Effect of Relaxin Signaling on ERBB2-Induced Breast Cancer

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Relaxin, a small peptide hormone, has been found to be highly expressed in several human metastatic cancers. Suppression of the relaxin/RXFP1 (Relaxin/Insulin like Family Peptide Receptor 1) signaling pathway decreases cancer progression in prostate cancer models *in vitro* and *in vivo*. However, there is contradictory published data on the role of relaxin/RXFP1 in breast cancer. Data collected in our laboratory has shown that the small molecule ML290 is a biased agonist of RXFP1 with anti-fibrotic properties. We are testing this compound in several preclinical models of fibrosis, as the therapeutic agent. The question remains whether ML290 treatment affects breast cancer progression or metastases. Thus, the aims of the project are to 1) analyze the role of endogenous relaxin signaling in breast cancer induced by transgenic overexpression of ERBB2 in mice and 2) study the effects of the small molecule agonist of the relaxin receptor, ML290, on ERBB2-induced tumor development and metastases. ML290 activates human, but not mouse, RXFP1. Therefore, to investigate the effect of ML290 on breast cancer development and progression, we used mice with the humanized RXFP1 gene. All of the mice being used in this study have transgenic overexpression of ERBB2 (erythroblastic oncogene B), which is frequently overexpressed in most aggressive breast cancers in human patients. Preliminary results indicate that ML290 treatment may decrease breast cancer progression. The complete results of this study will clarify the role of relaxin receptor activation by endogenous and synthetic agonists in breast cancer and will define RXFP1 as a potential target for cancer treatment.