# Good Fat, Bad Fat: How Niche Affects Breast Cancer Development

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## Abstract

**Introduction**. Most cancer studies are based solely on the study of tumor cells. However, here, we study how the microenvironment surrounding them affects the pathogenesis of the disease.
**Objective**. To study how tumor-associated fibroblasts (TAF) affect tumor cell gene expression in the context of the tumor microenvironment.
**Material and methods**. We compared the profile of gene deregulation induced in response to normal fibroblasts (NAF) vs CAF using the GSO public database **GSE70884.** Venn diagrams have been constructed to identify common genes. The functional analysis has been carried out using the Enrich platform. The association with forecast has been developed using the KM Plotter tool.
**Results.** We showed how the difference in gene expression induced by the factors secreted by CAF is greater than that of NAF. In addition, the number of overexpressed genes shared between different cell lines is greater when they are exposed to the environment conditioned by CAF. The functions of genes overexpressed in response to CAF are mostly related to the immune system. Finally, the combined analysis of genes overexpressed by CAF with poor disease progression (HR≥1) has a higher prognostic value.
**Conclusions.** CAF-induced deregulation of gene expression is more intense and homogeneous than NAF-induced. Besides the fact that the microenvironment influences the tumor cells, it is involved in the tumor's immune response and in the worse evolution of the tumor.

## Hypothesis

Factors secreted by tumor-associated fibroblasts (TAF), rather than normal fibroblasts (NAF), induce an overexpression of genes related to poor prognosis in breast cancer.

## Objectives

1. Compare the expression profiles of the deregulated genes in responses to the conditioned environment of normal (NAF) and tumor-associated fibroblasts (CAF)
2. Identify the overexpressed genes in breast cancer cells in response to conditioned medium of NAF and CAF.
3. Study the relationship between the identified overexpressed genes and the clinical evolution of breast cancer patients.
4. Determinate the functions involved in the over-expressed genes in response to conditioned medium of NAF and CAF.

