

Local GMCSF expression

Gene expression analysis of tumors demonstrates an induction of Th1 type immune response following intratumoral administration of ONCOS-102 in refractory solid tumor patients

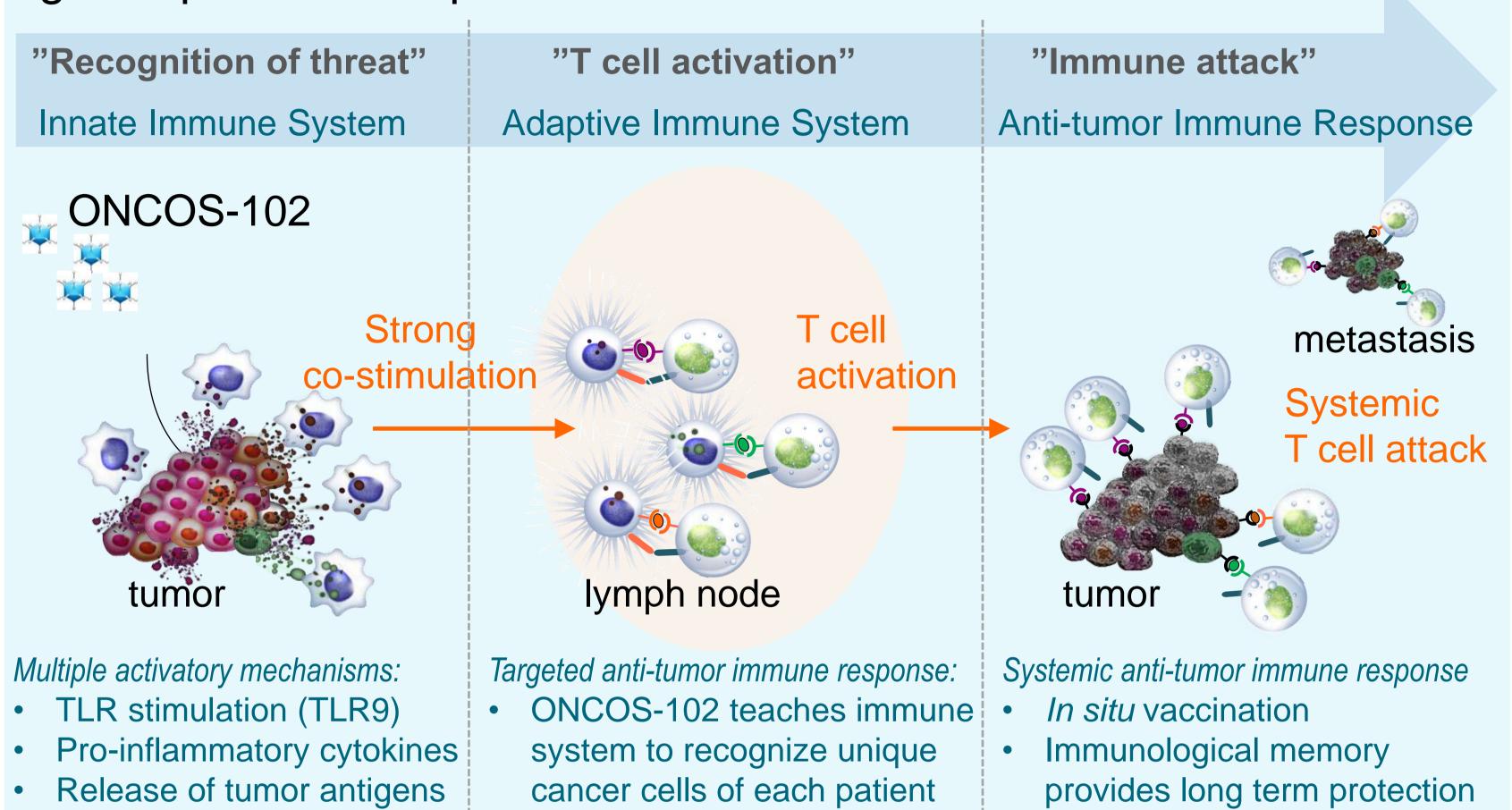
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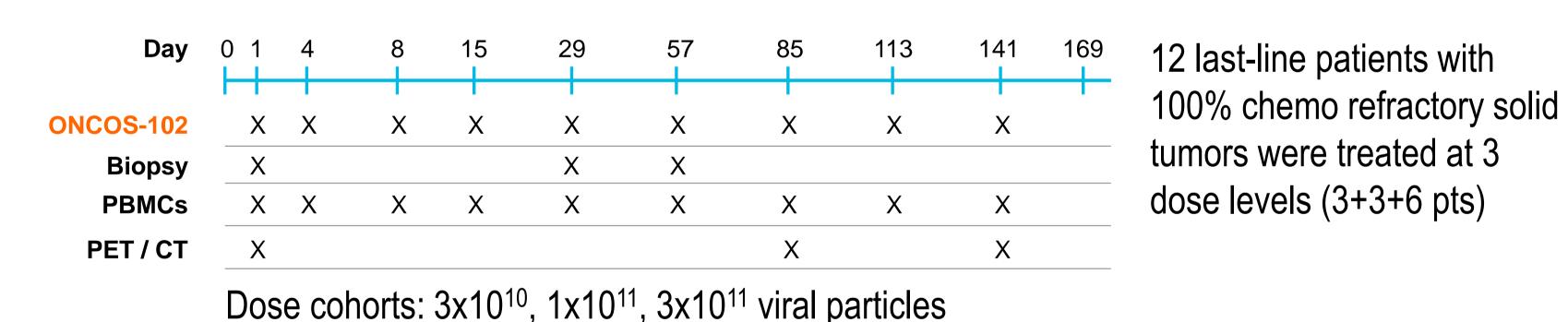
INTRODUCTION

