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Lipid Nanoparticle Encapsulated OX40L mRNA-2416

National Cancer Institute

Source

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A proprietary formulation consisting of a lipid nanoparticle encapsulating a synthetic messenger RNA (mRNA) encoding the human co-stimulatory protein tumor necrosis factor ligand superfamily member 4 (TNFSF4; OX40 Ligand; OX40L), with potential immunomodulatory and antitumor activities. Although the mechanism of action has not been completely characterized, following intratumoral injection of lipid nanoparticle encapsulated OX40L mRNA-2416, the lipid nanoparticle moiety presumably binds to the plasma membrane of nearby cells and releases the OX40L mRNA into the cell. The OX40L mRNA is then translated by the cellular protein translation machinery to produce OX40L protein, which is then expressed on the plasma membrane of the cells that internalized the OX40L mRNA. OX40L binds to and activates signaling pathways downstream of its cognate receptor tumor necrosis factor receptor superfamily member 4 (TNFRSF4; OX40), which is expressed on activated T-cells. OX40L/OX40 binding promotes increased cytokine production, which can induce proliferation of memory and effector T-lymphocytes. Altogether, this may enhance an immune response that promotes the killing of nearby tumor cells. OX40L, a cell surface glycoprotein and member of the tumor necrosis factor (TNF) ligand family, provides a co-stimulatory signal for the proliferation and survival of activated T cells.