## Conclusions

1. The difference in gene expression induced by CAF in MT is much more intense and varied than that induced by NAF. This leads us to affirm that TM has an influence on TK.
2. The intensity of CAF gene deregulation varies between subtypes. It is most evident in HER2+, through overexpressed genes.
3. The most heterogeneous tumor subtype is TNBC, which shares only three genes in all LCs (HR+ and HER2+ share 10). This allows us to confirm the relationship between heterogeneity and poor prognosis.
4. There are more common genes among the LCs before CAF than before NAF, which allows us to conclude that CAF helps to homogenize the characteristic heterogeneity of CM.
5. The functions carried out by genes overexpressed with CAF are mostly related to SI, i.e., MT is involved in both the immune response to CT and the subsequent mutations that allow the tumor to evade it.
6. Overall, genes overexpressed to CAF are synergistically associated with a worse tumor prognosis, especially in TNBC. Inhibiting this overexpression may therefore lead to an improved prognosis.
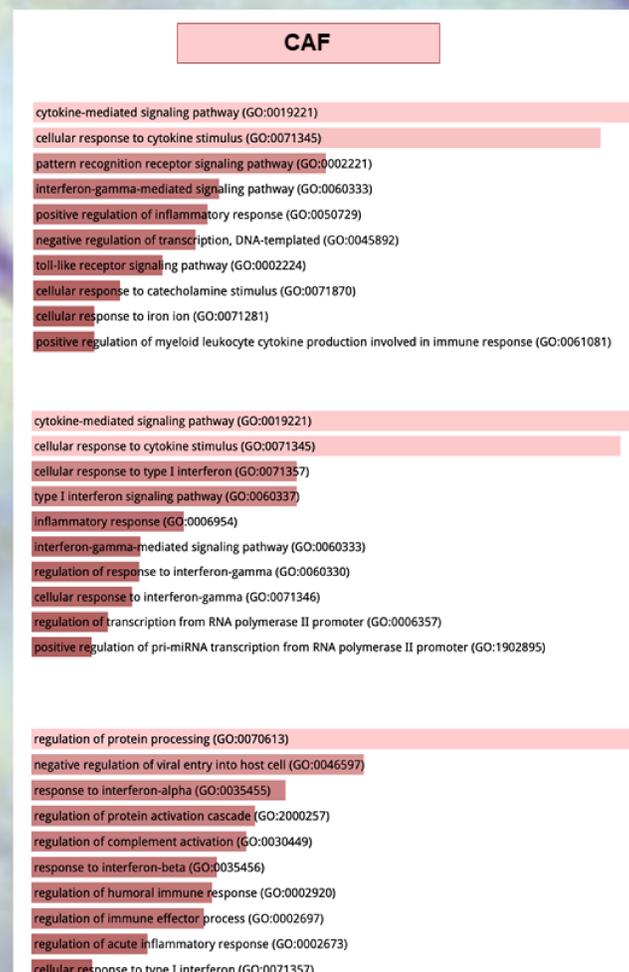
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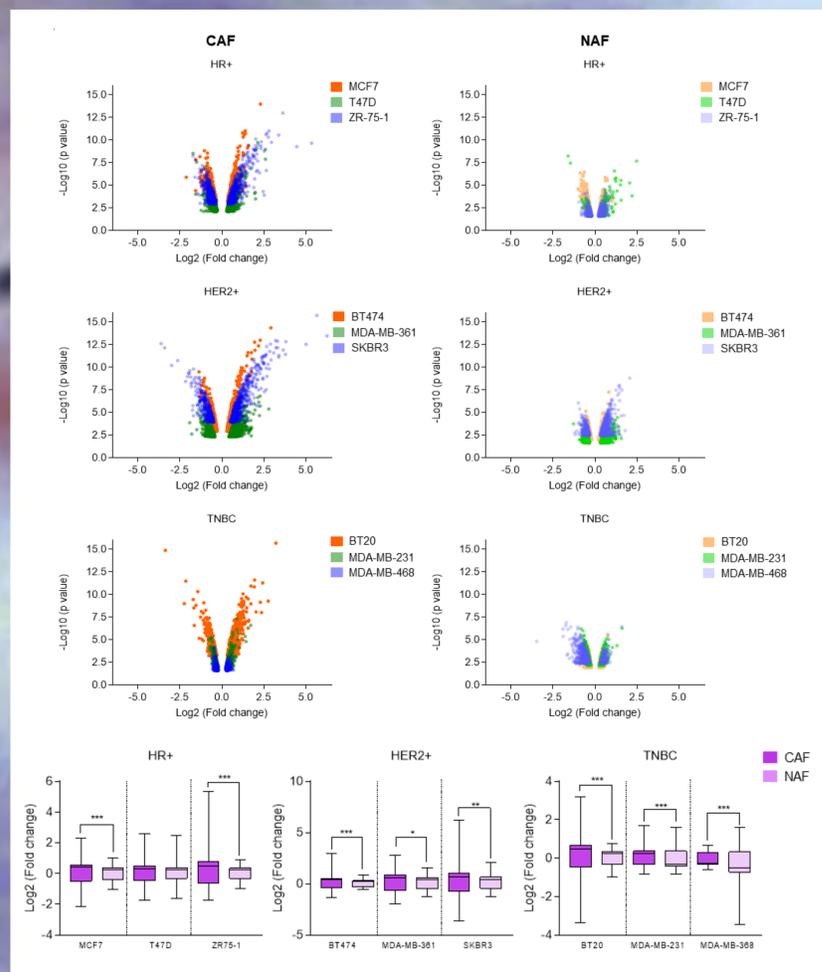
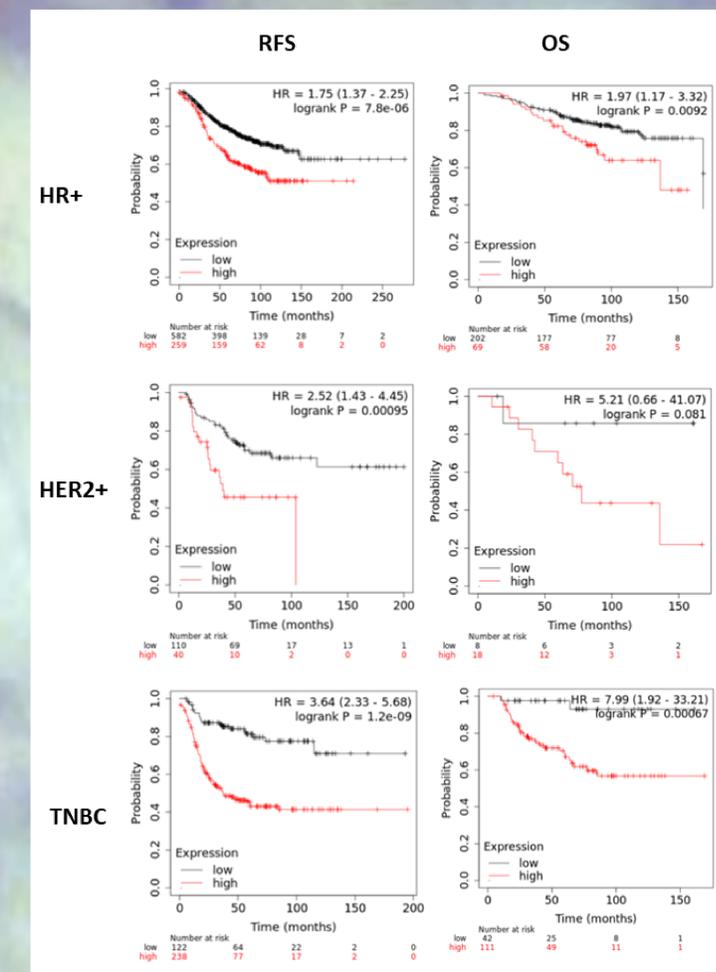

