

## Spera - recruitment of immune effector cells against astrocytoma by MHC-chlorotoxin chimeric proteins

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**G**lioblastoma Multiforme (GBM) is the most common malignant primary brain neoplasm having a mean survival time of 12 months. This figure remains constant despite progress in all areas of medical research and treatment. The lack of an efficient immune response to the tumor and its microinvasive nature has been explained by its immunosuppressive capabilities and the immunosuppressed local environment. We designed a molecule that specifically binds Matrix metalloproteinase 2 (MMP-2) expressed most abundantly on GBM cells, and through its effector domain mobilize and recruit elements of the immune system to mount an effective antitumor reaction. The targeting pole of the molecule is the small 36-amino acid chlorotoxin, derived from the venom of the Israeli Yellow scorpion. The effector end of the chimera is a single chain HLA-A2 (Human leukocyte antigen subtype A2) covalently bound to a protein derived from the cytomegalovirus, to which most of the human population has developed a specific immune response. This exemplifies a new family of molecules which contain a non-antibody compact and highly specific targeting domain, combined with the ability to recruit different lymphocyte populations using HLA-molecules bearing a single, preselected, highly antigenic peptide derived from immunogenic tumor, viral, or bacterial T cell epitopes. Moreover, the recruitment of potent memory CTLs to the tumor's milieu may be resistant to the previously described local immunosuppressive environment created in part by TH2 secretion profile, and may enable the shift to TH1 cytokine profile resulting in specific massive tumor destruction. Results are very encouraging.

### Biography

Or Cohen-Inbar has completed his M.D. at the Technion Israel institute of technology, currently completing his Ph.D studies at the field of molecular immunology and cancer immunotherapy. He is a 5<sup>th</sup> year resident of neurosurgery at the department of neurosurgery at Rambam health care campus. He is a member of both the Congress of neurological surgeons and the EANS, and has published over 6 peer review papers in both clinical and basic science fields.

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