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Research Category:	Translational/'Bench to Bedside' Research
Title of Abstract:	Semaphorin 7a Promotes Endocrine Resistance in ER+ Breast Cancer
Please copy and paste your abstract here: (no more than 300 words):	Estrogen receptor positive (ER+) breast cancers comprise approximately 70% of all breast cancer cases. ER-targeting endocrine therapies have facilitated the successful treatment of ER+ primary tumors; yet, 1 in 5 women with ER+ disease will experience recurrence, frequently in a metastatic site. These recurrent tumors uniformly develop resistance to endocrine therapies, rendering current treatments ineffective and identifying a need for novel molecular targets. We have identified semaphorin 7a (SEMA7A) as a potential driver of recurrence and metastasis in ER+ breast cancer. SEMA7A is a signaling protein that, when expressed, confers significantly decreased patient survival rates. We hypothesized that SEMA7A may promote ER+ recurrence and/or resistance to endocrine therapy. Using SEMA7A-overexpressing ER+ tumor cells, we demonstrate that SEMA7A overexpression is sufficient to induce numerous tumor-promotional phenotypes, including cell survival and invasion. Importantly, SEMA7A overexpression also confers resistance to endocrine therapies, including fulvestrant, tamoxifen, and estrogen deprivation in in vitro growth and clonogenic survival assays. Additionally, we verified this endocrine resistant phenotype using in vivo models, where we observe that SEMA7A renders MCF7 tumors insensitive to fulvestrant treatment and estrogen deprivation. Finally,

we report that SEMA7A-expressing tumors are capable of metastasizing to the lung in animals receiving fulvestrant. Our data support that SEMA7A may be a novel driver of endocrine resistance, recurrence, and metastasis in ER+ breast cancer.