Curriculum Vitae

Name	**Sarat Chandarlapaty**	
Current Position & Affiliation	**Associate Professor, Medicine; Associate Member, Human Oncology and Pathogenesis Program**	
Country	**USA**	

Educational Background and Professional Qualifications

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
College of William and Mary, VA	B.S.	05/1993	Chemistry
University of North Carolina, NC	Ph.D.	12/1998	Biochemistry
Wake Forest School of Medicine, NC	M.D.	06/2002	Medicine
New York Presbyterian Hospital, NY		06/2004	Internal Medicine
Memorial Sloan Kettering Cancer Center, NY		12/2008	Medical Oncology

Professional Experience

2008-2010	Instructor in Medicine, Memorial Sloan Kettering Cancer Center, New York, NY
2008-2012	Instructor in Medicine. Weill Cornell Medical Center, New York Presbyterian Hospital, New York, NY
2010-2018	Assistant Professor in Medicine. Memorial Sloan Kettering Cancer Center, New York, NY
2012-2018	Assistant Member and Lab Head, Human Oncology and Pathogenesis Program. Memorial Sloan Kettering Cancer Center, New York, NY
2012-2018	Assistant Professor in Medicine. Weill Cornell Medical Center, New York Presbyterian Hospital and Weill Cornell Cell and

	Developmental Biology Program, Weill Cornell Graduate School, New York, NY.
2018-Present	Associate Professor in Medicine. Weill Cornell Medical Center, New York Presbyterian Hospital and Weill Cornell Cell and Developmental Biology Program, Weill Cornell Graduate School, New York, NY.
2018-Present	Associate Professor in Medicine, Associate Member and Lab Head, Human Oncology and Pathogenesis Program. Memorial Sloan Kettering Cancer Center, New York, NY
2019-Present	Section Head, Translational Research, Breast Service, Department of Medicine, MSKCC, NY

Professional Organizations

2004 – Member, American Society of Clinical Oncology
2005 – Member, American Association of Cancer Research
2005 – Board certified in Internal Medicine
2007 – Working group member, Translational Breast Cancer Research Consortium
2008 – Board certified in Medical Oncology
2012 – Peer Reviewer for Susan G. Komen and Department of Defense BCRP (Ad hoc)
2013-19 Committee Member for ASCO/CCF Grants.
2013-14 Program Committee member – ASCO Annual Meeting
2014-16 Program Committee member – AACR Annual Meeting
2016 – Peer Reviewer for Department of Defense BCRP (Ad hoc)
2017-18 – Peer Reviewer NIH (Ad hoc)
2017-18 – Chair - ASCO/CCF Grants Committee
2019 – Member, Scientific Advisory Board – Breast Cancer Research Foundation
2020 – Associate Editor – Breast Cancer Research
2020 – Standing Member – NIH MCT-1 Study Section
2020 – Director, Developmental Research Program, MSK Breast SPORE

Main Scientific Publications

1) Understanding resistance to antiestrogen therapy in breast cancer. We have used detailed genomic analyses of human tumors samples and pharmacologic interrogation of well annotated cancer models to understand the basis for resistance to endocrine agents. This is highlighted by our ongoing work on characterizing the clinical and biological implications of *ESR1* mutations noted above and in:

a. **Chandarlapaty S**, Chen D, He W, Sung P, Samoila A, You D, Bhatt T, Patel P, Voi M, Gnant M, Hortobagyi G, Baselga J, and Moynahan ME. *ESR1* Mutations in Cell-Free DNA and Outcomes in Metastatic Breast Cancer. (2016) *JAMA Oncol*. Oct 1;2(10):1310-1315. PMCID: PMC5063698
b. Fanning, SW, Mayne, CG, Dharmarajan, V, Carlson, KE, Martin, TA, Novick, SJ, Toy, W, Green, B, Panchamukhi, S, Katzenellenbogen, BS, Tajkhorshid, E, Griffin, PR, Shen, Y, **Chandarlapaty, S**, Katzenellenbogen, JA, Greene, GL. (2016) Estrogen receptor alpha somatic mutations Y537S and D538G confer breast cancer endocrine resistance by stabilizing the activating function-2 binding conformation. Elife. Feb 2;5. Pii:e12792. PMCID: PMC4821807.
c. Bielski CM, Donoghue MTA, Gadiya M, Hanrahan AJ, Won HH, Chang MT, Jonsson P, Penson AV, Gorelick A, Harris C, Schram AM, Syed A, Zehir A, Chapman PB, Hyman DM, Solit DB, Shannon K, **Chandarlapaty** S, Berger MF, Taylor BS. (2018) Widespread Selection for Oncogenic Mutant Allele Imbalance in Cancer. Cancer Cell. Nov 12;34(5):852-862.e4. doi: 10.1016/j.ccell.2018.10.003. Epub 2018 Nov 1. PMCID: PMC6234065
d. Katzenellenbogen JA, Maybe CG, Katzenellenbogen, BS, Greene, GL., **Chandarlapaty, S**, (2018) Structural underpinnings of oestrogen receptor mutations in endocrine therapy resistance. *Nat Rev Cancer*. Jun; 18(6): 377-388. PMCID: PMC6252060

