 8, no. 1 (2018).
- Kaelberer, M., Buchanan, K., Klein, M., Barth, B., Wen, G., Montoya, M., **Shen, X.** and Bohórquez, V. (2018). A Gut-Brain Neural Circuit for Nutrient Sensory Transduction. *Science*, 361 (6408), doi: 10.1126/science.aat5236

Patents

- 6,789,246 M. Sunderarjan and X. Shen, “Method and apparatus for automatic layout of circuit structures”
- 6,802,050 X. Shen and M. Sunderarja, “Efficient layout strategy for automated design layout tools”
- US20150164053 A1 J.H.Chen, Lipkin, JM. And X. Shen, “Compositions and methods useful for making orthotopic tumors with controllable metastasis” (Under licensing with Morphotek.INC)
- US9681647 B2 J.H.Chen, Lipkin, JM. And X. Shen, “Mammal with an orthotopic tumor capable of metastasis, a method of making and a method of using”
- PCT/US18/53236, D. Hsu, X. Shen, “Patient Specific Clinical Trials And Associated Methods of Treatment”
- 62623065 Provisional, X. Shen, “Compositions and methods for targeting fructose metabolism for the treatment of cancer”

Former postdoctoral Fellows

Dr. Yong Jun Shin (Assistant Professor, UConn)

Dr. Kim Heiman Chow (Research assistant Professor, Division of Life Sciences, Hong Kong)
Dr. Christelle Haibi-Johnson (Field Application Scientist, Personalis Inc)
Dr. Yan Han (Principle Scientist, Curacloud Inc)
Dr. Pengcheng Bu (Assistant Professor, Institute of Biophysics of Chinese Academy of Sciences)
Dr. Kai-Yuan Chen (Senior research associate, Intellia Inc.)

Former PhD students

Huanhuan Joyce Chen (Beckman Postdoctoral Fellow, Harold Varmus group, Weill Cornell Medical College)
Daniel Jo (R&D engineer, Samsung)
Tara Srinivasan (R&D scientist, Sangamo Biosciences)
Lihua Wang (Postdoc, Duke)
Yitian Xu (Postdoc, Baylor)

Current Research Assistant Professor

Dr. Shengli Ding

Current Research Associates and Postdoctoral Fellows

Dr. Ian Williams, Dr. Zhiguo Sun, Dr. Lihua Wang, Dr. Qiang Huang,

Current Graduate Students

Bradley Barth (Duke, Biomedical Engineering)
Tianyi Chen (Duke, Molecular Genetics and Microbiology)
Ander Dolhman (Duke, Biomedical Engineering)
Nicholas Giroux (Duke, Biomedical Engineering)
Shaun Sze-Tse Lim (Duke, Biomedical Engineering)
Preetish Murthy (Cornell, Mechanical Engineering)
Robert Mines (Duke, Biomedical Engineering)
Aleisha O'Raw (Duke, Biomedical Engineering)
Nikolai Rakhilin (Cornell, Electrical and Computer Engineering)
Green Tung (Cornell, Biological and Environmental Engineering)
Ergang Wang (Duke, Biomedical Engineering)
Rui Xi (Duke, Biomedical Engineering)
Kun Xiang (Duke, Biomedical Engineering)

Current support as PI

U01 CA217514 NIH 09/01/2018-08/31/2023
Epigenomic reprogramming in patient derived models of colorectal cancer
Overall goal: To understand epigenetic reprogramming of tumor cells in PDO and PDX models.
Overlap: none

R35GM122465 NIH 04/01/2017-3/31/2022
MIRA: Robust Control of the Stem Cell Niche
Overall goal: This merit-based award aims to understand non-coding RNA, metabolic, and epigenetic control of the stem cell niche.
Overlap: none.

R01GM114254-01 NIH 04/01/2015-3/31/2018
Robustness of The Intestinal Stem Cell Niche

Overall goal: Develop new abdominal intravital imaging and laser ablation technology to track perturbed stem cell niche in live animals in order to understand its recovery from damage.

Overlap: none.

U01 CA214300 NIH 10/01/2017-9/30/2022

An Organotypic Model Recapitulating Colon Cancer Microenvironment And Metastasis

Overall goal: Using novel in vitro and in vivo models to study colon cancer microenvironment and metastasis.

