Early lymph node (LN) metastasis often precedes systemic metastasis and correlates with a 20% decrease in 10-year survival compared to patients without LN metastasis. Understanding biologic pathways involved in early LN metastasis could identify promising drug targets for early-stage breast cancer (EBC) treatment.

While tumor size modestly correlates with the probability of clinical or occult axillary metastases, small T1 tumors are often LN negative. Large tumors without evidence of LN metastasis are often LN negative. We compared large tumors without evidence of LN metastasis (pT2-3pN0) and small tumors with LN metastasis (pT1pN1+) by whole transcriptome analysis to elucidate molecular biological differences associated with the absence or presence of early LN metastasis at diagnosis.

Our primary comparison was between pT1pN1+ and pT2-3pN0 tumors, with pT1pN0 and pT2-3pN1+ as controls. This study provides a foundation for understanding the mechanisms that promote LN metastasis. Previous studies have correlated LN metastasis with EMT and immune function. Overall, we found most biological differences within MP HR tumors.

Proliferation-related pathways were upregulated and EMT and immune-related pathways were downregulated in pT2-3pN0 tumors compared with pT1pN1+ tumors. Our data suggests these pathways may be involved in early LN metastasis. Dysregulated immune pathways could activate immune evasion/suppression mechanisms to escape immune surveillance and ultimately metastasize. Future studies will investigate antineoplastic therapies for EBC that modulate these dysregulated pathways to reduce early LN metastasis and subsequent systemic metastasis.

The authors wish to thank our patients who inspire us everyday. Navigating a cancer diagnosis is never easy, doing so during a pandemic requires heroic personal strength.

References: