

## **TRAIL: The "smart" anticancer agent and its potential therapeutic applications**

The [Signal Mediated Gene Expression Research Laboratory of the IBRB/NHRF](#) has a strong interest on studies for the mechanisms of carcinogenesis and cell death (apoptosis). Within these scopes, we have developed activities for the exploitation of basic research knowledge towards the development of new anti-cancer approaches by using "smart" molecules, like TRAIL.

We have developed and tested new forms of TRAIL, which are highly active and potentially very effective anti-cancer agents. These activities are performed in the framework of the EUREKA program (E!2928 - RETRAIL) and the corresponding funding programs from Greek Secretariat of Research and Technology in cooperation with "Hygeia" hospital in Athens, the Czech Academy of Sciences and "Exbio Praha A.S". in Prague, Czech Republic,

Apo2L/TRAIL (Tumour Necrosis Factor Related Apoptosis Inducing Ligand / Apo2 Ligand) is a novel anticancer agent that can be potentially utilized as an alternative and/or complementary therapy. TRAIL is a cytokine with enhanced apoptotic activity in tumour cells, but normal cells seem to be resistant to its apoptotic effects.

In mice that have been injected with cancer cells derived from various tissues, TRAIL treatment results to a significant reduction of the tumour load either alone or in conjunction with conventional therapies. TRAIL, as well as specific monoclonal antibodies which can bind to and activate its receptors, are currently used with encouraging preliminary results in clinical trials phase I.

In order to investigate the mechanisms of TRAIL induced apoptosis and the selectivity that TRAIL exhibits towards the malignant tumour cells, we are using an *in vitro* model of human colon cell lines, representing the various stages of carcinogenesis from early adenoma to metastatic adenocarcinoma. K. Drosopoulos, a PhD student in the Signal Mediated Gene Expression Lab, has observed relative resistance of colon adenoma cells to TRAIL, as compared to carcinoma cells. On the other hand sensitivity to TRAIL can be associated with the presence of activated oncogenes.

Analysis of the particular mechanism of TRAIL signalling and the factors implicated in its regulation may not only contribute towards developing a more tolerable alternative therapy, but possibly also in the development of future drugs that will be, at least partially, individualized.

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