2) Understanding resistance to targeted therapies in the context of hormone dependent cancers. Activation of PI3K, AKT, CDK4, and HER2 have all been demonstrated to collaborate with ER activation to promote tumor growth and drug resistance. We have identified key mechanisms whereby tumors can develop resistance to drugs targeting oncogenic signals such as CDK4/6 specifically in the context of ER+ breast cancer. Alteration of ER signaling can play a critical role in the manifestation of resistance to the targeted agent.

a. Razavi P, Chang MT, Xu G, Bandlamudi C, Ross DS, Vasan N, Cai Y, Bielski CM, Donoghue MTA, Jonsson P, Penson A, Shen R, Pareja F, Kundra R, Middha S, Cheng ML, Zehir A, Kandoth C, Patel R, Huberman K, Smyth LM, Jhaveri K, Modi S, Traina TA, Dang C, Zhang W, Weigelt B, Li BT, Ladanyi M, Hyman DM, Schultz N, Robson ME, Hudis C, Brogi E, Viale A, Norton L, Dickler MN, Berger MF, Iacobuzio-Donahue CA, **Chandarlapaty S**, Scaltriti M, Reis-Filho JS, Solit DB, Taylor BS, Baselga J. (2018) The Genomic Landscape of Endocrine-Resistant Advanced Breast Cancers. *Cancer Cell*. Sep 10;34(3):427-438.e6. PMCID: NIHMSID997535
b. Yang C, Li Z, Bhatt T, Dickler M, Giri D, Scaltriti M, Baselga J, Rosen N, **Chandarlapaty S.** (2017) Acquired CDK6 amplification promotes breast cancer resistance to CDK4/6 inhibitors and loss of ER signaling and dependence. *Oncogene*. Apr 20;36(16):2255-2264. PMCID:PMC5393973
c. Bosch A., Li Z., Bergamaschi A., Ellis H., Toska E., Prat A., Tao J., Spratt D.E., Viola-Villegas N.T., Castel P., Minuesa G., Morse N., Rodon J., Ibrahim Y., Cortes J., Perez-Garcia J., Galvan P., Grueso J., Guzman M., Katzenellenbogen J., Kharas M., Lewis J.S., Dickler M., Serra V., Rosen N., **Chandarlapaty S.***, Scaltriti M.*, Baselga J.* (2015) PI3K inhibition results in enhanced estrogen receptor function and dependence in hormone receptor-positive breast cancer. *Science Translational Medicine*, Apr 15;7(283):283ra51. * = co-corresponding. PMCID: PMC4433148
d. Gala K, Li Q, Sinha A, Razavi P, Dorso M, Sanchez-Vega F, Chung Y, Hendrickson R, Hsieh J, Berger M, Schultz N, Pastore A, Abdel-Wahab O**, Chandarlapaty S.** (2018) KMT2C mediates the estrogen dependence of breast cancer through regulation of Era enhancer function. *Oncogene*. May 14; doi: 10.1038/s41388-018-0273-5. PMCID: PMC6107480

3) Characterization of the types and significance of feedback regulatory pathways governing the PI3K/AKT/mTOR pathway in cancer. A central hypothesis of our work is that physiologic feedback is exaggerated in oncogenically activated signaling pathways and this feedback has major significance for cancer therapy. My research has helped identify the specific types of feedback that regulate PI3K, AKT and mTOR individually and together and how these can promote resistance to drugs targeting these individual kinases. We have shown how combinations of inhibitors of PI3K/AKT/mTOR, and the relieved feedback (e.g. RTKs like HER3) can lead to substantial therapeutic benefits and these have spurred clinical trial efforts some of which are being led by me as PI or Co-PI.

