

## Adaptation to extracellular acidosis promotes cancer cell plastic

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Early ducts of breast tumors are unequivocally acidic, due to the combination of high rates of glycolysis with poor perfusion. Pre-malignant cells must adapt to this acidosis to thrive. Cancer cells plasticity promotes their diversity and contributes to tumor evolution through intratumoral heterogeneity. Plasticity of cancer cells enables them to shift between a more differentiated state and less or undifferentiated state. Here in, using RNA sequencing and small RNA sequencing and their differentially expressed, integrative network analysis using a motif exploring and motif ranking scheme we found a core regulatory sub-network in acid adapted breast cancer cells playing role in cancer plasticity. Our further integrative analysis of RNA sequencing and SILAC proteomics resulted in validation of two hubs of this sub-network. We further validated our finding both *in vitro* using q-RT-PCR, western blot and Immuno-cytochemistry (ICC) and in patient samples TMA by IHC analysis. We concluded that this cluster plays role in plasticity of breast cancer cells resulting from adaption to acidic microenvironment of early breast cancer. Survival analysis of patients showed lower survival of patients with higher expression of acid-induced plasticity clusters. Hence, this study suggests essential roles of acid adaptation in cancer cells plasticity and its derived heterogeneity mechanism that can be used as therapeutic strategy targeting both acid-adapted and plastic phenotype.

### Biography

Iliya Rafiei has completed his Bachelor's degree in Cellular and Molecular Biology from Shiraz University, Iran. He is currently working on his MSc thesis in Research Institute for Fundamental Science at Tabriz University, Iran. He has worked as a Research Assistant on multiple researches conducted at RIFS and also a couple of manuscripts with his participation have been submitted to peer-reviewed journals.

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