BIOGRAPHICAL SKETCH

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NAME: Chan, Chang S.

eRA COMMONS USERNAME (credential, e.g., agency login): chanc3

POSITION TITLE: Associate Professor of Medicine

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
Harvard University, Cambridge, MA	A.B.	06/1997	Physics and Mathematics
Princeton University, Princeton, NJ	Ph.D.	11/2003	Physics
Princeton University, Princeton, NJ	Postdoctoral	06/2007	Systems Biology
Institute for Advanced Study, Princeton, NJ	Postdoctoral	12/2011	Systems Biology

A. Personal Statement

My research interests include computational cancer genomics, cancer evolution, p53 biology, and gene regulation. I have a background in physics and mathematics, with specific training and expertise in systems and computational biology. As PI or co-Investigator on several federally- and NIH-funded grants, I have collaborated with basic research labs and clinicians in developing computational tools and pipelines for analyzing, integrating, and modeling immense biological data including whole-genome, exome, transcriptome, DNA methylation data, and precision oncology. As co-leader of the Genomic Instability and Cancer Genetics (GICG) research program, I solicit and review membership applications, recommend acceptance of program members and nominate members for new investigator awards, organize and chair monthly GICG program meetings, build pipeline of pilot projects with potential for future peer-reviewed funding, foster interactions and collaborations that can guide new investigators into the field, engage with the Committee to Expedite Translational Initiatives and clinical scientists in formulating new translational projects, work with the GICG COE Program liaison and office of the AD for Population Science and Community Outreach to maximize the potential impact of the basic discoveries on catchment priorities and cancer disparities.

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

NIH/NCI 5P30 CA072720
Libutti (PI); Role: Co-program leader
03/07/2019 – 02/29/2024
Cancer Center Support Grant (CCSG)

NETRF #831950
Chan (PI); Role: PI
01/03/2022 – 01/02/2024
Investigating PanNET tumorigenesis with single-cell genomics

NIH/NCI 1P01CA250957-01A1
Shen (PI) Role: Co-investigator
05/01/2021 – 04/30/2026
The BRCA Network in Medulloblastoma Responses to Replication Stress

NETRF Award #827464
Libutti (PI); Role: Co-investigator
01/03/2020 – 01/02/2024
The role of the B7x signaling pathway in the progression of neuroendocrine tumors

NIH/NCI R01 CA243547
Ganesan/White/Lattime (MPI); Role: Co-investigator
02/01/2020 – 01/30/2025
Impact of mutation burden on cancer growth and the immune landscape

NIH/NCI 1R01 CA227912-01
Feng/Hu (PI); Role: Co-investigator
03/01/2018 – 02/28/2023
Metabolic Reprogramming in Breast Cancer

NIH/NCI 1R01 CA237347
Guo (PI); Role: Co-investigator
02/01/2020 – 01/30/2025
Elucidate the mechanism of autophagy in supporting Lkb1-deficient lung tumorigenesis and metastasis

NIH/NIDK 1R01 DK124897
Zheng (PI); Role: Co-investigator
09/18/2020 – 07/31/2024
Amino Acids-Rab1A Nutrient Signaling in the Regulation of Glucose Homeostasis

Award #1546101
Chan (PI)
06/15/2016-05/31/2020
National Science Foundation Title: Collaborative Research: The genetic, epigenetic, and immunological foundation of cancer evolution.

Citations:

1. **Chan CS**[*], Laddha SV, Lewis PW, Koletsky MS, Robzyk K, Da Silva E, Torres PJ, Untch BR, Li J, Bose P, Chan TA, Klimstra DS, Allis CD, Tang LH (2018). ATRX, DAXX or MEN1 mutant pancreatic neuroendocrine tumors are a distinct alpha-cell signature subgroup. Nat Commun. 2018 Oct 12;9(1):4158. PMID:30315258; PMCID: PMC6185985 (* co-corresponding authors)
2. Laddha SV, da Silva EM, Robzyk K, Untch BR, Ke H, Rekhtman N, Poirier JT, Travis WD, Tang LH, **Chan CS** (2019). Integrative Genomic Characterization Identifies Molecular Subtypes of Lung Carcinoids. Cancer Res. 2019 Sep 1;79(17):4339-4347. PMID:31300474; PMCID:PMC6733269
3. Joshi S, Tolkunov D, Aviv H, Hakimi AA, Yao M, Hsieh JJ, Ganesan S, **Chan CS**[*], White E[*] (2015). The genomic landscape of renal oncocytoma identifies a metabolic barrier to tumorigenesis. Cell Rep., 13(9):1895-908. PMID:26655904; PMCID:PMC477919 (* co-corresponding authors)
4. Ariffin H, Hainaut P, Puzio-Kuter A, Choong SS, Chan AS, Tolkunov D, Rajagopal G, Kang W, Lim LL, Krishnan S, Chen KS, Achatz MI, Karsa M, Shamsani J, Levine AJ, **Chan CS** (2014). Whole-genome sequencing analysis of phenotypic heterogeneity and anticipation in Li-Fraumeni cancer predisposition syndrome. PNAS, 111(43):15497-501. PMID: 25313051; PMCID: PMC4217424

