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Innovative immunotherapies to treat cancers

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We report the development of anti-human mesothelin mRNA chimeric antigen receptor transfected peripheral blood lymphocytes (CARMA-hMeso), demonstrating the manufacture and cryopreservation of multiple cell aliquots for repeat administration from a single human leukapheresis. We show that CARMA-hMeso cells recognize and lyse tumor cells in a mesothelin-specific manner. Expression of CAR was detectable over approximately 7 days *in vitro* with a progressive decline of CAR expression that appears to correlate with *in vitro* cell expansion. In a murine ovarian cancer model, a single intra-peritoneal (IP) injection of CARMA-hMeso resulted in the dose-dependent inhibition of tumor growth and improved the survival of mice. Furthermore, repeat weekly IP administrations of the optimal CARMA-hMeso dose further prolonged disease control and survival. No significant off-target toxicities were observed. These data support further investigation of CARMA-hMeso as a potential treatment for ovarian cancer and other solid mesothelin-expressing cancers¹. In addition, we have successfully developed a strategy to specifically target a therapeutic chimeric protein to tumor loci, which elicits potent tumor-targeted killing through antigen-specific CD8⁺ immune responses. This strategy may provide a platform for the delivery various anti-cancer molecules to the tumor loci as well as for coating tumor cells to circumvent immune tolerance in order to generate therapeutic antitumor effects².

Biography

Chien-Fu Hung is an associate professor of pathology and oncology and a professor of gynecology and obstetrics at the Johns Hopkins University School of Medicine. He is a member of the Johns Hopkins Kimmel Cancer Center. His research focuses on the prevention and treatment of cervical and ovarian cancers.

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