Review of Methodology in Biomechanical Breast Cancer Research

Lalith Roopesh[1]; Keo Chhun[1]; Taman Kanchanapalli[1]
[1]University of South Florida

ABSTRACT

While the tumor microenvironment is an important topic in oncology, only recently has mechanotransduction been a focus due to its better-understood role in cell signaling. However, study of these mechanisms is difficult *in vivo* as it is hard to accurately measure force within organisms. To this end, we elucidated a specific mechanosensitive PIEZO pathway in triple-negative breast cancer and researched *in vivo* methodology in study. We complement this research by touching on bioinformatic techniques that complement *in vivo* and *in vitro* research as well as discuss *in silico* models. Overall, while *in vivo* and *in silico* study improve, increased integration will hasten development and lead to fully computational experimental models. This may allow ease of research as well as expedite simpler personalized medicine.

AUTHOR CONTRIBUTIONS

Keo Chhun researched and wrote the introduction. Taman Kanchanapalli researched and wrote *in vivo* methodology. Lalith Roopesh researched and wrote the bioinformatic work, conclusions, abstract, and put together the references.

All authors reviewed and put together the poster together.

CONTACT

Lalith Roopesh lalithr@usf.edu

Keo Chhun keoc@usf.edu

Taman Kanchanapalli tamank@usf.edu

INTRODUCTION

The tumor microenvironment (TME) is the cellular environment in which cancer cells reside. Within this environment, the body's immune cells struggle to perform their duties and the non-immune cells function to nourish the tumor[7, 10]. Mechanotransduction, the process of converting mechanical stimuli into electrochemical responses, has been shown to significantly impact the TME[3]. This is typically done via activation or deactivation of pathways that impact cell cycle fibers or structural formation[4].

The focus of this literary review is on the breast cancer PIEZO pathways. In this pathway, the PIEZO family of mechanical-gated ion channels plays a role in the development of cancer. PIEZO1 gate specifically assists in the migration of breast cancer cells, while the PIEZO2 gate causes various effects ranging from increased invasiveness of TNBC (triple negative breast cancer) cells to worse prognosis (prediction of disease progress) of TNBC[5]. Figure 1 demonstrates a possible pathway.

The review will touch upon how these pathways are studied and conclusions about the method and direction of this work.

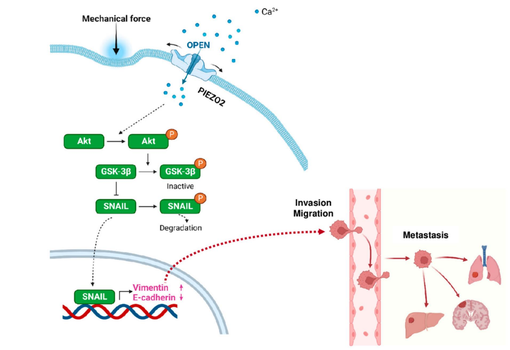

Figure 1. Model of PIEZO2's role in breast cancer. Adapted from Katsuta et al.[5]

IN VIVO METHODOLOGY

In vivo experimentation is generally harder due to higher difficulty in controlling every variable, stress indication variability, applicability to wider populations, and expensiveness. Novel imaging techniques offer a less invasive, but consequently slightly inaccurate, measurement strategy.

Elastography (Figures 2A-D) is the usage of ultrasound-based elasticity imaging which identifies heterogeneity *in vivo*, which offers hints to genotype, TME, spacial distribution, and oncogenesis due to stress [8].

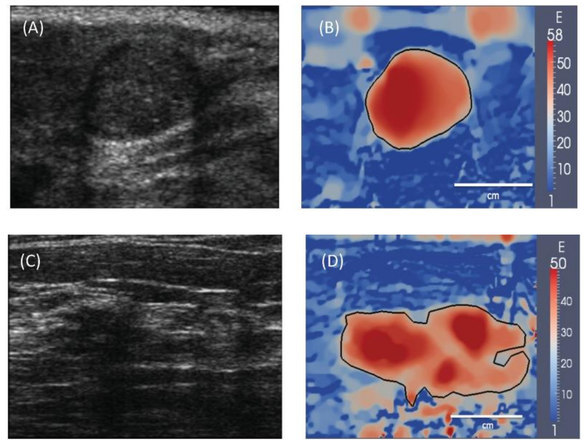

Figure 2. Ultrasound imaging of a homogenous (A, B) and a heterogeneous (C,D) fibroadenoma. Adapted from Liu et al.[8]

Compression optical coherence elastography (OCE) maps tissue strain with special resolution, allowing comparison with data from newly excised tissues to measure rigidities *in vivo*[6]. This method is useful for cells that cannot be detected well with regular elastography.

In vitro 3D-engineered anisotropic collagen scaffolds with grown tumors allow stronger measurement for models of tumor growth via immunofluorescence microscopy and optical coherence micrography. It is particularly useful in testing effects of therapeutic drugs[2].

BIOINFORMATIC WORK

Bioinformatic tools are applicable in assisting *in vivo* or *in vitro* studies as well as basic modeling. Genome data can be obtained from faster sequencing and novel platforms (such as cBioportal) that allow comparisons at a global scale[1]. Gene expression analysis with Gene Set Enrichment Analysis (GSEA) allows comparison of transcriptomic profiles to sort patients with high and low levels of PIEZO1 expression[5]. Figures 3A-D show how this data can be correlated to outcomes.

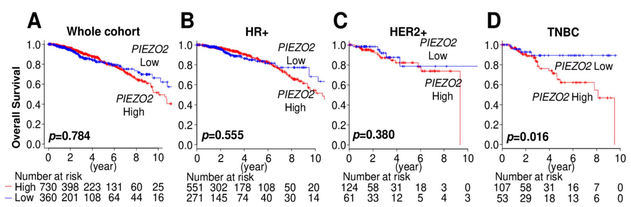

Figure 3. Correlation of PIEZO1 expression to outcomes across multiple types of breast cancer. Adapted from Katsuta et al.[5]

Mathematical and computational modeling of the environment is steadily improving. Focus is now given to modeling cells as individuals rather than tumors as a whole, using lattice-based, force-based, or repulsion/adhesion forces. More complex biochemical interactions with the extracellular matrix or fibers are also considered, and accurate mechanical modeling of breast cancer PIEZO1 pathways is possible[9]. As more advanced models develop, bioinformatic work may move from predictive to experimental research.

CONCLUSIONS

In vivo study of the biomechanical pathways in breast cancer proves difficult as mechanotransduction and related studies are relatively new, but recent imaging techniques combined with bioinformatic analysis shows strides. PIEZO1 mechanotransduction study in particular benefits from a combined imaging and bioinformatic technique. Focus should be given to developing more accurate bioinformatic models through greater integration with *in vivo* model study.

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