RUNX1 and breast cancer

University of Massachusetts Medical School

Asia N. Matthew-Onabanjo
University of Massachusetts Medical School

Leslie M. Shaw
University of Massachusetts Medical School

Follow this and additional works at: https://escholarship.umassmed.edu/metnet_pubs

Part of the Biochemistry Commons, Cancer Biology Commons, Cell Biology Commons, Cellular and Molecular Physiology Commons, and the Molecular Biology Commons

This work is licensed under a Creative Commons Attribution 3.0 License.

Repository Citation

This material is brought to you by eScholarship@UMMS. It has been accepted for inclusion in UMass Metabolic Network Publications by an authorized administrator of eScholarship@UMMS. For more information, please contact Lisa.Palmer@umassmed.edu.
RUNX1 and breast cancer

Jose Mercado-Matos, Asia N. Matthew-Onabanjo and Leslie M. Shaw

News on: Runx1 stabilizes the mammary epithelial cell phenotype and prevents epithelial to mesenchymal transition by Hong et al. Oncotarget. 2017; 8:17610-27. doi: 10.18632/oncotarget.15381

RUNX1 is a member of the RUNX family of transcription factors that also includes RUNX2 and RUNX3 [1]. Early studies identified RUNX1 as a key regulator of definitive hematopoiesis and the role of RUNX1 as a tumor suppressor in leukemia is well established [1]. In more recent sequencing studies of solid tumors, molecular alterations have been identified in other cancer types, suggesting a broader role for RUNX1 in epithelial cells and carcinomas. RUNX1 is the predominant RUNX protein expressed in the normal human breast epithelium and it is the only RUNX family member for which somatic mutations have been identified in human breast cancer. These mutations are primarily loss of function mutations that occur through nonsense, frameshift or missense mutations within the Runt DNA-binding domain [1]. These RUNX1 mutations occur almost exclusively in the ER+, luminal subtype of breast cancer and indicate a tumor suppressor role for RUNX1 [2]. In contrast, elevated levels of RUNX1 expression correlate with poor outcomes in triple negative breast cancers (TNBCs), indicating a positive, oncogenic role for RUNX1 in this breast cancer subtype [3]. These disparate findings support a cell-context dependent role for RUNX1 in breast cancer.

The functional consequences of RUNX1 loss or gain of expression that contribute to breast cancer development and progression have not been fully elucidated. A role for RUNX1 in suppressing ER oncogenic signaling is suggested by the fact that combined loss of Runx1 with either TP53 or Rb1 leads to hyperproliferation of ER+ luminal cells in the mouse mammary gland [2]. Inactivating mutations of RUNX1 may be an early event that enhances estrogen signaling, creating a permissive environment for the development of ER+ luminal tumors. Regulation of ER signaling would explain the luminal phenotype that occurs with EMT, tumor cells can also rely upon E-Cadherin expression for collective invasion from the tumor [7]. Moreover, in a recent study investigating the role of cancer associated fibroblasts (CAFs) in tumor invasion, a heterotypic interaction between N-Cadherin on CAFs and E-Cadherin on tumor cells was required for efficient invasion of squamous cell carcinoma (SCC) cells [8]. Therefore, either high or low levels of RUNX1 could regulate invasion and promote tumor progression in breast cancer through a mechanism involving regulation of E-Cadherin expression.

In summary, increasing evidence supports a role for RUNX1 in breast cancer progression. Understanding how RUNX1 functions in a cell context-dependent manner will be essential for determining the mechanism(s) by which this transcription factor impacts tumor biology.

Leslie M. Shaw: Department of Molecular, Cell and Cancer Biology, University of Massachusetts Medical School, Worcester, MA, USA

Correspondence to: Leslie M. Shaw, email leslie.shaw@umassmed.edu

Keywords: breast cancer, E-Cadherin, estrogen receptor, EMT, RUNX1

Received: March 08, 2017
Published: April 19, 2017
REFERENCES