Alpha-galactosyl ceramide analogs and their use as immunotherapies

本院覽號

28A-951222

公告日期

智財權狀態

台灣(發明)已申請、美國已申請、美國臨時案已申請、PCT已申請、歐盟已申請、加拿大已申請、日本已申請

摘要

Alpha-Galactosylceramide is a glycolipid that was reported to have the capability to boost the human immune system in fighting cancers back in 1995. The research went pass various pre-clinical studies and raised hope. However, it failed to go beyond phase I trial. It turned out that while boosting the immunity fighting cancers, it also induces substances that suppress the immune functions, resulting in weak overall anti-cancer effects. By using computer modeling technique, we have successfully designed and synthesized a series of compounds to have better binding to CD1 molecule than α-GalCer. Qualifying test against these compounds with human Natural Killer T cells showed glycolipids with an aromatic ring like attached to the tail end displayed higher IFN-g/IL-4 ratio than α-GalCer. In vivo experiment on mice with aggressive lung cancer tumors and breast cancer tumors was performed. In breast cancer-bearing mice, treatment with the new glycolipids (C11, C13, C14, C16) inhibited the tumor growth rate by 75% of untreated group, as compared to 50% inhibition in mice treated with α-GalCer (C1). Meanwhile, the lung cancer-bearing mice treated with the new glycolipid had significantly prolonged survival time compared to those treated with α-GalCer. The treated mice appeared much healthier than the untreated group. The invention indicates that novel α-GalCer analogs can be designed to favor Th1 biased immunity with greater anticancer efficacy than α-GalCer.

技術優勢

Glycolipids are expected to have minimal or no toxicities. Glycolipids have more potent adjuvant activities for vaccines than exiting adjuvants. There is a paucity of effective anti-viral agents. Glycolipids may ameliorate the severity of viral illness.

應用範圍

Treatment of cancer Use as adjuvant for vaccine Treatment of autoimmune disorders Treatment of viral infection

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