

Brachyury Goes Clinical

Debalina Sarkar*

Brigham and Women's Hospital, Boston, USA

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It takes several years, for a gene of interest in basic science to get into clinical trial. These developments are much hoped for but never are easy and certainly not fast. These steps usually involve many years of basic science research, financial support and yet no conclusion for a clinical trial.

One of the genes, which climbed these steps very fast, is the mesoderm-inducing gene and T-box transcription factor 'Brachyury'. Brachyury was not studied extensively in cancer until the recent years. Its role in the cancer was merely known until very recently.

Brachyury was originally shown to play central role in mesoderm development in mouse where the mice were arrested in mesoderm formation [1]. Brachyury is been shown to be expressed in chordomas [2] and embryonal carcinoma (EC) cell line, NTERA2 where it is expressed in absence of mesodermal differentiation. Brachyury was also described as a candidate of T-cell mediated cancer immunotherapy and its expression was associated with many tumour types, including colorectal tumour cell lines [3]. But, studies to link the presence of brachyury with cancer are very recent. Over the last 5 years, this gene has been investigated in many basic science laboratories.

Brachyury is shown by various research groups to be highly expressed in a variety of cancers, including breast, colon, lung and prostate [3]. This made brachyury an interesting candidate for clinical trial.

Furthermore, understanding the role of brachyury is also crucial to study this gene as a stem cell marker [4]. Brachyury has been shown to be a potential marker for colorectal cancer and also as a colon cancer stem cell marker. A possible link between the expressions of brachyury with the regulation of the pluripotency gene Nanog, has been shown in human colon cancer cell line [4]. The oncoprotein β -catenin, which is itself a modulator of 'stem' signaling pathways, is known to influence the levels of brachyury [4]. This would suggest that, the latter may be an important factor in transducing the β -catenin signaling pathway in the maintenance of cells with a CSC-like phenotype. Brachyury regulates expression of the pluripotency gene Nanog, by binding to

brachyury with upstream regulatory elements in the Nanog promoter in mesenchymal-like cancer cells.

Decisively, in February 2012, GlobeImmune, a Colorado based company, announced the beginning of Phase 1 clinical trial to be performed at the National Cancer Institute (NCI). This study will focus on the safety and tolerability of GI-6301, a Tarmogen product that is meant for patients with metastatic cancers containing brachyury protein [5]. In May 2012, Clinical Cancer Research has published another significant research confirming brachyury can be a potential target for Lung Cancer Therapy [6]. Successful completion of this project will open far more branches of research in cancer than before. Following this interesting publication, NCI published an editorial on brachyury's potential to be a significant target [7].

Although, brachyury moved from basic science to clinical trial significantly fast, many answers are yet unknown about its fundamental role in human body. Completion of the clinical trial will definitely tell a lot more in this field of study, but continuation of brachyury to be studied in basic science is still needed to answer many questions.

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*Corresponding author: Debalina Sarkar, Ph.D, Brigham and Women's Hospital, Boston, USA, E-mail: drds14@yahoo.com

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