Search for New Ways to Improve Immune Response against Cancer: Modulation of FASL (CD95L) by Lipid Mediators on Lymphocytes

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Searching mechanisms to improve the immune system against cancer can be an alternative for treatments used nowadays. In that way, my project studies the relation of lipid mediators (such as prostaglandins and leukotriene) with two important immune cells in cancer defense: natural killer (NK) and LTCD4 lymphocyte. LTCD4 plays an important role in tumor context by releasing cytokines that activate other cells, especially in tumor context. These lymphocytes can undergo apoptosis by AICD (activated induced cell death) after constant stimulation on TCR/CD3 complex, increasing FASL (pro-apoptotic protein) levels. Based on the capacity of prostaglandin E2 (PGE2) in reducing AICD in LTCD4, my goal was to identify other lipid mediators that could protect those cells from death. Thus, I cultured LTCD4 hybridomas (D011.10), induced AICD and treated them with some lipid mediators (PGF2, PGD2, PGJ2 and leukotriene B4). After performing flow cytometry, and statistical analysis (One Way ANOVA, and Tukey), I conclude that PGF2 and LTB4 were able to reduce, in significant ways, the death in LTCD4. This discovery, besides innovating, can be beneficial because these mediators protect important lymphocytes from death, improving immunotherapy. In addition, their potential suggests a reduction of FASL, which could be controversially related with NK cells that kill tumor trough FASL. So in this case, PGD2 and LTB4 would be reducing a mechanism of killing tumor cells, related with my first hypothesis that PGE2 down regulate NK cytotoxicity by reducing FASL (tumor immune evasion). Therefore, this result also shows the complexity of lipid mediators (different actions depending on the microenvironment) demonstrating the importance of this research in the adoption of a more effective therapy.

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