

Featured Publication Note

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A key role for polarity signalling in breast cancer metastasis

Metastasis, the spread of cancer cells from the primary tumor site to distant organs, accounts for over 90% of deaths in breast cancer patients. Metastasis has been associated with epithelial-to-mesenchymal transition (EMT), in which polarized epithelial cells convert into single fibroblastoid cells capable of locomotion. The Par6 polarity complex is an important regulator of the morphological transitions associated with epithelial cell plasticity. In this study, researchers show that par6 signalling, which is regulated directly by TGF β , plays a key role in breast cancer metastasis.

To explore the role of the TGF β -Par6 pathway in breast cancer progression, researchers used 3D culture models of mammary gland epithelial cells, and an orthotopic mouse model of breast cancer. Mouse mammary epithelial cells (NMuMg) were cultured in 3D cultures, immunostained for polarity markers, and analyzed using confocal microscopy. Images were acquired and visualized using **Volocity**[®] software (figure 1). In addition, the measurement features of **Volocity Quantitation** were used to compare cytoplasmic vs. junctional staining of the polarity marker, ZO-1. The results showed that interference with Par6 signaling blocks the morphological changes associated with EMT. Par6 signaling was also shown to be critical for the distinctive protrusive morphology of metastatic breast tumor cells, and blocking it *in vivo* suppressed metastasis to the lungs.

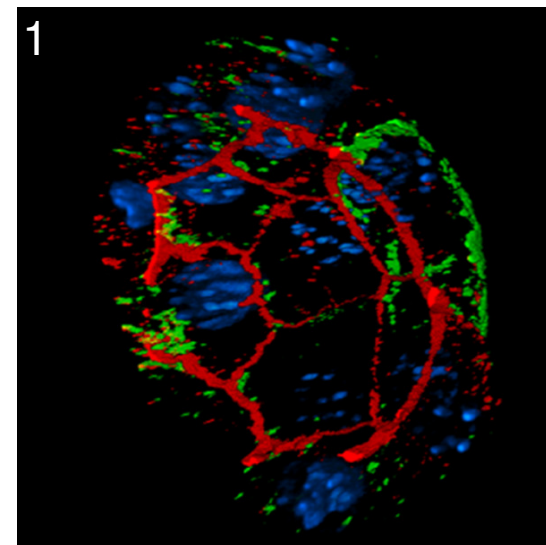
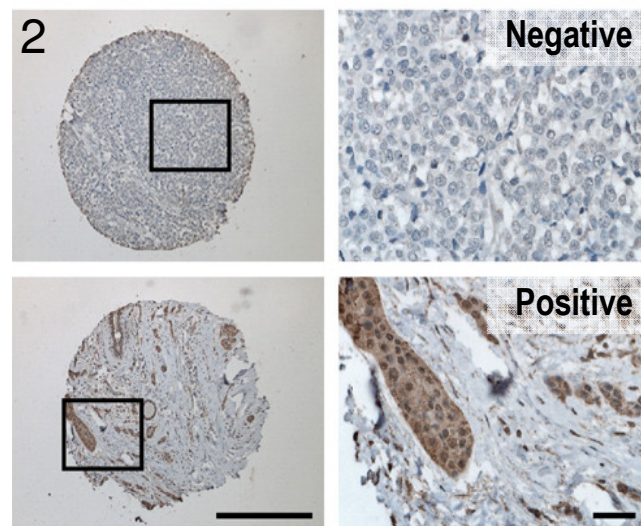


Figure 1: 3D reconstruction of a 12-day NMuMg polarized acini-like structure with a well defined lumen, characterized by ZO-1 (red) localized to the apical tight junction region and E-cadherin (green) localized to the adherens junction, basal to ZO-1. Nuclei are shown in blue.



Researchers used Tyramide Signal Amplification (TSA[™]) technology to explore the Par6 pathway in tissue microarrays (TMA) of human breast tumors. The levels of pPar6 were analyzed in TMAs by immunohistochemical staining of pPar6 on paraffin sections, using the **TSA[™] Plus DNP HRP System** (figure 2). With the increased signal sensitivity provided by this system, researchers were able to show that the Par6 pathway was highly active in a subset of human breast tumors with basal subtype features, which are generally more aggressive.

By furthering the knowledge of the processes involved in breast cancer metastasis, this research may contribute towards future treatments of breast cancer.

Figure 2: pPar6 immunostaining in human breast cancer TMAs. Examples of positive and negative staining are shown at lower (left images; scale bar, 500 μ m) and at higher magnification (right images, scale bar, 50 μ m).