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Invariant natural killer T cell activation by α-GalCer analogues and novel anti-epidermal growth factor receptor -antibody glycol-conjugates for onco-immunotherapy

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Abstract

Invariant NKT (iNKT) lymphocytes recognize lipids presented by CD1d and respond by a rapid release of cytokines that regulate innate and adaptive immune responses. They also show potent cytotoxic activity against cancer. α-GalactosylCeramide (α-GalCer) is the canonical iNKT agonist. With the aim to mediate a local immune response close to EGFR-tumour environment α-GalCer derivatives have been associated to the anti-EGFR monoclonal antibody. Biological activities of α-GalCer analogues and MoAb-conjugates were assessed to highlight dual cytotoxic performances. In comparison with the canonical α-GalCer (KRN7000), novel α-GalCer analogues proved to be more potent by several orders of magnitude using APC that express CD1d for interferon secretion were discovered. Intriguingly, unlike α-GalCer, they also proved to be active when loaded on several human cancer cell lines known as not expressing CD1d. This latter result reveals a paramount effect of modified α-GalCer on CD1d/TCR complex stabilization that occurs on cancer cell bed without recruitment of usual APCs. Thus, association of α-GalCer analogues to anti-EGFR monoclonal antibody is also able to restore iNKT stimulation and to increase antibody cytotoxicity.

Biography

Didier Dubreuil completed his PhD at ICSN (Institut de Chimie des Substances Naturelles Gif/Yvette), France. He is currently a full professor at the University of Nantes in CEISAM laboratory (CNRS 6230) working at the interface of chemistry and biology. He has over 80 publications and 14 international patents.

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