**Lay Summary**

The incidence of invasive breast cancer has been increasing since 2004, with more than 2 million cases reported worldwide in 2023. In ER+ breast cancer, endocrine therapy has proven successful in the treatment of hormone-responsive breast cancer since its early adoption in the 1940s as an ablative therapy. Despite the efficacy of endocrine therapy, resistance arises in about 30% of patients with early-stage disease and in almost all patients who develop metastasis, leading to poor clinical outcome.

Overcoming these outcomes is a major challenge in the ER+ breast cancer therapeutic arena. Thanks to the invaluable support from METAvivor, our laboratory has achieved remarkable progress in unraveling the intricate molecular mechanisms underpinning metastatic breast cancer. In our efforts to identify new potential therapeutic targets, we discovered that CoREST and BAF, two major epigenetic machineries that physically interact, are key determinants of resistance to endocrine therapies in breast cancer. Notably, loss of CoREST and BAF complexes, inhibits proliferation, primary tumor, and metastasis of endocrine resistant breast cancer and TNBC.

Additional results revealed a functional interplay between CoREST-BAF and the AXL signaling pathway in metastatic breast cancer. The AXL signaling pathway is associated with tumor cell growth, metastasis, invasion, drug resistance, and stem cell maintenance. Our investigations are poised to furnish compelling evidence advocating the incorporation of AXL inhibitors synergistically with CoREST and BAF complexes inhibitors as a promising strategy for the treatment of ER+ metastatic breast cancer.