

Enhancement of Cancer Immunotherapy Using Immune Modulating Peptides

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Abstract:

Immune Peptide Therapeutics (IPT) LLC, an Indiana-based small business and its research partner Indiana University previously identified a novel property of lunasin as a distinct class of immune modulating agent that enhances anti-tumor immunity, which may promote disease-free survival by limiting tumor progression, and thus prolong lives of cancer patients. Lunasin, a synthetic 43-amino acid peptide, was originally isolated from soybeans. Our studies have demonstrated that lunasin exerts robust synergistic effects with cytokines on augmenting IFN γ and granzyme B expression by Natural Killer (NK) cells, which is associated with increased tumoricidal activity of NK cells. In addition, this combination regimen is capable of rescuing IFN γ production *ex vivo* by NK cells from chemotherapy-treated Non-Hodgkin's Lymphoma (NHL) patients who are immunocompromised with acquired immune deficiency. The long-term goal is to develop an efficacious immunotherapy which will impact the treatment and improve the clinical outcomes for NHL patients. The dose-response study indicates the optimum concentration of lunasin is at the range of μM , which would undermine its use in clinical studies. To enhance the medicinal value lunasin must be optimized for *in vitro* and *in vivo* efficacy. The objective is to develop a second generation of lunasin, which will increase its potency to improve the performance. In this study we have implemented several strategies to design and modify the prototype. The newly developed peptide called IPT.103 has 15 amino acids that are in the D-isoform configuration. Activity of IPT.103 has been tested *in vitro* with EC₅₀ of 0.78 μM as compared to 4.54 μM for lunasin. IPT.103 also has *in vivo* activity on enhancing the serum levels of IFN γ production using a mouse model. Taken together, we have developed a peptide derivative (IPT.103) that deviates from its parental type lunasin to increase intellectual merit for commercialization as well as support clinical application.