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Investigation of LRRC24, a putative negative regulator of ErbB receptor tyrosine kinases

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Lrrc24 is a 513 amino acid transmembrane protein with a domain organization very similar to Kekkon-1. Preliminary data from the Fennell lab has revealed that Lrrc24 decreases ErbB receptor expression as efficiently as Lrig1 strongly suggesting that Lrrc24 is a negative regulator of the ErbB family of RTKs. Furthermore, Lrr24 is expressed in the murine mammary gland and the epithelium of the healthy human breast but may be decreased in breast cancer. Analysis of the Weigelt breast cancer dataset demonstrates that Lrrc24 expression inversely correlates with time to metastasis, suggesting that Lrrc24 could be a metastasis suppressor. Furthermore, Lrrc24 is decreased in prostate adenocarcinoma compared to normal prostate. Collectively, our preliminary data highlight several key features of Lrrc24 which suggests that it could be an important growth suppressor including its ability to negatively regulate oncogenic ErbB RTKs, its expression in normal tissue in which ErbBs are expressed and its potential loss in cancer. Through this study we hypothesize that Lrrc24 is a novel negative regulator of the ErbB family of RTKs and that it functions to suppress ErbB-driven tumor cell proliferation, motility and/or invasion.

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