Identifizierung des TMX2-Transmembranprotein-Netzwerks
Identification of TMX2 transmembrane protein network

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Introduction: TMX2 is a thioredoxin-related transmembrane protein that possesses not only a thioredoxin consensus pattern, but also an endoplasmic reticulum membrane retention signal, an N-terminal signal peptide, and a Myb DNA-binding domain repeat signature. The participation of thioredoxin in redox reactions explains its role in cell signaling and homeostasis. Any abnormal regulation could contribute to carcinogenesis. According to previous data, TMX2 overexpressed in breast CSCs and downregulation contribute in downregulation of specific transcription factors involved in stemness. However, no many data about TMX2 pathway and interaction with other proteins exist. The present study aimed to identify potential interactions among TMX2 and other genes and design a potential pathway.

Methods: MDAMB231 and MCF7 breast cancer cell lines tested for TMX2 expression with qPCR and western blot. Then were transfected with siRNA for TMX2 and KD evaluated. RNA extracted from control and siRNA - KD cells and whole gene expression microarrays followed. Genes that downregulated were selected for further analysis. It included clustering analysis and then design of potential interactions among all these genes based on biochemical experimental data.

Results: The qPCR post KD revealed decrease in gene expression of TMX2 up to 82 % for MCF7 and 52% for MDAMB231. More than 200 genes (encoding proteins) downregulated. A potential network designed, including the above proteins and interactions among them or other known proteins. This network consisted of more than 1000 proteins. Sub-networks created, eliminating interactions not correlated direct or indirect with TX2. Approximately 150 proteins participated on the finally network. TMX2 has 14 directed edges and the average shortest path length is approximately 10.7. The closeness is 0.092 and radiality is high enough for TMX2 (0.72) compared with the entire network (max 0.79).

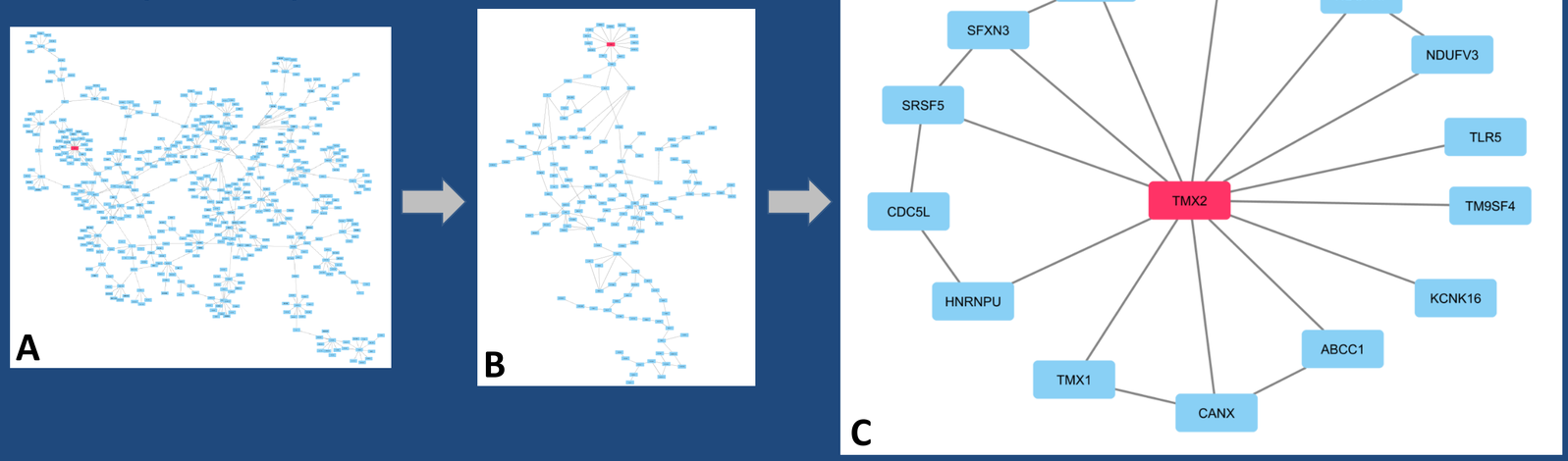

Figure 1: Diagramatic representation of identification of TMX2 network. The initial network (**A**) consisted of 508 proteins, the second (**B**) of 108. TMX2 interacts with 14 different proteins (**C**). The red square indicated TMX2 protein.

Conclusion: According to experimental data, TMX2 overexpressed in breast cancer and correlated with stemness. Therefore, apart from a potential biomarker TMX2 might be a drug-able target. The identification of TMX2 pathway is required in order to understand the mechanisms of action, since no direct connection with stemness transcription factors revealed from the above data. The TMX2 pathway might be useful for determination other molecules involved in stemness process, and enable the identification of new drug-able targets.

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Disclosure of Potential Conflicts of Interest

None of the authors of the above study has declared any conflict of interest

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