

## **Translational Breast Cancer Research**

A postdoctoral training position is available in the <u>laboratory</u> of <u>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:

- Acquired secondary HER2 mutations enhance HER2/MAPK signaling and promote resistance to HER2 kinase inhibition in breast cancer. Cancer Res. 2023 Jul 5:CAN-22-3617. doi: 10.1158/0008-5472.CAN-22-3617. Online ahead of print.PMID: 37404061
- 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.
- Hyperactivation of TORC1 Drives Resistance to the Pan-HER Tyrosine Kinase Inhibitor Neratinib in HER2-Mutant Cancers.
   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.
- ER+ Breast Cancers Resistant to Prolonged Neoadjuvant Letrozole Exhibit an E2F4 Transcriptional Program Sensitive to CDK4/6 Inhibitors. Clin Cancer Res. 2018 Jun 1;24(11):2517-2529.
- 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.
- An Acquired HER2(T798I) Gatekeeper Mutation Induces Resistance to Neratinib in a Patient with HER2 Mutant-Driven Breast
   <u>Cancer. Cancer Discov.</u> 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. A track record of productivity and publications in well-established journals would be a strength.

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

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

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