

3.2. Mechanism of Action of the NANT Cancer Vaccine

Mechanistically, the spatiotemporal deliver of combination immunotherapeutic products (The NANT Cancer Vaccine) will immunomodulate the tumor microenvironment, induce immunogenic cell death (ICD) and result in long term sustainable remission of multiple tumor types with lower toxicity and higher efficacy than current standards of care by:

- Penetrating** the tumor microenvironment to overcoming the tumor immunosuppressed state, informed by tissue and liquid biopsies, with low-dose metronomic chemotherapeutic agents capable of inducing immunogenic cell death (ICD) with inhibitors of immunosuppressive cytokines.
- Upregulating** induction of damaged associated molecular pattern (DAMP) signals, upregulate tumor associated MHC restricted antigens and stress receptors (NKG2D) through low-dose radiation, IMiDs and HDAC agents
- Activating** dendritic cells, natural killer cells, cytotoxic T-cells, memory T & NK cells through cytokine fusion protein, checkpoint inhibitor administration and NK cell therapy infusion.
- Maintaining** the equilibrium state through vaccine, NK and fusion protein boosters

We hypothesize that this **Combination Product of Cell Therapy, Biological Proteins, and Genetically Engineered Vaccines (NANT Cancer Vaccine)** will induce immunogenic cell death and result in durable responses across multiple tumor types with lower toxicity than the traditional treatment regimens administered as the current standards of care.

Figure 9: NANT Cancer Vaccine Mechanism of Action to Induce ICD

