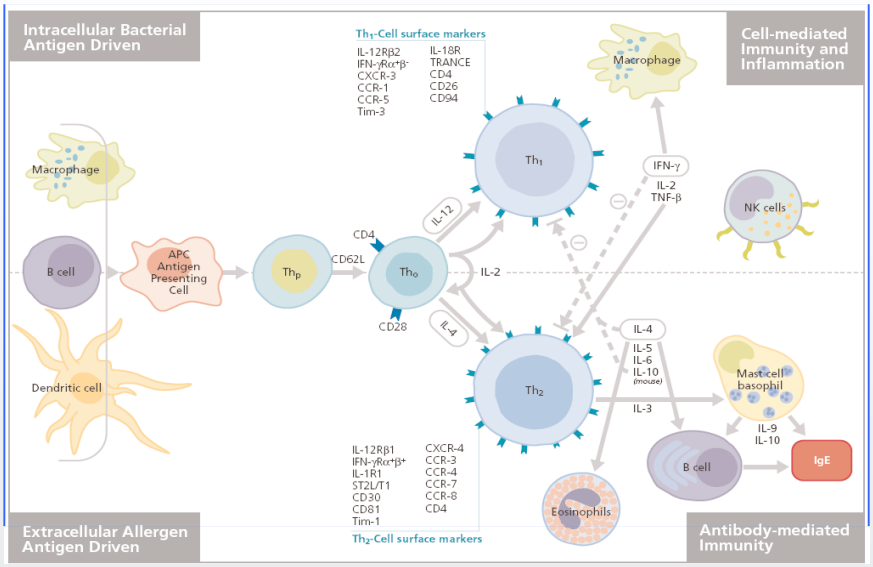
VACCINE ADJUVANT

BACKGROUND AND MECHANISM

Two central factors involved in the mechanisms of action for adjuvants in enhancing the immunogenicity of an antigen include T-cell proliferation and activation, as well as antigen-presenting cell (APC) mobilization and activation. Importantly, both T-cells and APCs (dendritic cells and Langerhans' cells) have been found to express the neurokinin-1 receptor (NK1-R).

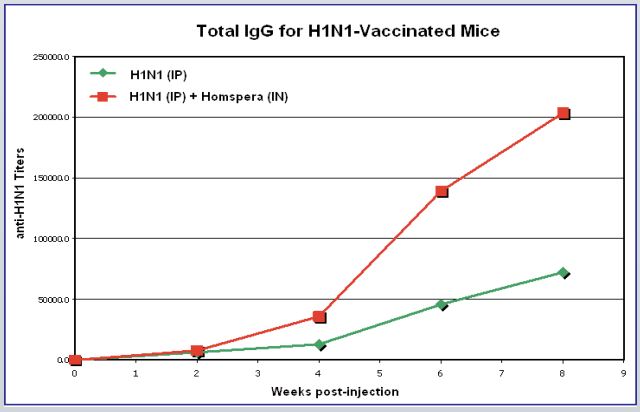
Antigens, depending on their chemical nature, are processed by different pathways within the immune system and this phenomenon may underlay Homspera's adjuvant activity. Intracellular pathogens, such as viruses and some bacteria, replicate within the cellular cytoplasm and are processed and presented by MHC class I molecules (present on nearly all cells in the body) to CD8+ T-cells. Pathogens processed via this pathway typically induce the TH1-associated, cell-mediated immune response that is marked by IFN-? release. Alternatively, antigens such as bacteria and proteins from extracellular pathogens are taken up (mostly by phagocytic macrophages and B cells of the hematopoietic system) into endocytic vesicles that fuse intracellularly with endosomes and lysosomes enabling antigen digestion. The resulting antigen-derived immunogens are subsequently processed and presented by MHC class II molecules to CD4+ T cells. Pathogens processed via this pathway typically induce the TH2-mediated, humoral immune response that is marked by interleukin-4 (IL-4) release.



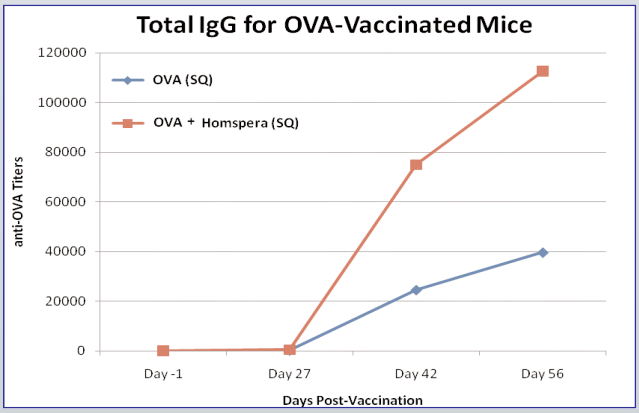
FINDINGS

HOMSPERA INDUCES TH1 AND TH2-MEDIATED RESPONSES

- Homspera elicits an increase in antibody responses via intranasal (IN) and subcutaneous (SQ) modes of administration (see figures below)
- Peer-reviewed literature demonstrates that the active ingredient in Homspera (Sar9, Met(O2)11-Substance P) is capable of the following:
  - Stimulates the loading of antigens into APCs
  - Activates APCs to migrate to the skin-draining lymph nodes
  - Suggests stimulation of T cell proliferation
  - Induces strong cytotoxic T-lymphocyte (CTL) responses
  - Increases the expression of both TH1 (IFN-?) and TH2 cytokines (IL-4)



Homotypic antibody titers in animals vaccinated with H1N1 influenza vaccine increase in the presence of Homspera.



Homspera increases OVA-specific antibody titers in vaccinated animals.

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