Evaluation of the Yes-associated Protein as a Target for Breast Cancer Therapy

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The Yes-associated protein (YAP) is a transcriptional regulator that has been linked to various cellular processes such as tissue regeneration and metabolism. Typically, the Hippo pathway regulates the YAP pathway and it remains cytoplasmic. However, deregulation causes the YAP pathway to localizes to the nucleus where it drives cell processes. Unregulated YAP, thus, may lead to tumorigenesis. The purpose of this project is to prove the connection between YAP localization and cancerous proliferation (reflected by the production of Antigen Ki67 (Ki67), a cellular marker for proliferation), and to further investigate if inhibiting YAP could suppress cancerous proliferation and shed light on potential breast cancertherapy. First, this experiment increases the spreading area of MCF10A cells to 1040μm^2 to manipulate YAP localization. The cell lines were then subject to immunofluorescence microscopy to visualize YAP and proliferation. To quantify the effect of increasing the spreading area on localization of YAP, a MATLAB algorithm calculated the nucleus-cytoplasmic ratio of YAP intensity in 50 cells. Another MATLAB algorithm calculated the intensity of Ki67 production across 20-30 cells to indicate whether the population was proliferative. Lastly, cells with a greater production of Ki67 across thepopulation were treated with a YAP inhibitor. The Ki67 production was analyzed using immunofluorescence microscopy and western blot. After analyzing all the data, the project concludes that YAP localization in the nucleus does indeed increase Ki67 production. Furthermore, inhibiting YAP function significantly decreases Ki67 production. Overall, the entire project demonstrates that developing drugs targeting YAP may improve current cancer treatment/therapy.