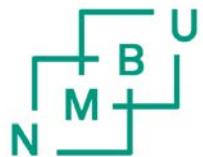




# ILA vaksine – forskningsnytt

Espen Rimstad,  
NMBU- Veterinærhøgskolen



# Ultimate fish vaccine - requirements?

- Efficient
  - Induce disease protection
  - Reduce/stop shedding
  - Long-lasting immunity
  - Administrated once
- Safe
  - No/little side effects
  - No/little environmental effects
  - No effect for consumer
- Low cost?
- Easy to administrate
  - Injectable versus oral or dip?



# VIVAFISH

## Platform for Fish Virus Vaccines



- ViVaFish is a platform project funded by Research Council of Norway (RCN)



Primary institutions

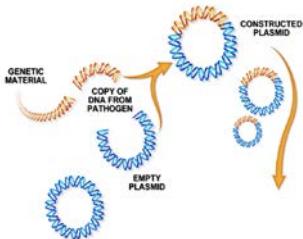


National and international partners

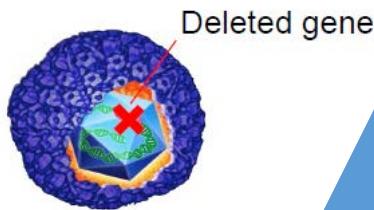


Industrial partners

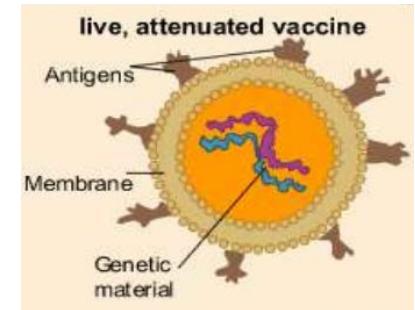
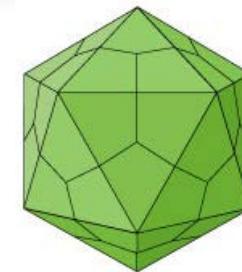
## Vaccine concepts



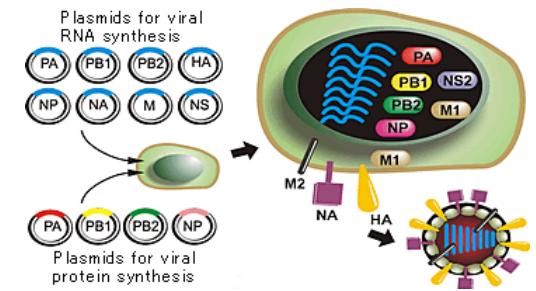
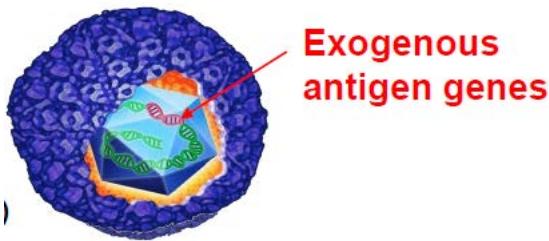
Whole virus and subunit preparations



Live attenuated virus



Vectorized, propagation-defective

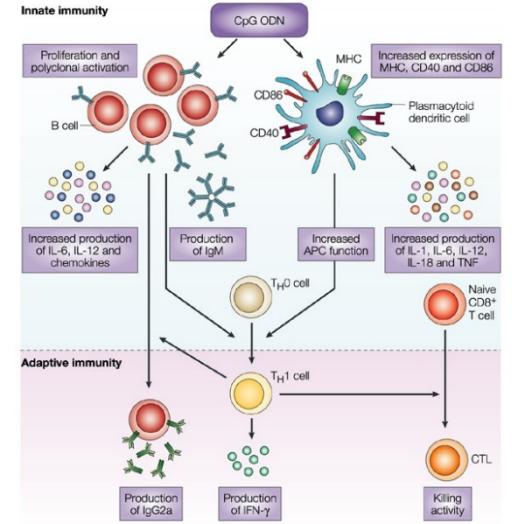


Immunology of long term protection

Link between innate and adaptive immune responses

Analyze adaptive CTL responses

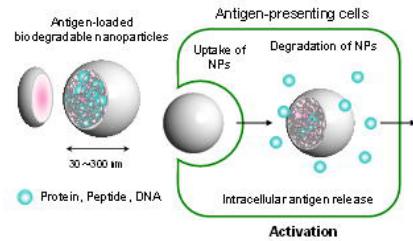
B-cell responses involved in long term protection



