Modulating NK-mediated Immunity by Lunakine

Hua-Chen Chang[1, 4], Chun-Yu Tung[1], David Lewis[1], Ling Han[1], Mythily Srinivasan[2], Michael J. Robertson[3], and Wu-Kuang "WK" Yeh[4]

[1]Department of Biology, Indiana University-Purdue University Indianapolis School of Science, Indianapolis, IN; [2]Department of Oral Pathology, Medicine & Radiology, Indiana University School of Dentistry, Indianapolis, IN; [3]the Bone Marrow and Stem Cell Transplantation Program, Lymphoma Program, and the Division of Hematology/Oncology, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN; and [4]Immune Peptide Therapeutics (IPT), LLC, Indianapolis, IN.

Despite the plethora of immune modulating agents available in cancer treatment, their effectiveness relies on a functional immune system. However, the adverse side effects by chemotherapy impede the therapeutic benefits from immunotherapy. It remains a major challenge to prevent relapse for cancer patients who have already undergone rigorous chemotherapy. Lunasin, a 43-amino acid peptide, was originally isolated from soybeans. Our team has recently discovered a novel function of lunasin as an immune modulating agent that exerts robust synergistic effects imposed by several therapeutic cytokines. Such synergism strongly augments IFNγ and granzyme B expression by Natural Killer (NK) cells, which is associated with increased tumoricidal activity. The combination regimen with lunasin and cytokine is capable of restoring NK activation from lymphoma patients with chemotherapy-induced immune dysfunction. Our results support the potential application of lunasin to improve the therapeutic effects of existing cytokine treatment that has been used to eliminate residual tumors cells from lymphoma patients after chemotherapy. We designate lunakine as new formulation by combing lunasin and selected cytokine (filed for US Patent Cooperation Treat). In working with Indiana University and Technology Corporation (IURTC), we have started a startup company, Immune Peptide Therapeutics (IPT), LLC. Our mission is to develop a more efficacious immunotherapy that prevents relapse and confers progression-free survival for cancer patients. With the support from FORCES, our team has successfully developed a second generation of lunasin called IPT.103 that deviates from its parental type. Activity of IPT.103 has been tested in vitro with EC_{50} of 0.78 µM as compared to 4.54 µM for lunasin, indicating an improved potency to induce IFNγ production by NK cells. The newly developed peptide IPT.103 is expected to strengthen the intellectual property (IP) position for commercialization. We are currently working on tumor models for preclinical assessment of IPT's regimens in immunotherapy for lymphoma.