ST-001: nanoFenretinide Therapeutic Profile

Multiple Mechanisms of Action (MoA) Including Modulation of Tumor Immunity

Clinical Hypothesis in CTCL: 2-prong MoA that Restores Tumor Immunity

- treats deficient adaptive immunity
  → reverse cytokine suppression of CD8+ CTL TILs (likely RAR & RXR)
- treats lack of innate immunity by NK cells
  → upregulates NKR ligands (likely RXR)
- plus direct action on malignant cells (RAR & DES-1/ceramide apoptosis)
- minimal side effects may be due to immune homeostasis in healthy tissues
- proven clinical activity in the treatment and prevention settings

Implications

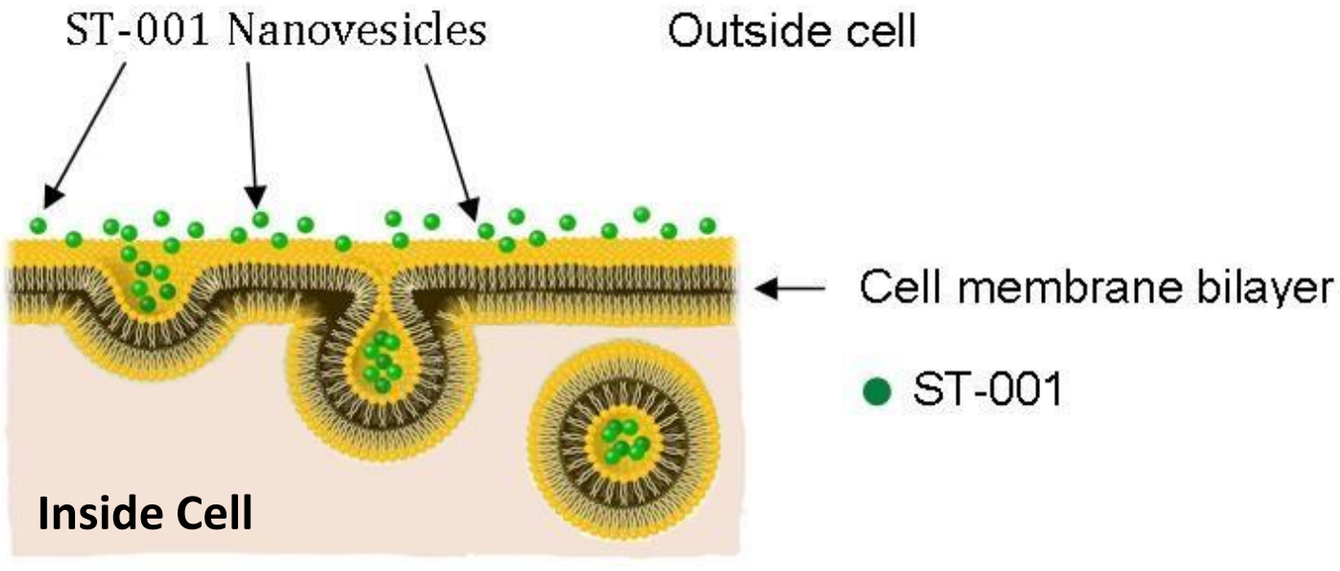
- personalized immuno-Rx → w/o need to identify individual patient's antigens (unlike immuno-targeted therapeutics)
- multiple MoA's offer advantages over first-generation retinoids (RA's)

ST-001 Delivery and Direct Mechanism of Action

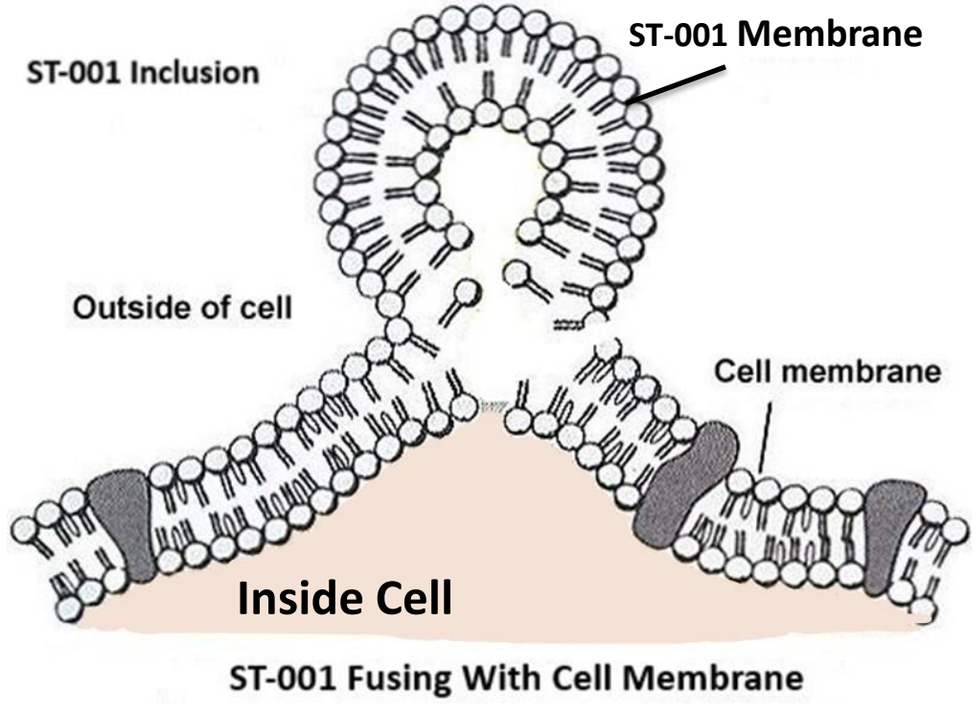
Once inside the cancer cell Fenretinide affects multiple biochemical pathways ultimately causing cell death via apoptosis

*These pathways include retinoid receptors, oxygen radicals and inhibition of ceramide (unlike retinoic acid)**

Direct Targets:
RAR/RARE, DES-1,
Mitrochondrial OXPHOS



Membrane Fusion



Systemic ST-001 nanoparticles may enter cells like Exosomes and Ectosomes

*Kalemkerian, G.P., et al., Growth inhibition and induction of apoptosis by fenretinide in small-cell lung cancer cell lines. J Natl Cancer Inst, 1995. 87(22): p. 1674-80.