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HONORS PROGRAM APPLICATION TO CANDIDACY: ABSTRACT

**Transforming growth factor beta, periostin and transforming growth factor
induced expression in breast cancer**

Breast cancer is the second leading cause of death among US woman. One in eight women will be diagnosed in their lifetime (1). Breast cancer patients have benefited from early detection. Advances in surgery and chemotherapy continue to act as the primary therapeutic measures while immunomodulation plays a significant role in tertiary prevention. Despite significant improvements, the development of aggressive cancers, including inflammatory breast cancer and metastatic disease still have poor prognoses (1,2).

Although the somatic mutation theory (SMT) dominates the current understanding of cancer progression, Sonnenschein et al. (5) developed an alternative theory: tissue organization field theory (TOFT). The latter theory defines cancer as a tissue-based disease and postulate that all cells by default proliferate in the absence of paracrine regulation (6). Regardless of the theory behind cancer progression, dynamic interactions between cancer cells, supportive stromal cells, extracellular matrix (ECM), and the immune system are critical to breast cancer progression (3,4). An independent parameter of breast

cancer progression is alterations in the ECM, notably accumulation of collagen I (8). In addition to collagen I accumulation, local fibrosis within the breast tumor microenvironment stimulates production of other ECM proteins especially periostin (POSTN) and transforming growth factor beta induced (TGFBI) (8,9). POSTN is an ECM protein that is upregulated in many carcinomas and is associated with poor prognosis in breast cancer (10,11,12). POSTN plays a role in development and tissue repair but is generally not expressed in healthy adult tissue (11,12,13). POSTN possesses similar protein structure and binding domains to TGFBI however they likely play opposite roles in cancer progression (13). Interestingly, both are regulated in part by the pro-fibrotic cytokine transforming growth factor beta (TGF- β). Additionally, our lab observed that breast cancer cells secreted periostin, leading to expression and activation of the cytokine TGF- β in a positive regulatory loop (13).

These studies are novel, as they will provide further evidence of the role of TGF β , POSTN and TGFBI in breast cancer progression. As well as give further clues to the mechanistic pathways involved in cancer progression. Overall the proposed experiments will provide a better understanding of the TGF- β , angiotensin II pathways and POSTN-TGFBI interactions in breast cancer progression.