ONCOS-102 (Ad5/3-D24-GMCSF) is a tumor-targeted oncolytic adenovirus coding for human GM-CSF

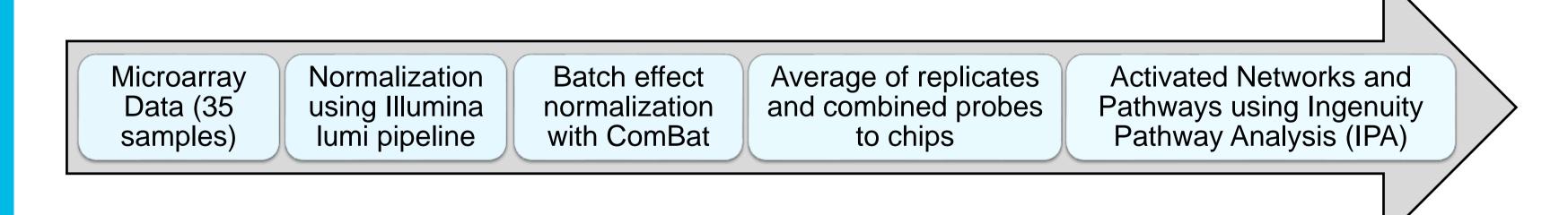
Intratumoral ONCOS-102 induces a systemic CD8+ T cell response against patient's unique cancer cells:



Phase I study - design



Gene expression analysis: Work flow



Induction of systemic anti-tumor CD8+ T cell response

Patient FI1-14 with malignant pleural mesothelioma (MPM)

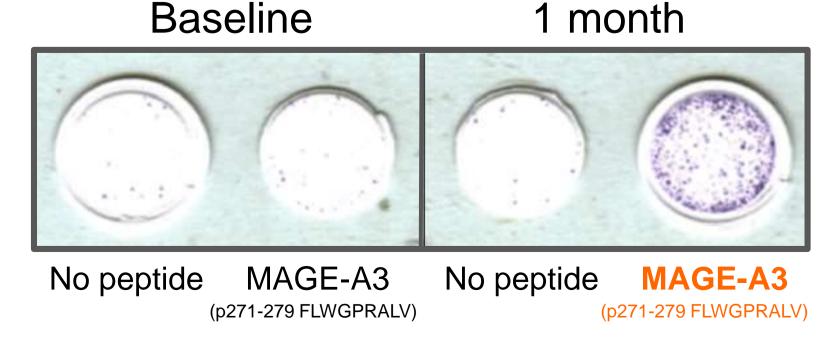
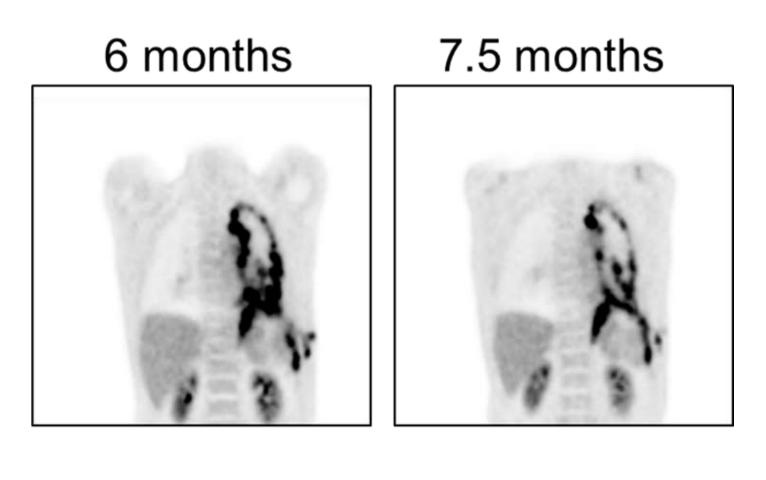


