IDENTIFICATION OF GENES REGULATED BY NFAT1 IN MELANOMA: An *IN SILICO* APPROACH

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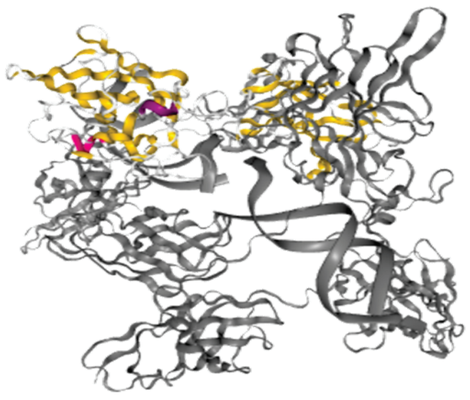

Figure 1: NFAT1's tertiary structure (PDB ID 1P7H.L).

INTRODUCTION

Nuclear factor of activated T-cells (NFAT) is a family of transcription factors expressed in different vertebrate cells and tissues that plays important roles in cellular development, including in the immune system. It is already know that the deregulation of NFAT expression is involved in tumor progression, including in cutaneous melanoma, a type of skin cancer that originates from melanocytes. Although it corresponds to a rare type of malignant neoplasm, it is clinically relevant because of a high risk of metastasis. In melanoma, it is common to observe high expression of two NFAT family members, NFAT1 and NFAT2, and it has been shown that the silencing of NFAT1 in melanoma cells causes apoptosis. However little is known about NFAT1 related-gene regulation in melanoma.

OBJECTIVE

This project aims to understand the role of NFAT1 and its interaction network in melanoma through an in silico approach.

METHODOLOGY

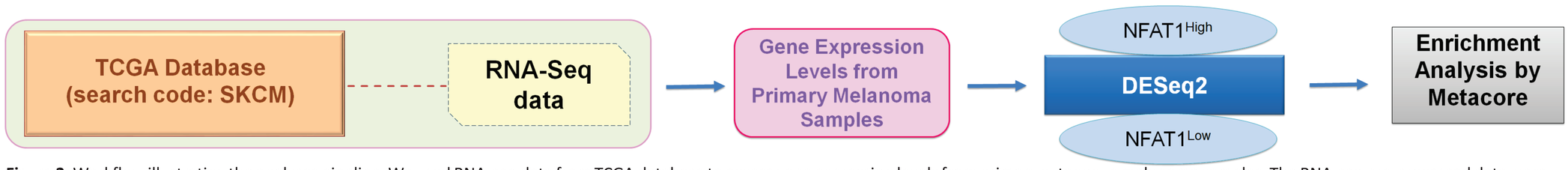

Figure 2: Workflow illustrating the analyses pipeline. We used RNA-seq data from TCGA database to access gene expression levels from primary cutaneous melanoma samples. The RNA-seq pre-processed data were downloaded and normalized using the DESeq2 package. Samples were then separated into NFAT1^{High} and NFAT1^{Low} expression groups.

RESULTS

Table 1: Classification of primary melanoma samples according to NFAT1 expression. From the 103 samples downloaded from the TCGA database, 11 samples were classificated into NFAT^{High}, and 11 into NFAT1^{Low} (Padj < 0.01).

Primary Melanoma Samples		
Total	**NFAT1^{High}**	**NFAT1^{Down}**
103 samples	11 samples	11 samples

Table 2: Different Expression Genes (DEG). We found 512 differentially expressed genes in the NFAT^{High} group, of which 152 were up-regulated (LFC > 0) and 360 were down-regulated (LFC < 0).

DEG in NFAT1^{High} samples		
Total	**Up-regulated**	**Down-regulated**
512 genes	152 (0.78%)	360 (1.9%)