B. Positions, Scientific Appointments, and Honors

2011-Present	Resident Member, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ
2018-Present	Associate Professor, Department of Medicine, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ
2016-Present	Co-leader of Genome Instability and Cancer Genetics Research Program, Rutgers Cancer
2016	Most highly cited research article in Molecular Cancer Research in 2014 Award Institute of New Jersey, New Brunswick, NJ

2011-2018	Assistant Professor, Department of Medicine, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ
2008-2010	Charles L. Brown Membership, Institute for Advanced Study, Princeton, NJ
2004-2010	Fellow of Forbes College at Princeton University
1997-2000	National Science Foundation Graduate Fellowship
1997	Magna Cum Laude with highest honors in physics, Harvard University
1993-1994	John Harvard Scholarship
1993	International Physics Olympiad
1991-1993	Member of US Physics Olympiad Team

C. Contributions to Science

1. I have applied computational genomics to neuroendocrine tumors to molecularly classify subtypes defined by transcriptional program and mutation profile. We discovered that pancreatic neuroendocrine tumors with mutations in MEN1, ATRX, or DAXX comprise a phenotypically distinct subgroup and has a gene expression profile similar to pancreatic alpha cell. We also discovered three distinct subgroups of lung carcinoids with different mutational, gene expression and DNA methylation patterns.

    a. **Chan CS**[*], Laddha SV, Lewis PW, Koletsky MS, Robzyk K, Da Silva E, Torres PJ, Untch BR, Li J, Bose P, Chan TA, Klimstra DS, Allis CD, Tang LH (2018). ATRX, DAXX or MEN1 mutant pancreatic neuroendocrine tumors are a distinct alpha-cell signature subgroup. Nat Commun. 2018 Oct 12;9(1):4158. PMID:30315258; PMCID: PMC6185985 (* co-corresponding authors)
    b. Laddha SV, da Silva EM, Robzyk K, Untch BR, Ke H, Rekhtman N, Poirier JT, Travis WD, Tang LH, **Chan CS** (2019). Integrative Genomic Characterization Identifies Molecular Subtypes of Lung Carcinoids. Cancer Res. 2019 Sep 1;79(17):4339-4347. PMID:31300474; PMCID:PMC6733269
    c. Wong C, Laddha SV, Tang L, Vosburgh E, Levine AJ, Normant E, Sandy P, Harris C, **Chan CS**, Xu EY. The bromodomain and extra-terminal inhibitor CPI203 enhances the anti-proliferative effects of rapamycin on human neuroendocrine tumors. Cell Death Dis, 5:e1450, 2014.
    d. Contractor T, Kobayashi S, da Silva E, Clausen R, **Chan C**, Vosburgh E, Tang LH, Levine AJ, Harris CR. Sexual dimorphism of liver metastasis by murine pancreatic neuroendocrine tumors is affected by expression of complement C5. Oncotarget. 2016 May 24;7(21):30585-96. PMID:27105526; PMCID:PMC5058703.

2. I applied genomics to study the role of autophagy in cancer. BECN1 was long thought to be a tumor suppressor in cancers because it was frequently deleted in tumors. We showed that in most cases this is due to BECN1 being in close proximity to BRCA1, a known tumor suppressor, in the genome. Deletion of BECN1 without co-deletion of BRCA1 was not significantly increased in cancer. We also studied the role that autophagy and more specifically mitophagy played in renal oncocytomas, a benign tumor with high abundance of defective mitochondria. We characterized two subtypes of oncocytomas with distinct mutational landscape and cancer driver mutations.