Nature Reviews | Immunology

# VIVAFISH

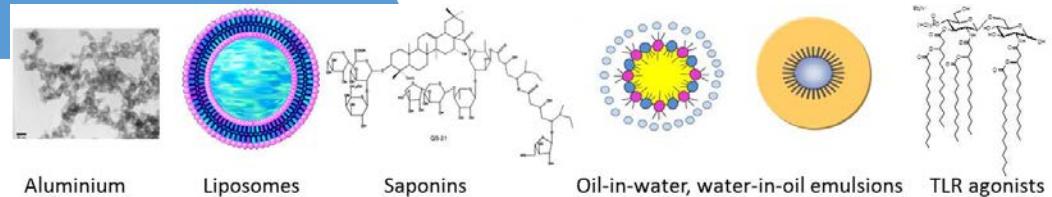
## Platform for Fish Virus Vaccines



Optimization of delivery systems

Assays for long-lasting antiviral immunity

RNA seq / Array



## Efficacy

## Safety

In target species

Dissemination

Reversion

Latency

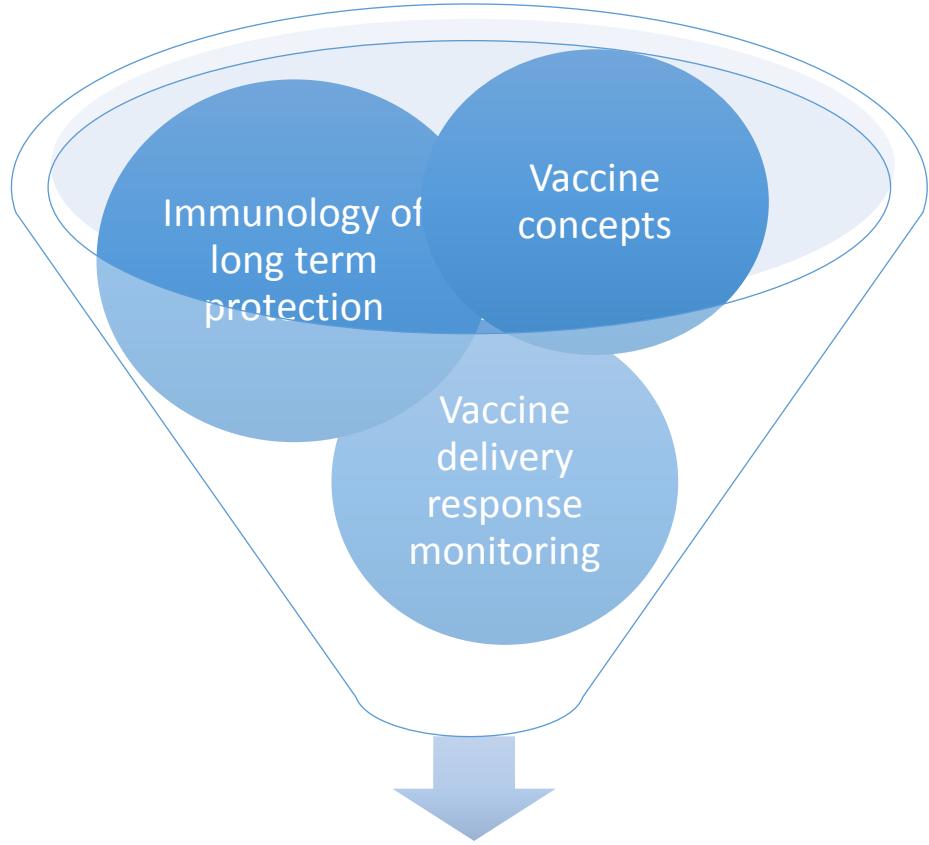
## Ecotoxicity

Target versus non-target species

Host range.