Figure 1. Purified CD8+ cells were pre-sensitized with peptide-pulsed, irradiated autologous PBMCs depleted of CD4 and CD8 T cells and tested on day 10 by IFN-gamma ELISPOT assay for recognition of autologous antigen-presenting cells.



47% reduction in total tumor burden (PET) between 6 and 7.5 months

Expression of Th1 response genes in tumor biopsies

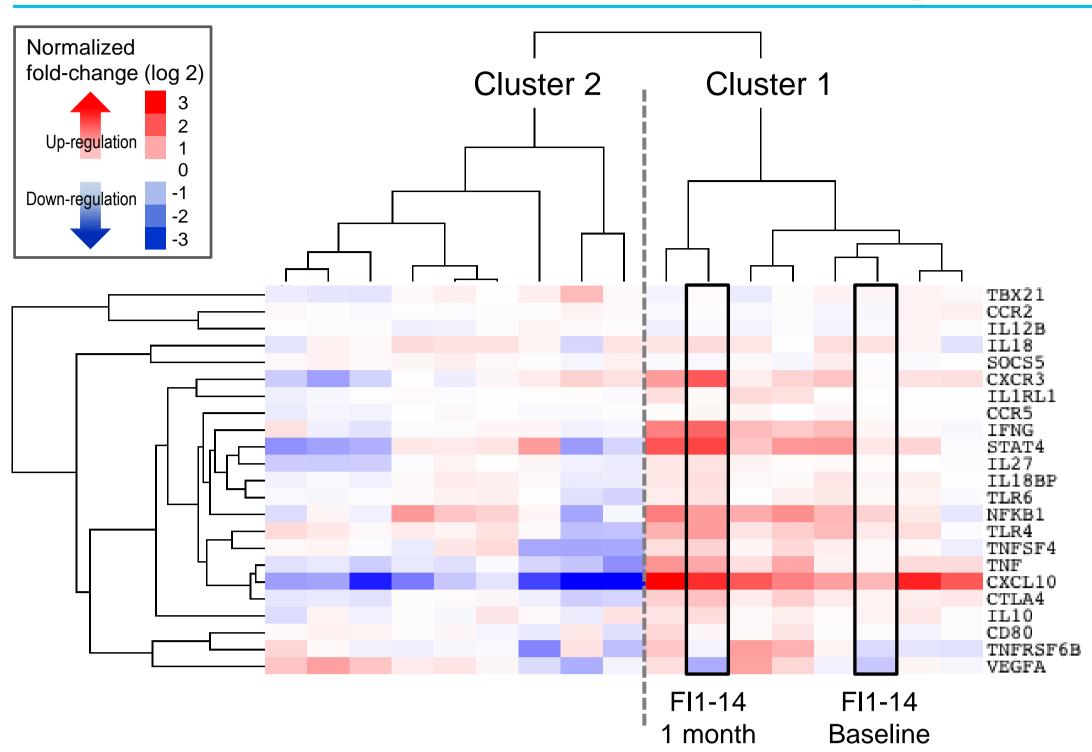


Figure 2. The expression of Th1 markers and cytokines in tumor biopsies divides patients into two separate clusters. Cluster 1 shows higher expression of Th1 related genes compared to Cluster 2. Patient FI1-14 shows upregulation of CXCR3, IFN-γ, STAT4, and CXCL10 concomitantly with the induction of tumor-specific CD8+ T cells (see Figure 1). Data is presented as normalized fold-change from healthy control tissue.

