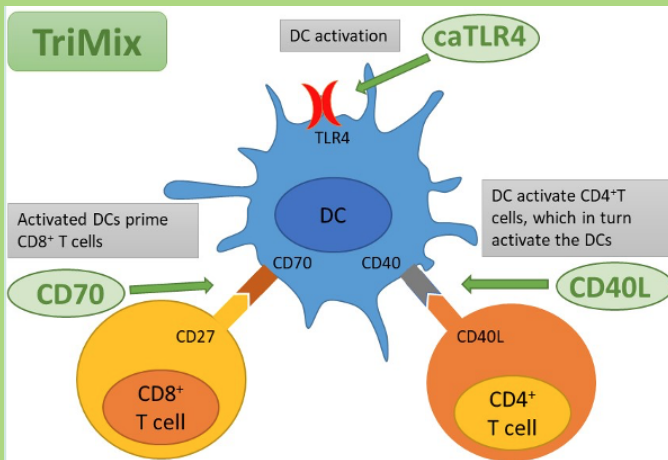


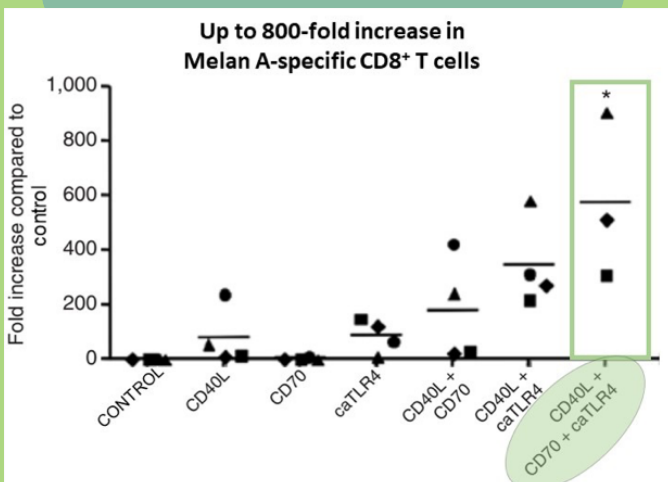
TriMix mRNA Technology

TriMix is composed of three mRNAs encoding; **caTLR4**, **CD40L**, **CD70**. They act on three different immuno-stimulatory pathways. T-cells fight cancer cells and infectious agents. The three TriMix mRNA molecules **induce the proliferation of T-cells** into either mature helper T-cells and cytotoxic T-cells.

TriMix



By combining TriMix with tumor-specific antigens or neoantigens, a patient's dendritic cells can be stimulated to produce a more potent and larger population of antigen specific cytotoxic and helper T-cells compared to tumor antigens alone.



Vaccine adjuvant

TriMix has been shown to amplify the T-cell response against vaccine antigens which can lead to tumor regressions in different in vivo models when delivered by different routes of administration: ex vivo, intranodal, intravenous and intramuscular.

Activation of tumour-infiltrating dendritic cells:

Naked TriMix mRNA injected intratumorally has been shown to exert anti-tumour efficacy and to prolong the survival of tumour-bearing mice.

Ex vivo dendritic cell-based vaccine

TriMix mRNA (in combination with antigen mRNAs) has been administered successfully to 109 metastatic melanoma patients in 4 different clinical studies. A favorable risk benefit profile could be demonstrated in both melanoma patients with no evidence of disease and in advanced melanoma patients when combined with ipilimumab.

TriMix to boost intranodal administered naked antigen mRNA - naked mRNA (TriMix and antigens)

has been administered successfully intranodally in the lymph nodes of 20 melanoma patients undergoing resection of stage IIc/III/IV melanoma. The product was reported to be well tolerated and immunogenic.

TriMix can boost intravenous administered antigen mRNA and TriMix formulated in eTheRNA's proprietary LNP for intravenous administration in in vivo models. This product is expected to enter a first-in-human study in Q4 of 2021.

TriMix as an activator of tumour-infiltrating dendritic cells

- an ongoing clinical study is examining the effect of naked TriMix mRNA injected intratumorally in breast cancer patients.