



Propuesta de Trabajo Fin de Máster

Año académico 2023-2024

MÁSTER EN MÉTODOS COMPUTACIONALES EN CIENCIAS

Proyecto Nº 5

Título: PRECISION MAPPING OF A LYMPHEDEMA GENETIC SIGNATURE IN RADIOTOXICITY IN BREAST CANCER PATIENTS.

Departamento/ Laboratorio: Bioquímica y Genética /Inmunoterapia CIMA

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Resumen:

Breast cancer (BC) remains a major health concern and is the most common cancer affecting women worldwide. It is well established how cancer treatment (surgical or radiation induced) associated lymphedema is a common complication in breast cancer patients caused by therapy-induced vessel destabilization and compromised immune function. This debilitating condition known as secondary lymphedema can damage lymphatic vessels leading to edema, fibrosis, inflammation and dysregulated adipogenesis, which result in profound swelling of an affected limb.

Lymphedema patients often exhibit impaired immune function which predisposes them to a variety of infections and may compromise the efficacy of immunotherapy-based therapeutic endeavors. In addition, in few cases radiation may induce angiosarcoma with characteristics of lymphatic endothelial cells as a consequence of intense tissue fibrosis.

Recent findings suggest the possibility of having genetic predisposition to secondary lymphedema and signal polymorphisms in 18 different genes as predisposing patients to develop this vascular disease following breast cancer therapy. If this holds true, a new possibility to foresee which patients will need particular medical follow up or preventive care before the onset of therapy. This approach will improve patient quality of life, response to treatment and alleviate the financial costs of medical care.

To probe these, in this project we will download BC data from the TCGA database and GEO database, on which we will perform in depth single-cell sequencing analysis (scRNA-seq), weighted co-expression network analysis, and transcriptome differential expression analysis. Then seven lymphangiogenesis-related genes (LARGs) will be identified using Cox regression, least absolute shrinkage, and selection operator (Lasso) regression analysis to construct a prognostic model for BC patients. Finally, the expression and function of the key genes found in the model were verified by in vitro experiments.

To further corroborate our findings, we will perform an additional analysis of the relationship between the expressions of lymphedema-associated genetic signatures and responses to radio and/or immune therapy in clinical samples in a separated cohort obtained from breast cancer patients

OPTATIVAS RECOMENDADAS

1. Análisis de imagen
2. Machine Learning I
3. Machine Learning II