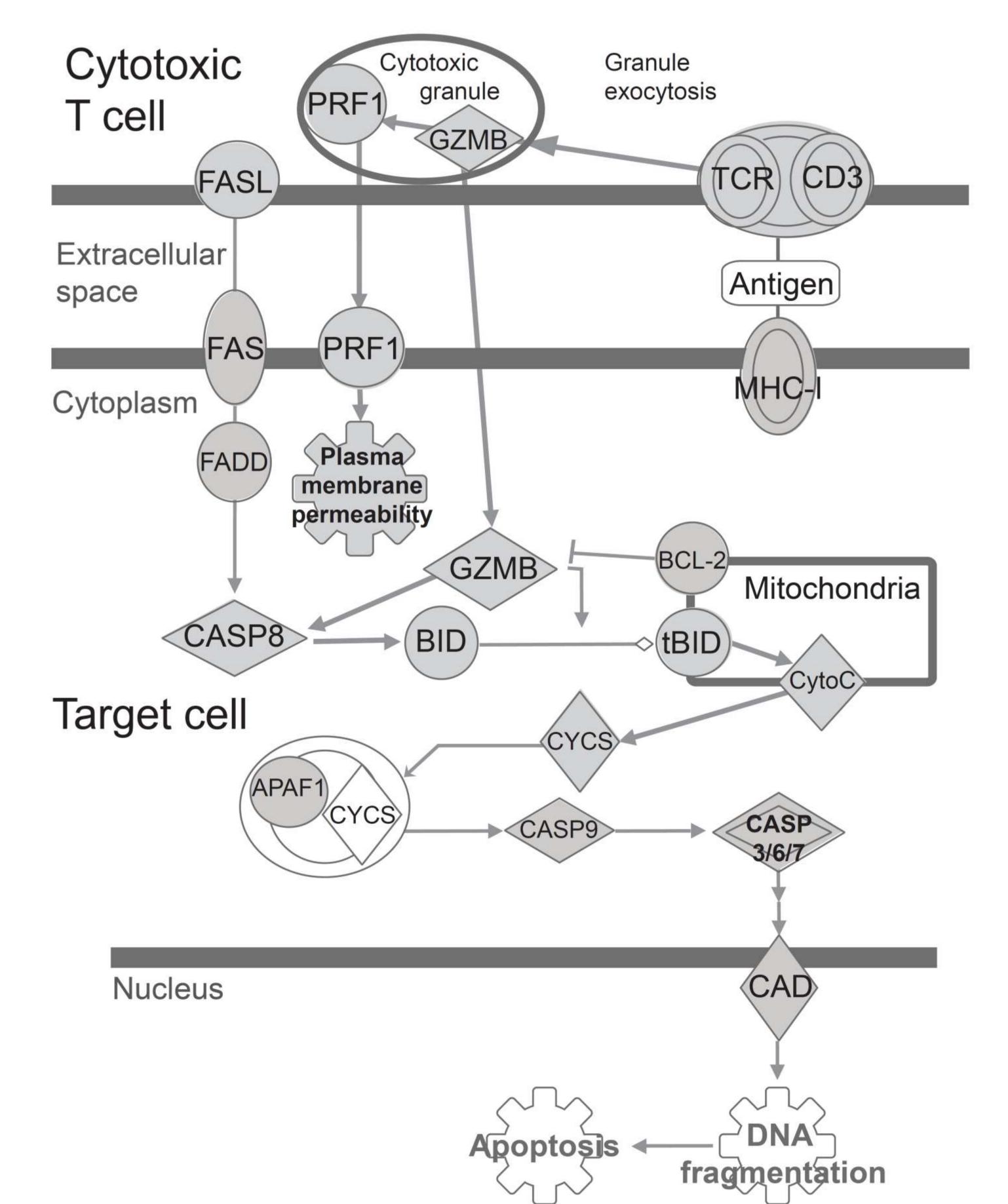
CONCLUSIONS

- ONCOS-102 monotherapy induced a systemic tumor-specific cytotoxic CD8+ T cell response
- Tumor-specific CD8+ T cell response was related to clinically significant tumor size reduction in last-line cancer patient
- ONCOS-102 induced Th1 polarization and T cell mediated apoptosis in chemotherapy refractory tumor tissue

ONCOS-102 triggered cytotoxic T cell mediated apoptosis in tumor cells (Patient FI1-14)

more extreme less more confidence less Predicted Relationships — Leads to activation — Leads to inhibition — Leads to inhibition — Effect not predicted