a. **Chandarlapaty, S**, Sawai, A, Scaltriti, M, Rodrik-Outmezguine, V, Grbovic-Huezo, O, Serra, V, Majumder, PK, Baselga, J, Rosen, N. (2011) AKT inhibition relieves feedback suppression of receptor tyrosine kinase expression and activity. *Cancer Cell*, Jan 18;19(1):58-71. PMCID: PMC3351275.

b. Carver B, Chapinski C, Wongvipat J, Hieronymous H, Chen Y, **Chandarlapaty S**, Arora V, Le C, Koutcher J, Scher H, Scardino PT, Rosen N, Sawyers CL. (2011) Reciprocal feedback regulation of PI3K and androgen receptor signaling in PTEN-deficient prostate cancer. *Cancer Cell*, May 17;19(5): 575-586. PMCID: PMC3142785.
c. Schwartz S, Wongvipat J, Trigwell CB, Hancox U, Carver BS, Rodrik-Outmezguine R, Will M, Yellen P, de Stanchina E, Baselga J, Scher HI, Barry ST, Sawyers CL, **Chandarlapaty S**, Rosen N. (2015) Feedback Suppression of PI3Kα Signaling in PTEN-Mutated Tumors Is Relieved by Selective Inhibition of PI3Kβ. *Cancer Cell*, Jan 12;27(1): 109-22. PMCID: PMC4293347
d. **Chandarlapaty S.** (2012) Negative Feedback and Adaptive Resistance to the Targeted Therapy of Cancer. *Cancer Discovery*, Apr;2(4):311-9. PMCID: PMC3351275

4) Therapeutic approaches to activated PI3K signaling. Apart from the implications of feedback, we have sought to understand rational and effective approaches to targeting activated PI3K signaling in cancer. This has included development of novel, selective inhibitors of kinases within the pathway as well as indirect approaches such as HSP90 inhibitors used to selectively destabilize components such as HER2 in HER2+ breast cancer. Going further, we have attempted to understand the molecular context in which specific PI3K pathway inhibitors are most likely to be effective such as our demonstration that PI3K but not AKT regulation of RAS in RAS/RAF wild type tumors will make direct PI3K inhibition a more effective strategy for select breast cancer subtypes.

a. Will, M, Qin, A, Toy, W, Yao, Z, Rodrik-Outmezguine, V, Scheider C, Huang, X, Monian, P, Jiang, X, De Stanchina, E, Baselga, J, Liu, N, **Chandarlapaty, S***, Rosen, N*. (2014) Rapid Induction of apoptosis by PI3K inhibitors is dependent upon their transient inhibition of RAS-ERK signaling. *Cancer Discovery*. Mar; 4(3): 334-47. PMCID: PMC4049524. * = equal contribution, co-corresponding.
b. Hyman DM, Smyth LM, Donoghue MTA, Westin SN, Bedard PL, Dean EJ, Bando H, El-Khoueiry AB, Pérez-Fidalgo JA, Mita A, Schellens JHM, Chang MT, Reichel JB, Bouvier N, Selcuklu SD, Soumerai TE, Torrisi J, Erinjeri JP, Ambrose H, Barrett JC, Dougherty B, Foxley A, Lindemann JPO, McEwen R, Pass M, Schiavon G, Berger MF, **Chandarlapaty** S, Solit DB, Banerji U, Baselga J, Taylor BS. (2017) AKT Inhibition in Solid Tumors With AKT1 Mutations. *J Clin Oncol*. Jul 10;35(2):2251-2259. PMCID: PMC5501365.

c. Castel P, Ellis H, Bago R, Toska E, Razavi P, Carmona J, Kannan S, Verma C, Dickler M, **Chandarlapaty S**, Brogi E, Alessi D, Baselga J, Scaltriti M. (2016) PDK1-SGK1 signaling sustains AKT-independent mTORC1 activation and confers resistance to PI3Ka inhibition. (2016) *Cancer Cell* Aug 8;30(2):229-42. PMCID: PMC4982440.
d. Liu B, Liu, Z, Chen S, Ki M, Erickson C, Reis-Filho JS, Durham B, Chang Q, deStanchina E, Sun Y, Rabadan R, Abdel-Wahab O, **Chandarlapaty S.** (2020) Mutant SF3B1 promotes AKT and NF-KB driven mammary tumorigenesis. *J Clin Invest*. Oct 8;138315. Doi:10.1172/JCI138315. PMCID pending.