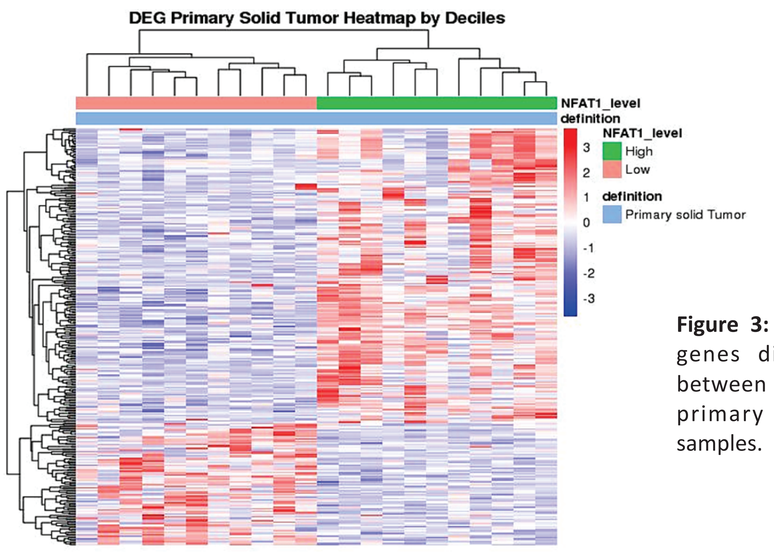

Figure 3: Heatmap illustrating the genes differentially expressed between NFAT1^{High} and NFAT1^{Low} primary cutaneous melanoma samples.

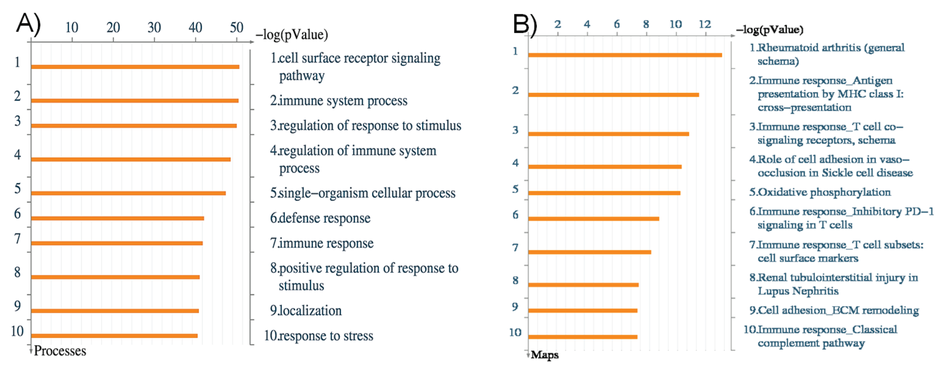

Figure 4: Pathway analyses enrichment using the software MetaCore. A) First 10 GO Processes found enriched with DEG. B) First 10 differently regulated Pathway Maps.

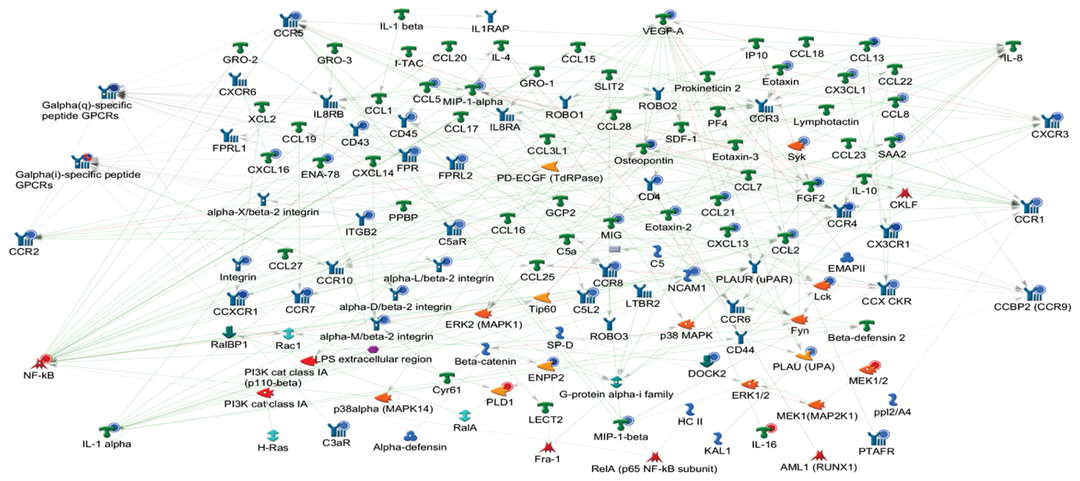

Figure 5: The Chemotaxis Network is illustrated as an example of an enriched network identified by the MetaCore analyses. DEG is represented by red (up-regulated) and blue (down-regulated) circles.

CONCLUSION

Primary melanomas express high and low levels of NFAT1. Classification of melanoma samples by NFAT1 expression levels allows the identification of almost 1500 differentially expressed genes. These genes are enriched in different networks and pathways, most of which related to the communication between tumor cells and the microenvironment including receptor signaling, chemotaxis and immune response. A more detailed analysis of the functional role of these genes in melanoma, as well as the relationship with NFAT1 expression is ongoing.

REFERENCES AND ACKNOWLEDGEMENTS

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