    a. Laddha SV, Ganesan S, **Chan CS**[*], White E[*] (2014). Mutational landscape of the essential gene BECN1 in human cancers. Mol Cancer Res., 12(4):485-90. PMID:24478461; PMCID: PMC3989371 (* co-corresponding authors)
    b. Joshi S, Tolkunov D, Aviv H, Hakimi AA, Yao M, Hsieh JJ, Ganesan S, **Chan CS**[*], White E[*] (2015). The genomic landscape of renal oncocytoma identifies a metabolic barrier to tumorigenesis. Cell Rep., 13(9):1895-908. PMID:26655904; PMCID:PMC477919 (* co-corresponding authors)
    c. Guo JY, TengX, Laddha SV, Ma S, Van Nostrand SC, Yang Y, Khor S, **Chan CS**, Rabinowitz JD, White E. Autophagy provides metabolic substrates to maintain energy charge and nucleotide pools in Ras-driven lung cancer cells. Genes Dev. 2016 Aug 1;30(15):1704-12. PMID:27516533; PMCID:PMC5002976
    d. Poillet-Perez L, Sharp DW, Yang Y, Laddha SV, Ibrahim M, Bommareddy PK, Hu Z, Vieth J, Hass M, Bosenberg MW, Rabinowitz JD, Cao J, Guan J, Ganesan S, **Chan CS**, Mehnert JM, Lattime EC, White E. Autophagy promotes growth of tumors with high mutational burden by inhibiting a T-cell immune response. Nature Cancer 2020 Sep 18;1:923-934.

3. P53 is a tumor suppressor whose function is crucially important in guarding genome stability. It is the most commonly mutated gene across all human cancers. I have studied the role of p53 in tumorigenesis in Li-Fraumeni Syndrome and p53 knockout mouse models. Loss of p53 is associated with increased genome instability in cancers but whether p53 plays a similar role in the germline is not well understood. I studied families with Li-Fraumeni Syndrome and showed no evidence for germline genome instability by analysis of genome sequencing. I created a genetic model termed, genetic regression, which explains the apparent observation of genetic anticipation in Li-Fraumeni Syndrome and identified genetic modifiers that affect heterogeneity of phenotypes. I studied the evolution of thymic lymphoma in p53 knockout mice and identified the temporal sequence of additional mutations required for tumorigenesis.

    a. Ariffin H, Hainaut P, Puzio-Kuter A, Choong SS, Chan AS, Tolkunov D, Rajagopal G, Kang W, Lim LL, Krishnan S, Chen KS, Achatz MI, Karsa M, Shamsani J, Levine AJ, **Chan CS** (2014). Whole-genome sequencing analysis of phenotypic heterogeneity and anticipation in Li-Fraumeni cancer predisposition syndrome. PNAS, 111(43):15497-501. PMID: 25313051; PMCID: PMC4217424
    b. Dudgeon C*, **Chan C***, Kang W, Sun Y, Emerson R, Robins H, Levine AJ (2014). The evolution of thymic lymphomas in p53 knockout mice. Genes Dev, 28(23):2613-20. PMID:25452272; PMCID: PMC4248292 (* co-first authors)
    c. **Chan CS** (2017). Prevalence and penetrance of Li-Fraumeni cancer predisposition syndrome. Current Opinion in Systems Biology. 2017 Feb 24;1(1):48-53.
    d. **Chan CS*,** Sun Y, Ke H, Zhao Y, Belete M, Zhang C, Feng Z, Levine AJ, Hu W (2020). Genetic and stochastic influences upon tumor formation and tumor types in Li-Fraumeni mouse models. Life Sci Alliance. 2020 Dec 29;4(3):e202000952. PMID:33376133 (* co-corresponding author)

4. I used computational genomics to make contributions to the understanding of post-transcriptional regulation by microRNAs and transcriptional regulation by estrogen. Estrogen induces the transcription of hundreds of genes but identifying the direct target genes is challenging because they lie far away from where the estrogen receptors bind. I identified CTCF binding to the genome to act as insulators for estrogen transcriptional regulation and incorporated this information in a Bayesian model to identify potential direct gene targets of estrogen regulation. I also used computational genomics to identify novel miRNAs as well as targets of miRNAs in human. Importantly, I identified some of the first miRNAs that are predicted to regulate p53 and in collaboration with biologists validated them.

    a. **Chan CS**, Elemento O, Tavazoie S (2005). Revealing posttranscriptional regulatory elements through network-level conservation. PLoS Comput Biol, 1(7), e69. PMID:16355253; PMCID: PMC1309705
    b. **Chan CS**, Song JS (2008). CCCTC-binding factor confines the distal action of estrogen receptor. Cancer Res, 68(21):9041-9. PMID: 18974150
    c. Hu W, **Chan CS**, Wu R, Zhang C, Sun Y, Song JS, Tang LH, Levine AJ, Feng Z (2010). Negative regulation of tumor suppressor p53 by microRNA miR-504. Mol Cell. 38(5):689-99. PMID:20542001; PMCID: PMC2900922
    d. Zhang C, Liu J, Wang X, Wu R, Lin M, Laddha S, Young KH, **Chan CS**, Feng Z (2014). MicroRNA-339 inhibits colorectal tumorigenesis through regulation of the MDM2/p53 signaling. Oncotarget, 5(19):9106-17. PMID:25193859; PMCID: PMC4253422

Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/myncbi/1v7kyfLe1K35H/bibliography/public/