Establishment in the environment

Potential for recombination



Improved prototypes for vaccines

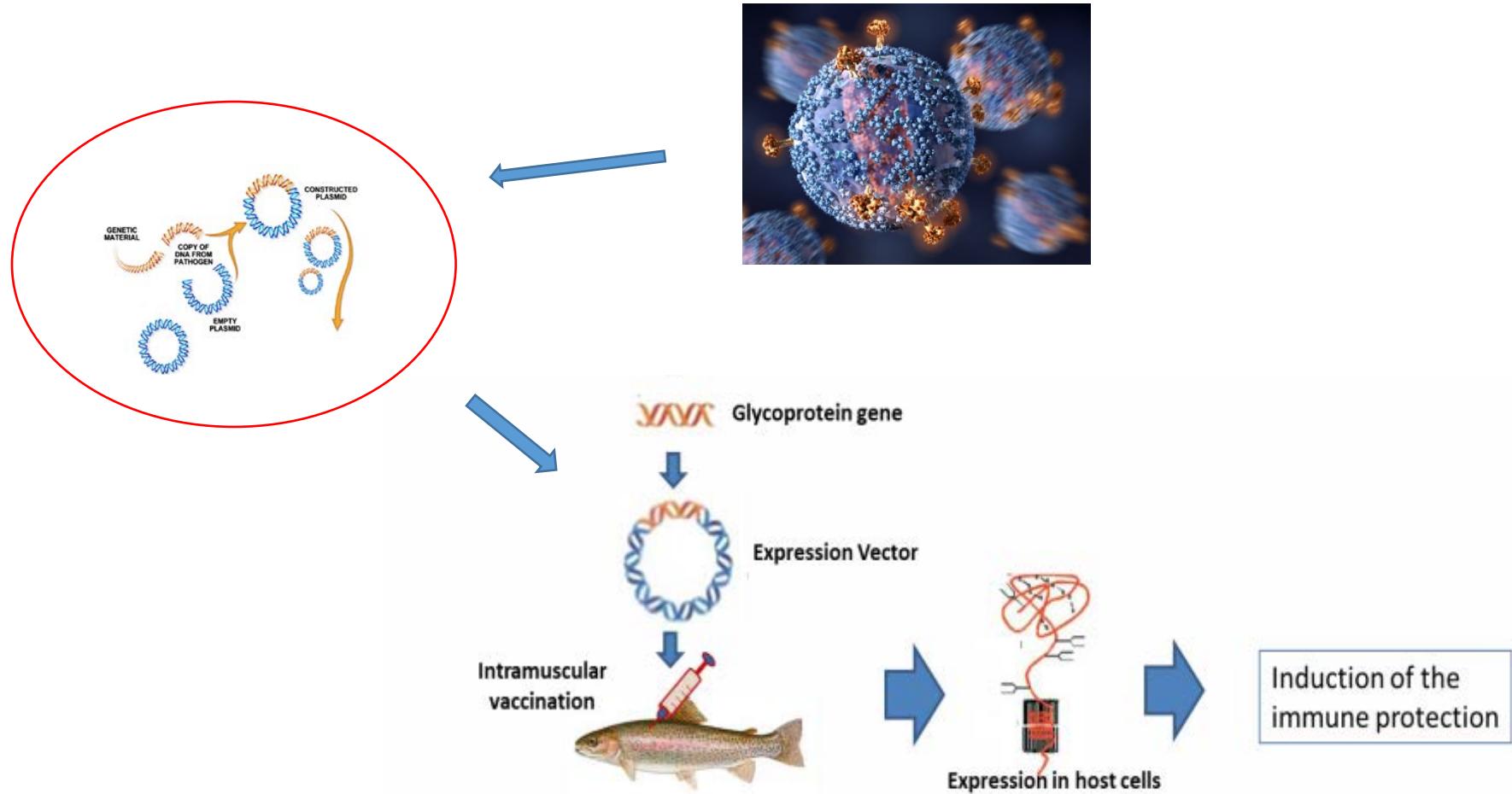


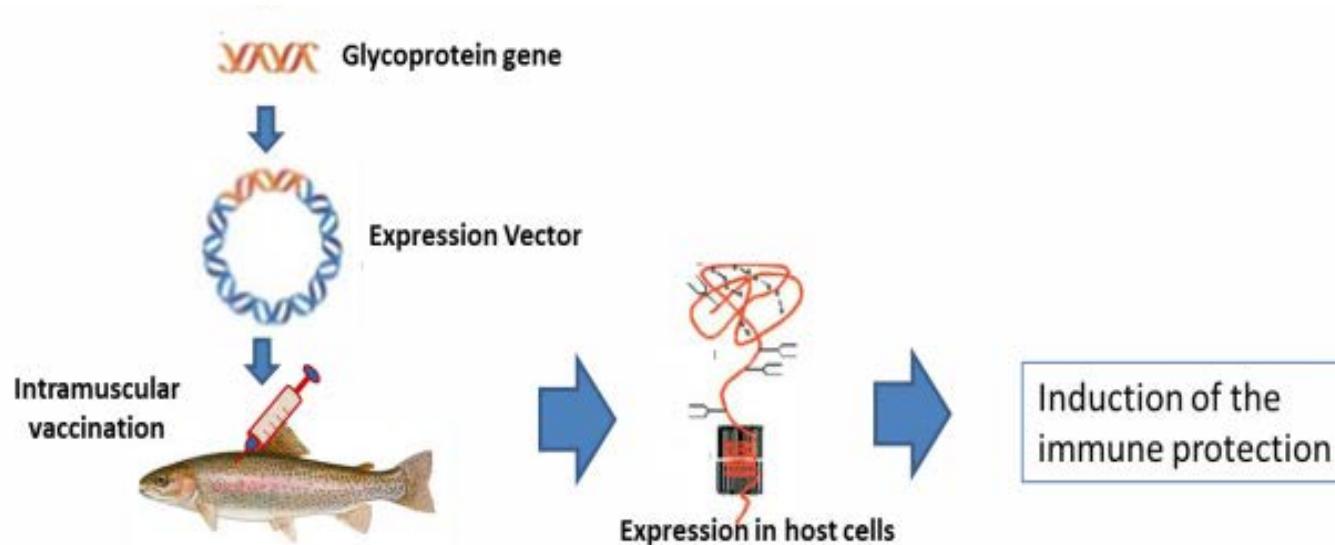
## ILA vaksine

- Robertsen B, Chang CJ, Bratland L. IFN-adjuvanted DNA vaccine against infectious salmon anemia virus: Antibody kinetics and longevity of IFN expression. *Fish Shellfish Immunol.* 2016 Jul;54:328-32. doi: 10.1016/j.fsi.2016.04.027. PubMed PMID: 27108379.
- Caruffo M, Maturana C, Kambalapally S, Larenas J, Tobar JA. Protective oral vaccination against infectious salmon anaemia virus in *Salmo salar*. *Fish Shellfish Immunol.* 2016 Jul;54:54-9. doi: 10.1016/j.fsi.2016.03.009. PubMed PMID: 26994669.
- Tobar I, Arancibia S, Torres C, Vera V, Soto P, Carrasco C, Alvarado M, Neira E, Arcos S, Tobar JA. Successive Oral Immunizations Against *Piscirickettsia Salmonis* and Infectious Salmon Anemia Virus are Required to Maintain a Long-Term Protection in Farmed Salmonids. *Front Immunol.* 2015 May 27;6:244. doi: 10.3389/fimmu.2015.00244. PubMed PMID: 26074916; PubMed Central PMCID: PMC4445318.
- Chang CJ, Robertsen C, Sun B, Robertsen B. Protection of Atlantic salmon against virus infection by intramuscular injection of IFN $\gamma$  expression plasmid. *Vaccine*. 2014 Aug 6;32(36):4695-702. doi: 10.1016/j.vaccine.2014.05.059. PubMed PMID: 24996122.
- Wolf A, Hodneland K, Frost P, Hoeijmakers M, Rimstad E. Salmonid alphavirus-based replicon vaccine against infectious salmon anemia (ISA): impact of immunization route and interactions of the replicon vector. *Fish Shellfish Immunol.* 2014 Feb;36(2):383-92. doi: 10.1016/j.fsi.2013.12.018. PubMed PMID: 24374059.
- Wolf A, Hodneland K, Frost P, Braaen S, Rimstad E. A hemagglutinin-esterase-expressing salmonid alphavirus replicon protects Atlantic salmon (*Salmo salar*) against infectious salmon anemia (ISA). *Vaccine*. 2013 Jan 11;31(4):661-9. doi: 10.1016/j.vaccine.2012.11.045. PubMed PMID: 23200939

