

## **Translational Breast Cancer Research**

Postdoctoral training positions are available in the <u>laboratory of Carlos L. Arteaga, M.D.</u> in the Simmons Comprehensive Cancer Center at UT Southwestern Medical Center. The laboratory has a longstanding interest in understanding the molecular pathways that drive breast cancer progression and influence response to therapies. Our laboratory has a strong mechanism-based translational focus, aimed at developing therapeutic strategies and identifying biomarkers of drug sensitivity and resistance.

## Current projects include:

- Discovery of **mechanisms of resistance** to breast cancer therapies (i.e., estrogen receptor antagonists, CDK4/6 inhibitors, HER2 inhibitors, PI3K/AKT inhibitors)
- Genomic and transcriptomic profiling of drug-resistant breast cancers
- Identifying rational combinations to overcome resistance to targeted therapies

We incorporate molecular profiling (DNA/RNA sequencing, single cell-seq) of patient tumors and cell lines, CRISPR, whole genome screens, and mechanistic studies using breast cancer cell lines, cell line-derived xenografts, and patient-derived organoids and xenografts, with the goal of using insights from the laboratory to inform clinical trials.

Relevant recent publications that apply to these topics include:

- PRMT5 is an actionable therapeutic target in CDK4/6 inhibitor-resistant ER+/RB-deficient breast cancer. Nat Commun. 2024 Mar 13;15(1):2287. doi: 10.1038/s41467-024-46495-2. PMID: 38480701
- Acquired secondary HER2 mutations enhance HER2/MAPK signaling and promote resistance to HER2 kinase inhibition in breast cancer. *Cancer Res.* 2023 Sep 15;83(18):3145-3158. doi: 10.1158/0008-5472.CAN-22-3617
- Co-occurring gain-of-function mutations in HER2 and HER3 modulate HER2/HER3 activation, oncogenesis, and HER2 inhibitor sensitivity. *Cancer Cell* 2021 Aug 9;39(8):1099-1114
- Proline rich 11 (PRR11) overexpression amplifies PI3K signaling and promotes antiestrogen resistance in breast cancer. *Nat Commun.* 2020 Oct 30;11(1):5488.
- <u>Hyperactivation of TORC1 Drives Resistance to the Pan-HER Tyrosine Kinase Inhibitor Neratinib in HER2-Mutant Cancers.</u> *Cancer Cell* 2020 Feb 10;37(2):183-199.e5.
- Aberrant FGFR signaling mediates resistance to CDK4/6 inhibitors in ER+ breast cancer. Nat Commun. 2019 Mar 26:10(1):1373.
- Genomic profiling of ER+ breast cancers after short-term estrogen suppression reveals alterations associated with endocrine resistance. *Sci Transl Med.* 2017 Aug 9;9(402):eaai7993.
- <u>An Acquired HER2(T798I) Gatekeeper Mutation Induces Resistance to Neratinib in a Patient with HER2 Mutant-</u> Driven Breast Cancer. *Cancer Discov.* 2017 Jun;7(6):575-585.

Applicants with a Ph.D., M.D., or M.D./Ph.D. and a strong background in molecular & cell biology and genomics with an interest in translational research in cancer are encouraged to apply.

Information on our postdoctoral training program, benefits, and a virtual tour can be found at <a href="http://www.utsouthwestern.edu/postdocs">http://www.utsouthwestern.edu/postdocs</a>.

Interested individuals should send a CV, statement of interests, and a list of at least two references (email preferred) to:

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