1. The difference in gene expresion (FC) induced by condicional media prepared from CAF is much larger than NAF-induced.
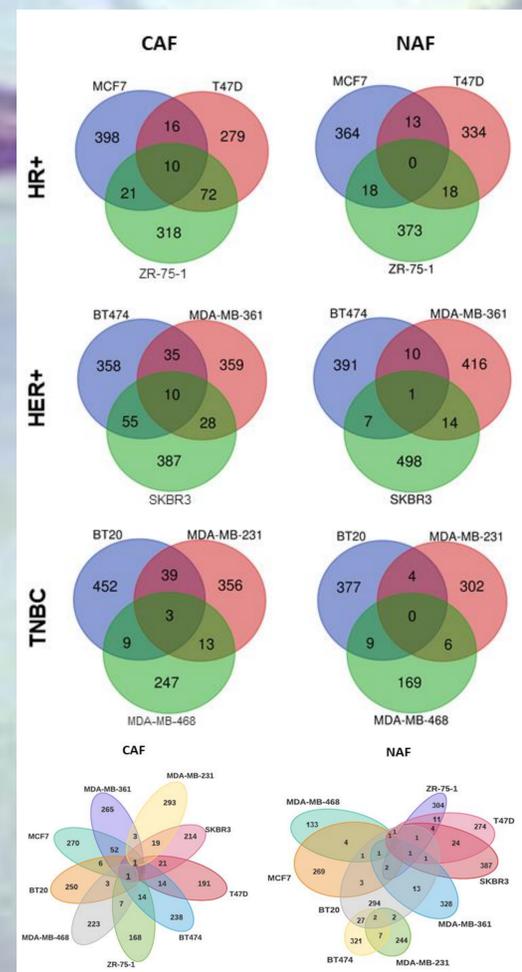
2. CAF-stimulated cell lines have many more overexpressed genes in common than NAF-stimulated cell lines

3. The overexpressed CAF genes common to at least two cell lines share functions related to the immune system.

4. Genes overexpressed for factors secreted by CAF common to at least two cell lines are associated with a worse prognosis of the disease. .