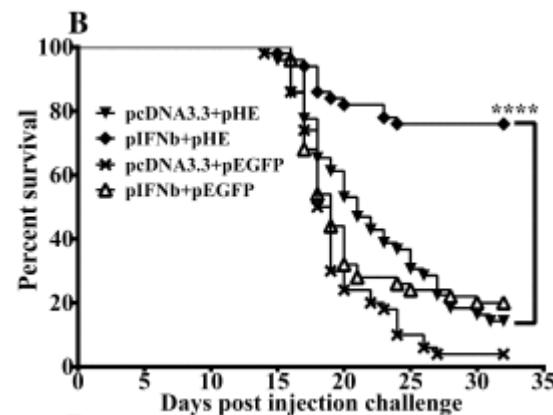
# VIVAFISH

## Platform for Fish Virus Vaccines

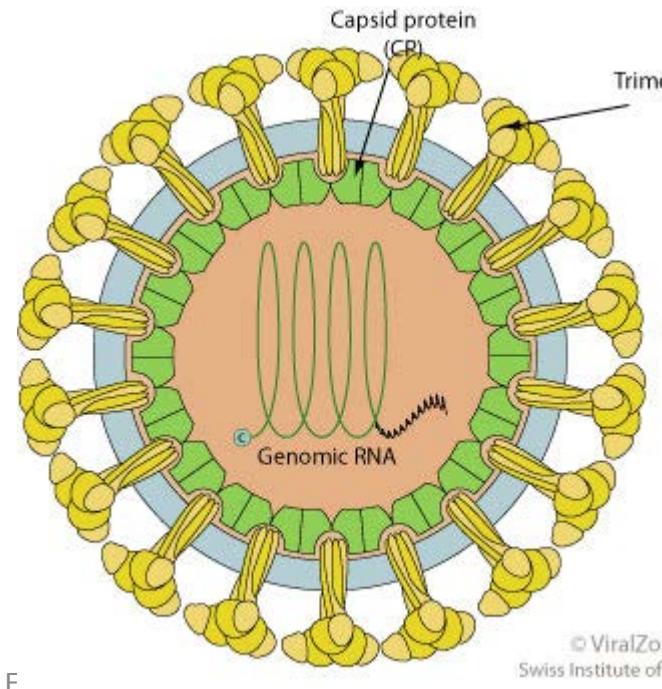
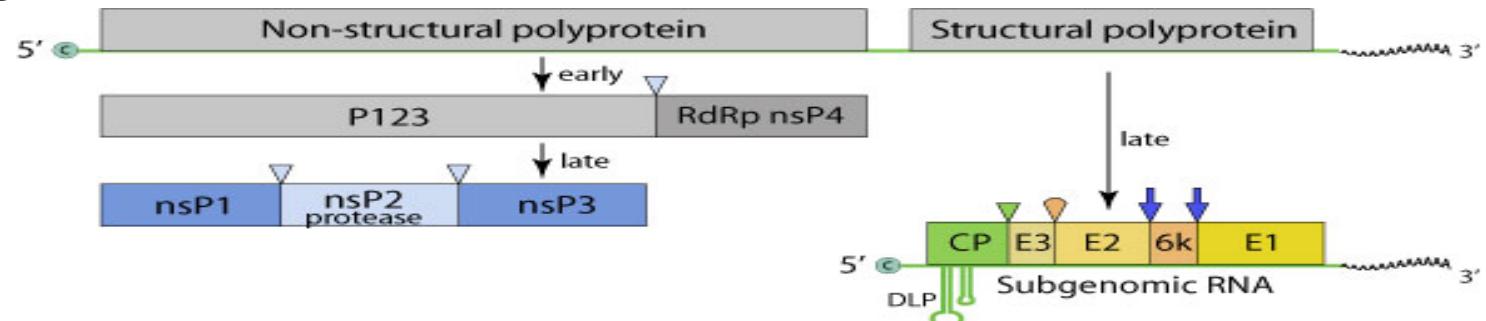


