

## **Abstract**

This study is part of ongoing research on the relationship between nutrition and neoplastic diseases. Numerous *in vitro* and *in vivo* analyses showed the ability of several nutritional factors to affect carcinogenesis and tumor progression processes. n-3 polyunsaturated fatty acids (PUFAs), such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), present at high levels in fish products, showed many beneficial effects on cardiovascular diseases. Furthermore, various biochemical and cellular activities of these nutrients suggest that they could interfere with onset and progression of different kind of neoplasia, including breast cancer. However, molecular mechanisms by which these nutrients may affect breast carcinogenic processes have not been completely clarified. Therefore, the aim of this project was to further analyze the effects of these nutrients on the mechanisms underlying breast cancer development.

Following treatments with different concentrations of DHA, we examined cell viability, mortality and cell cycle progression in breast cell lines with different degree of transformation and biochemical characteristics (MCF-10A, MCF-7, SK-BR-3, ZR-75-1). Viability of MCF-7 and ZR-75-1 showed low sensitivity to DHA treatment, while an high anti-proliferative effect was caused by this nutrient in MCF-10A and SK-BR-3 cell lines. In particular, DHA induced a strong G0/G1 arrest of MCF-10A cells which was not detected in the other examined mammary cell lines. Possibly involved molecular factors were also assessed at protein and mRNA levels. The activation of ERK1/2 and STAT3 pathways and the expression of some molecules involved in cell cycle regulation (p21<sup>Waf1/Cip1</sup> and p53) resulted differentially regulated by DHA treatments in each cell line.

Data showed that DHA is able to affect cell viability, cell cycle and proliferation factors activity, in a different way in each breast cell line assayed. Although by different mechanisms, DHA produced a relevant growth inhibition of two breast cell lines with different transformation degrees and biochemical characteristics. These findings suggest a possible variable role of DHA in etiology and in development of breast cancer, which might be dependent on the molecular properties and the malignancy degree of each individual neoplasia.