ABSTRACT

Glioblastoma multiforme (GBM) is an incurable brain tumor with 75% of patients dead two years after diagnosis. A limitation of past immunotherapeutic vaccines against GBM has been the difficulty in inducing a potent tumor-specific response, due in part to the poor immunogenicity of tumor-associated antigens, the means of formulation/delivery of the vaccine, or a combination of both.

Human cytomegalovirus (CMV) is a ubiquitous, generally asymptomatic virus that is present in over 90% of GBM tumors. Memory CD8+ and CD8+ T cells are most frequently directed against the gB and pp65 antigens, respectively. Thus, CMV gB and pp65 represent attractive, highly immunogenic “foreign” antigen components of a vaccine against GBM. A recent phase I clinical trial based on vaccination against CMV pp65 demonstrated significant improvement in overall survival, and identified chemokine CCL3 as a correlate of efficacy.

Bivalent gB/pp65 eVLPs Stimulate Both CD4+ and CD8+ Human T Cell Responses Ex Vivo

GBM Patient PBMCs Respond to Bivalent CMV eVLP & GM-CSF Stimulation

Design of GBM CMV eVLP Vaccine Candidate

Rationale for vaccine components/mechanisms of action

<table>
<thead>
<tr>
<th>Vaccine Component</th>
<th>Immune Response</th>
<th>Scientific Support</th>
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<tr>
<td>CMV gB</td>
<td>Antibody response against gB expressed on surface of tumor cells</td>
<td>Present gB vaccination of PD-1/PD-L1 signaling in tumor cells (Cobbs C et al., 2014)</td>
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<td>CMV pp65</td>
<td>Polyvalent CD4+ T helper cell &amp; CD8+ CTL responses</td>
<td>CMV pp65 vaccination in concert with dendritic cell activation confers overall survival of GBM patients (Mitchel SA et al., 2011)</td>
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<tr>
<td>eVLP Formulation with GM-CSF</td>
<td>Augment tumor-specific IFN-γ and CCL3 responses</td>
<td>Clinical data demonstrate IFN-γ and CCL3 as key biomarkers of efficacious tumor immunity (Gaber Jet al., 2006; Mitchell SA et al., 2013)</td>
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Cryo-EM & Immunogold Labeling Demonstrates Location of CMV Antigens in Bivalent gB/pp65 eVLPs

Characterization of Purified eVLPs

SDS PAGE & Western Blot analysis confirm good quality of bivalent gB/pp65 eVLP materials

Poster #1003 CMV gB/pp65 eVLPs Formulated with GM-CSF as a Therapeutic Vaccine Against GBM

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