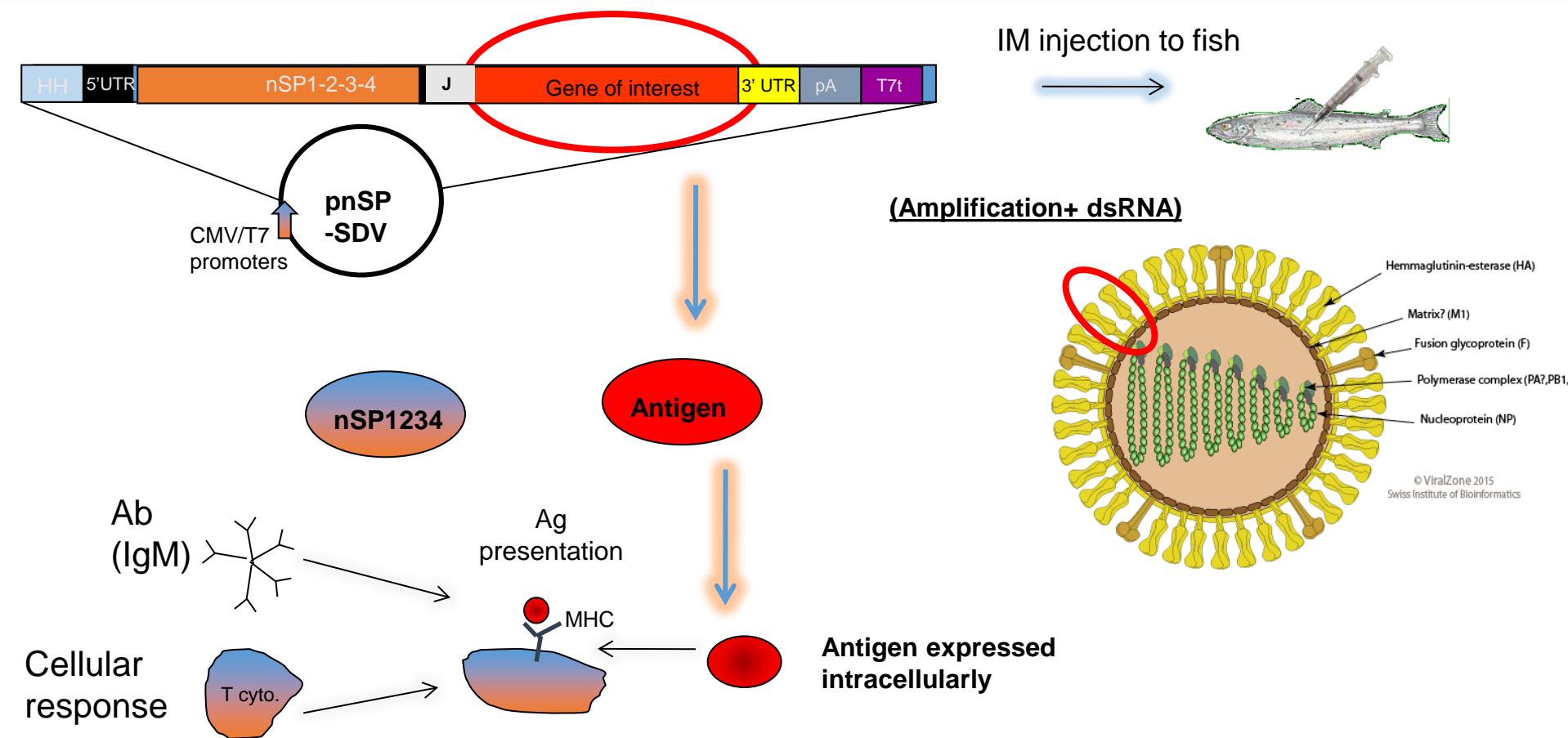


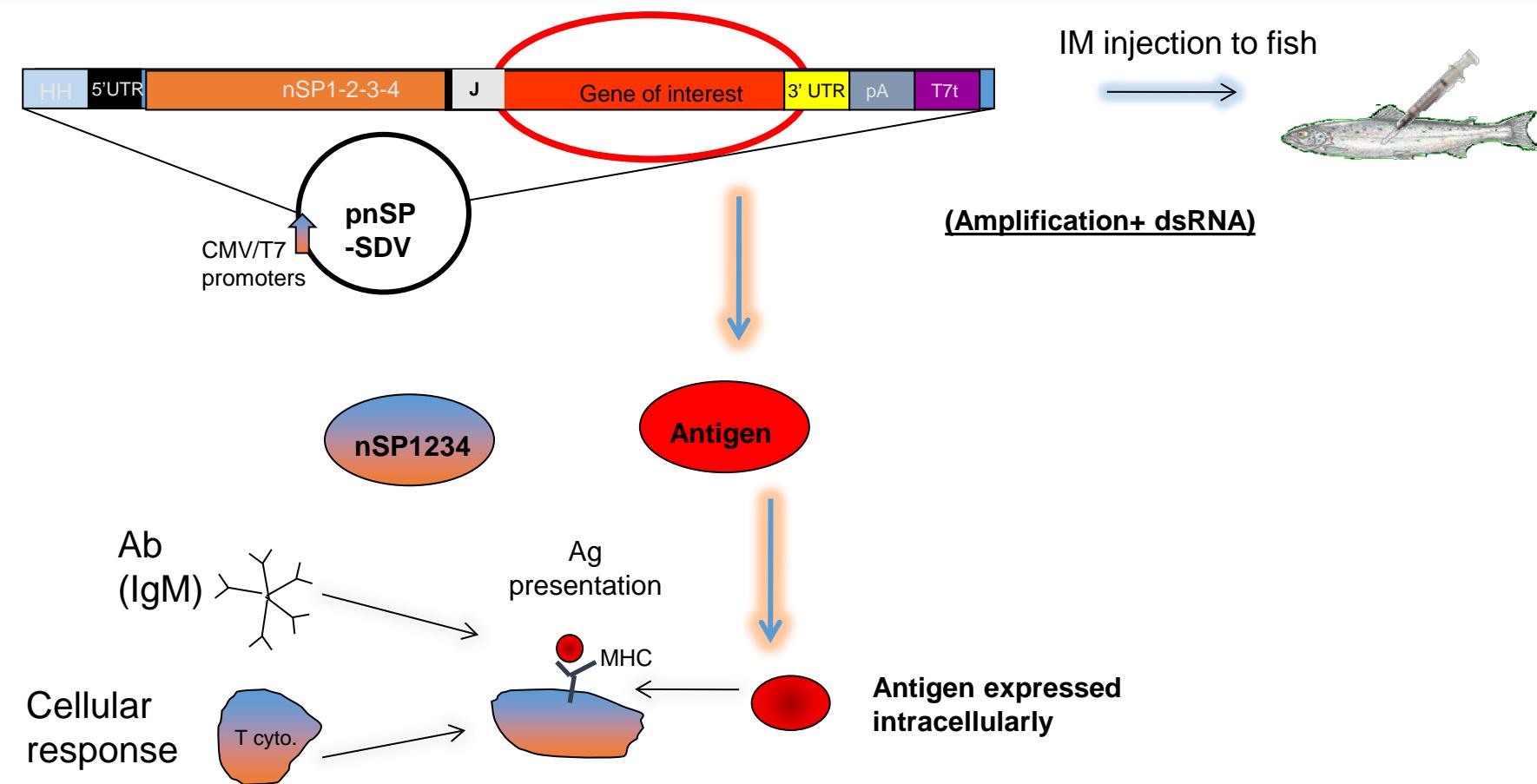
