

# Salmonella vector (L-12259)

## Highlights

Promising approaches for delivering antigens and generating a protective response against cancers and infectious diseases currently employ existing vaccine strain bacteria or closely-related attenuated bacteria. Human clinical trials have shown excellent safety profiles with various recombinant vaccine strain bacteria, but generally poor efficacies for promoting immunity against the targeted diseases. Finding the right vaccine vector and antigen production system to rapidly induce an immune response while causing minimal toxicity has been challenging. To address this problem, the NRC has developed a recombinant attenuated *Salmonella* vaccine system capable of producing rapid cell-mediated immune protection against infectious diseases and cancers.

## Technology Transfer

- › Commercial exploitation license
- › R&D agreement for development

## Market Applications

- › Delivery vector for vaccines against infectious diseases or cancer

## How It Works

*Salmonella* is an invasive bacterium that resides in phagosomes of infected cells; it is able to avoid immune detection and induce chronic

infection. Mutants of *Salmonella typhimurium* have been considered for developing oral vaccine delivery systems using the recombinant expression of disease-associated antigens. However, vaccination with attenuated *Salmonella* is associated with several problems, including failure to activate rapid T cell production, poor immune stimulation with over-attenuated strains, and immune suppression.

To address these problems, the NRC has built upon research making use of a bacterial Type III secretion system to deliver foreign antigens from the bacteria into the host cell cytosol. Processing of the foreign antigens from the cytosol of infected antigen-presenting cells enables a good induction of T cell immunity. Further refinements of this system involve the augmentation of inflammation and reduction of immune suppression induced by the attenuated *Salmonella* through the introduction of immunomodulators along with the foreign antigen expression cassette.

Preclinical studies conducted in mice have shown that the vector is efficacious in inducing a rapid immune

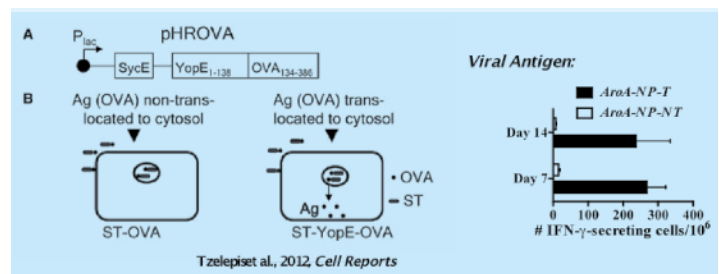


Figure. Antigen secretion from invasive *Salmonella* stimulates a T cell response (IFN $\gamma$  secretion) targeting the antigen. The viral antigen tested here is Lymphocytic Choriomeningitis Virus NP protein.

response against test antigens from lymphocytic choriomeningitis virus and melanoma.

## Benefits

- › Ideal for oral vaccine administration
- › Can be used with a wide range of antigens
- › Rapid, persistent cellular immune response

## Patents

**NRC file 12259:** Patents pending in Canada, the United States, Europe and India.

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