**Geminian Protein’s Dual Nature Plays Key Role in Metastasis, According to Texas-Based Study**

A team of investigators from Texas research institutions [MD Anderson Cancer Center (MD Anderson)](http://bionews-tx.com/news/news-category/ut-md-anderson-cancer-center/), The University of Texas Graduate School of Biomedical Sciences, and [Baylor College of Medicine](http://bionews-tx.com/news/news-category/baylor-college/) have recently made an important discovery in the field of **metastatic cancer research**.  The discovery was made while they were studying the mechanisms that cause [transforming growth factor beta (TGF-β)](http://www.ncbi.nlm.nih.gov/pubmed/20495575), a tumor suppression protein blocking progression in pre-malignant cells, to become a catalyst for metastasis (spread of cancer from its original site within the body). Their findings were published in the most recent issue of [*Cancer Cell*](http://www.cell.com/cancer-cell/abstract/S1535-6108%2814%2900476-0).

In a recent [news release](http://www.business-standard.com/article/news-ani/here-s-why-jekyll-and-hyde-protein-prevents-as-well-as-spreads-cancer-115021000732_1.html), [Dr. Dihua Yu, M.D., Ph.D.](http://faculty.mdanderson.org/Dihua_Yu/Default.asp?SNID=1120754774), deputy chair of the[Department of Molecular and Cellular Oncology at MD Anderson](http://www.mdanderson.org/education-and-research/departments-programs-and-labs/departments-and-divisions/molecular-and-cellular-oncology/index.html), Hubert L. & Olive Stringer Distinguished Chair in Basic Science, and lead study investigator explained the significance of the results, stating, “TGF-β has a dual role as both a tumor suppressor in normal and pre-malignant cells, and a metastasis promoter in late-stage cancer. The molecular mechanism by which TGF-β switches its role has long been an unsolved mystery for cancer researchers.”

“TGF-β’s known critical role in cancer has led to numerous efforts to develop TGF-β inhibitors for anti-cancer therapeutics, but its penchant for both suppressing tumor progression while serving as a springboard for cancer metastasis has been a major obstacle in the development of anti-TGF-β therapies,” said Dr. Yu. “We have developed a model that proposes that TGF-β’s complicated nature may be governed by the cellular effects of SMAD’s partner proteins.”

Their model was developed by using premalignant mammary epithelial cells in an experimental protocol to study the effects of different downstream protein partners, known as [SMAD proteins, on the dual functions of TGF-β](http://www.cellsignal.com/contents/science-pathway-research-stem-cell-markers/tgf-smad-signaling-pathway/pathways-tgfb).  SMAD proteins help regulate the activity of cell growth and division.  They have also been shown to promote the dual nature of TGF-β.  Their key findings showed that a regulatory protein [14-3-3ζ](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3017465/), plays an integral role through the following mechanisms:

* 14-3-3ζ switches TGF-β’s function by providing contextual partners for SMADs
* 14-3-3ζ inhibits YAP1-induced 14-3-3σ to disrupt p53/Smads complex
* 14-3-3ζ stabilizes Gli2/Smads complex to activate PTHrP and induce bone metastasis
* 14-3-3ζ is associated with TGF-β’s functional switch during breast cancer development

When asked about the significance of these results for future therapeutic drug target research, Dr. Yu explained, “Because TGF-β plays important roles in various physiological functions, it is crucial that we look at how to develop more specific drugs that selectively target TGF-β in cancer so as to discourage its ability to cause metastasis while maintaining its tumor suppression abilities in pre-cancerous cells.”