Overlap none.

1350659 NSF 04/01/2014-03/31/2019

Career: The Versatility of microRNA regulation

Overall Goal: Study dynamic switching and oscillatory properties of microRNA regulation

Overlap: none.

R24DK110492 NIH (PI: John Rawls, Duke) 9/25/2016-8/31/2021

A comprehensive research resource to define mechanisms underlying microbial regulation of host metabolism in pediatric obesity and obesity-targeted therapeutics

Goals: To establish a comprehensive research resource to define microbial regulation of host metabolism in adolescents with obesity before and after weight loss intervention.

Overlap: none.

HR0011-16-C-0138 DARPA 10/1/16-9/30/20

Engineering Signaling Specificity to Program Intestinal Organoid Development

Goals: This project will engineer synthetic feedback circuits based on the Bone Morphogenetic Protein (BMP) signaling pathway to control cellular composition of intestinal organoid culture.

Overlap: none.

Completed support

CBET-1106153 NSF (Michael L. Shuler – lead PI) 08/15/2011-07/31/2014

Targeting Cancer Stem Cell Self-Renewal and Proliferation Mechanisms Using in vitro Microscale Models

Overall goal: Engineer physiologically relevant lab-on-chip devices for screening drugs against colon cancer stem cell

19-1091726 DARPA 08/01/2011-12/31/2015

Programming Stem Cell Fate Using a Novel Synthetic Platform

Overall Goal: Engineer synthetic regulatory elements for manipulating mammalian cells.

19-1091638 NSF (Michael Elowitz – lead PI) 09/01/2011-08/31/2015

EFRI: MIKS: Notch Signaling in Colon Cancer Stem Cells

Overall Goal: Study the role of Notch signaling in colon cancer stem cell differentiation and proliferation.

R01GM095990-05 NIH 09/19/2011-08/31/2016

Multi-scale Modeling of Asymmetric Cell Division

Overall Goal: Study asymmetric division of *Caulobacter crescentus* and colon cancer stem cells using modeling and robust control theory.

C029543 NYS DEPT OF HEALTH 06/01/2014-05/31/2016

Versatile microRNA Regulation for Cell Fate Decision

Overall Goal: The kinetics of microRNA regulation in intestinal stem cells and colon cancer stem cells will be analyzed using computational modeling and quantitative experiments. The role of microRNA circuits in cell fate decision will be investigated.

W911NF-15-1-0177 ARMY RESEARCH OFFICE (DARPA) 04/28/2015-04/27/2016
Increasing Anti-Microbial Capacity Through Transient Gene Expression In The Lung

Overall Goal: The goal of this project is to demonstrate transient expression of biomodulators at the disease site to manipulate immune and tissue environments, and that such manipulations could both enhance the anti-microbial capacity of frontline antibiotics and confer pre-exposure protection against respiratory pathogens.

21-708253 DARPA (PI: Phil Santangelo, Georgia Tech) 10/1/2015-9/30/2017
mRNA-Based Expression Of Therapeutic Proteins And Antibodies In The Lung Targeting Bacterial And Viral Pathogens

1511357 NSF 09/05/2015-8/31/2018
Systems Biology Tools to Study Cancer Metastasis
Overall goal: Develop tools to study reprogramming of metastatic cancer cells.
Overlap: none.

R21CA201963 NIH 1/13/2016-12/31/2017
Metabolic Reprogramming of Colon Cancer Liver Metastasis
Overall goal: Characterizing metabolic reprogramming of metastatic cells in the liver microenvironment.
Overlap: none.

OT2OD023849 NIH 08/01/2016-1/31/2018
Functional Mapping of Efferent Gut Neuroepithelial Circuits
Overall goal: Understand the vagus nerve-enteric nervous system-enteroendocrine axis.
Overlap: none.

N66001-15-2-4059 DARPA (PI: Jiande Chen, Johns Hopkins) 10/1/2015-9/30/2017
Closed-Loop Sacral Nerve Stimulation for Inflammation
Overall goal: Study the anti-inflammatory effect of sacral neuromodulation on gut inflammation and microbiota.
Overlap: none.