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TAZ Defines Breast Cancer Stem Cell Properties Downstream of Epithelial-Mesenchymal Transition and Cell Polarity

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Cancer Stem Cells (CSCs) are proposed to drive tumor initiation and progression. Yet, our understanding of the cellular and molecular mechanisms that underlie CSC properties is limited. Here we show that the activity of TAZ, a transducer of the Hippo pathway, is a determinant of key biological traits of breast CSCs. TAZ is required to sustain self-renewal and tumor-initiation capacities. TAZ protein levels and activity are elevated in prospective CSCs and in poorly differentiated human tumors, and have prognostic value. Gain-of-TAZ endows CSC behaviors to non-CSCs. In epithelial cells, TAZ forms a complex with the cell polarity determinant Scribble, and loss-of-Scribble - or induction of EMT - disrupt the inhibitory association of TAZ with the core Hippo kinases MST and LATS. This study links the CSC concept to the Hippo pathway in breast cancer, and reveals a mechanistic basis of the control of Hippo kinases by cell polarity.