BASELINE



AFTER ONCOS-102

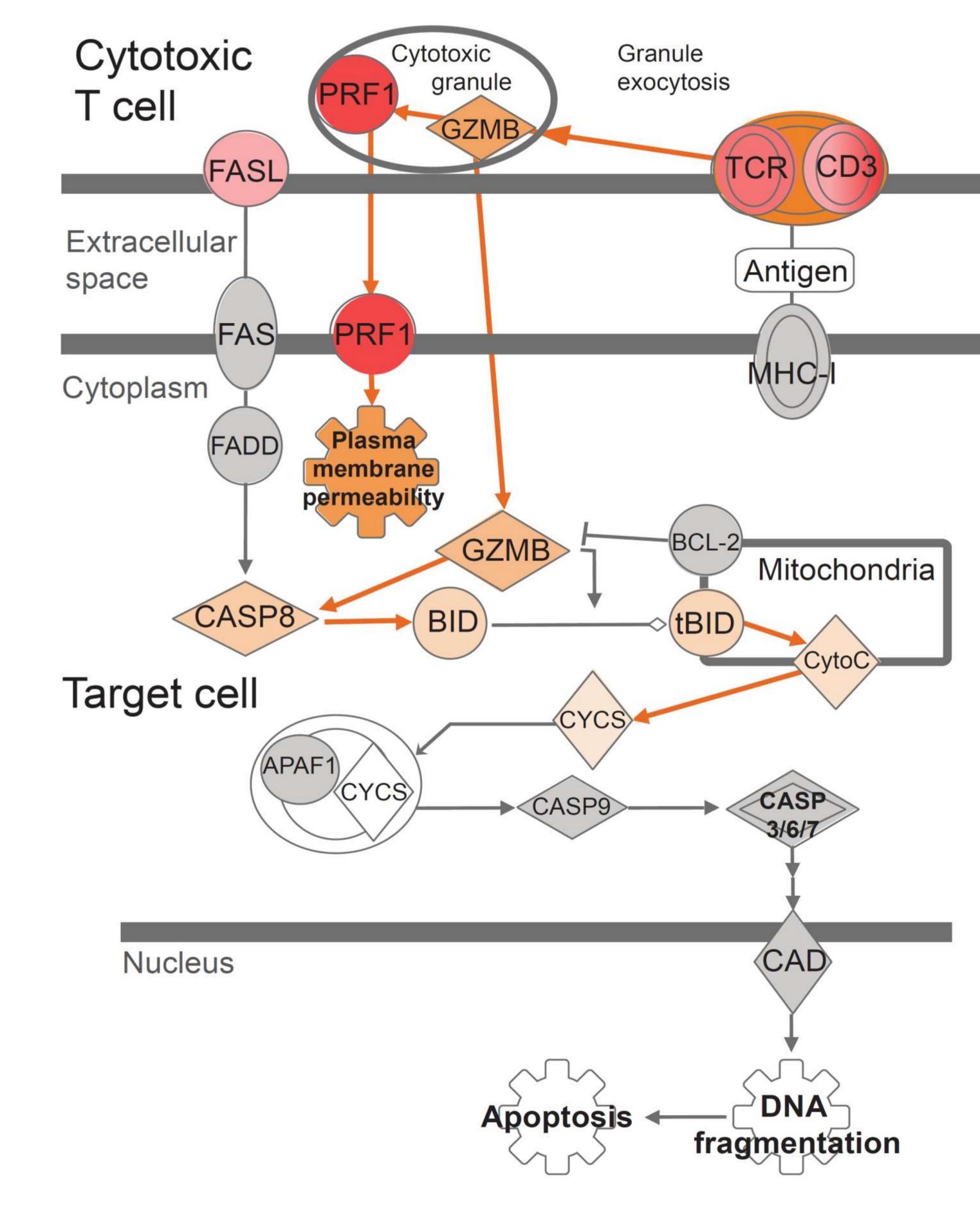


Figure 3. ONCOS-102 induced cytotoxic T cell mediated apoptosis of tumor cells in the last-line chemorefractory MPM patient as demonstrated by IPA. Other activated signaling pathways included: Leukocyte extravasation, Leukocyte adhesion and diapedesis, Crosstalk between Dendritic Cells and Natural killer cells, and Antigen presentation.