Research Grant Proposal
University of Pittsburgh Cancer Institute
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Title: Actively Personalized Vaccines for Newly Diagnosed Glioblastoma Patients

Personalized medicine can be achieved by stratification of patients according to biomarkers predicting therapeutic benefit. Ideally, this would mean the grouping of patients to different kinds of therapies, with *all* of the patients benefiting from the respective treatment. In reality, however, treatment is often restricted to the biomarker-positive patient population; patients, who are not eligible for the available treatments are neglected (e.g., EGFRviii+ and HLA-A2+ etc.). Additionally, few disease-specific features are addressed by current biomarker-driven therapies. The Glioma Actively Personalized Vaccine Consortium (GAPVAC) will be the first multi-center trial where vaccines will be specifically designed for the individual needs of patients and therefore will take personalization to the next level. In the GAPVAC, University of Pittsburgh Cancer Institute (UPCI) will be the only participating center in the USA, while all the other participating centers are in Europe. Recently, the potential of immunotherapy has been proven in various tumor entities, improving survival of patients with minimal adverse events. In this phase I GAPVAC trial, a total of 30 patients with newly diagnosed glioblastoma multiforme (GBM) will be enrolled. Each patient's GBM tissue will be analysed by cutting-edge gene sequencing systems to identify genes that are uniquely expressed in the tumor tissue. Those genes are ones that have mutations (alterations in the DNA sequence) and ones that are expressed much higher levels compared with normal tissues of the same patient.

Peptides (i.e. short protein fragments) designed from these genes are likely to induce effective immune responses when used as vaccines. We estimate that those peptides will be available for vaccines within 6 months after the patient undergoes the initial tumor resection, during which time, the patient will undergo standard of care chemo-radiotherapy. The primary endpoint is to evaluate safety and feasibility of the approach. This will be a proof of principle for a potentially paradigm-changing novel immunotherapy for patients with GBM.