Chang et al 2014, Robertsen et al 2016

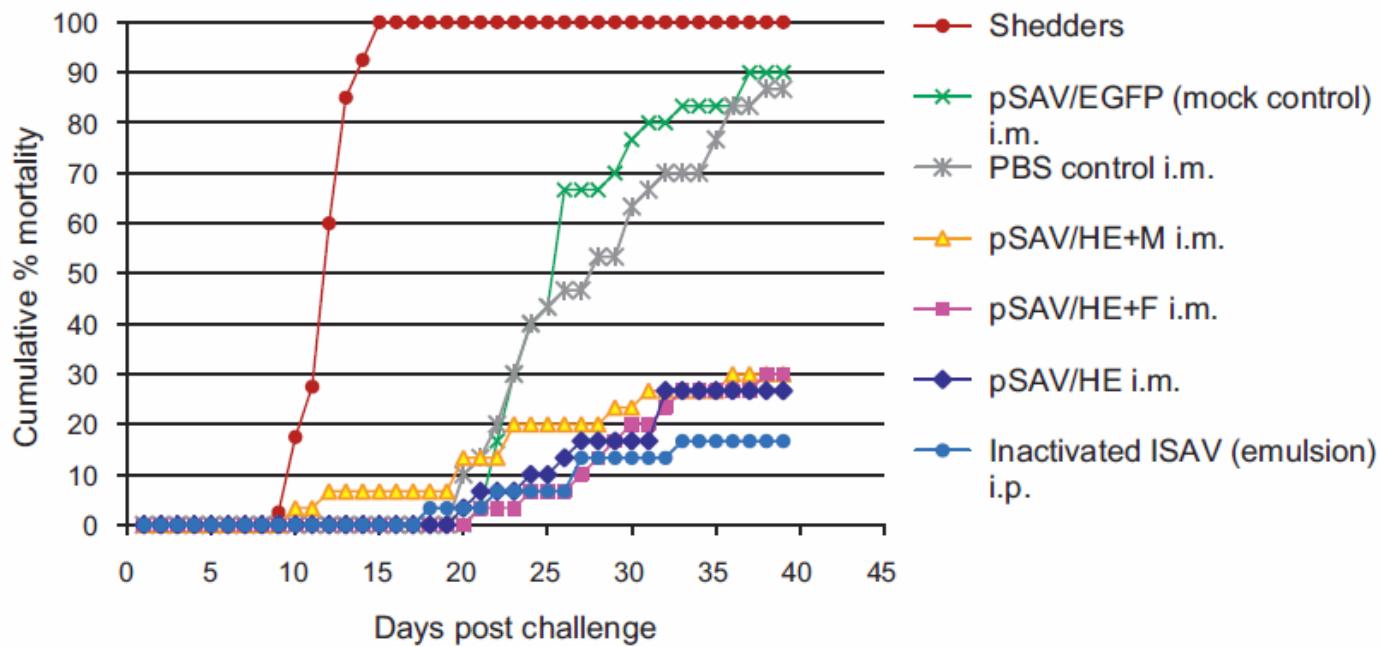


Pancreas disease  
virus is an  
Alphavirus



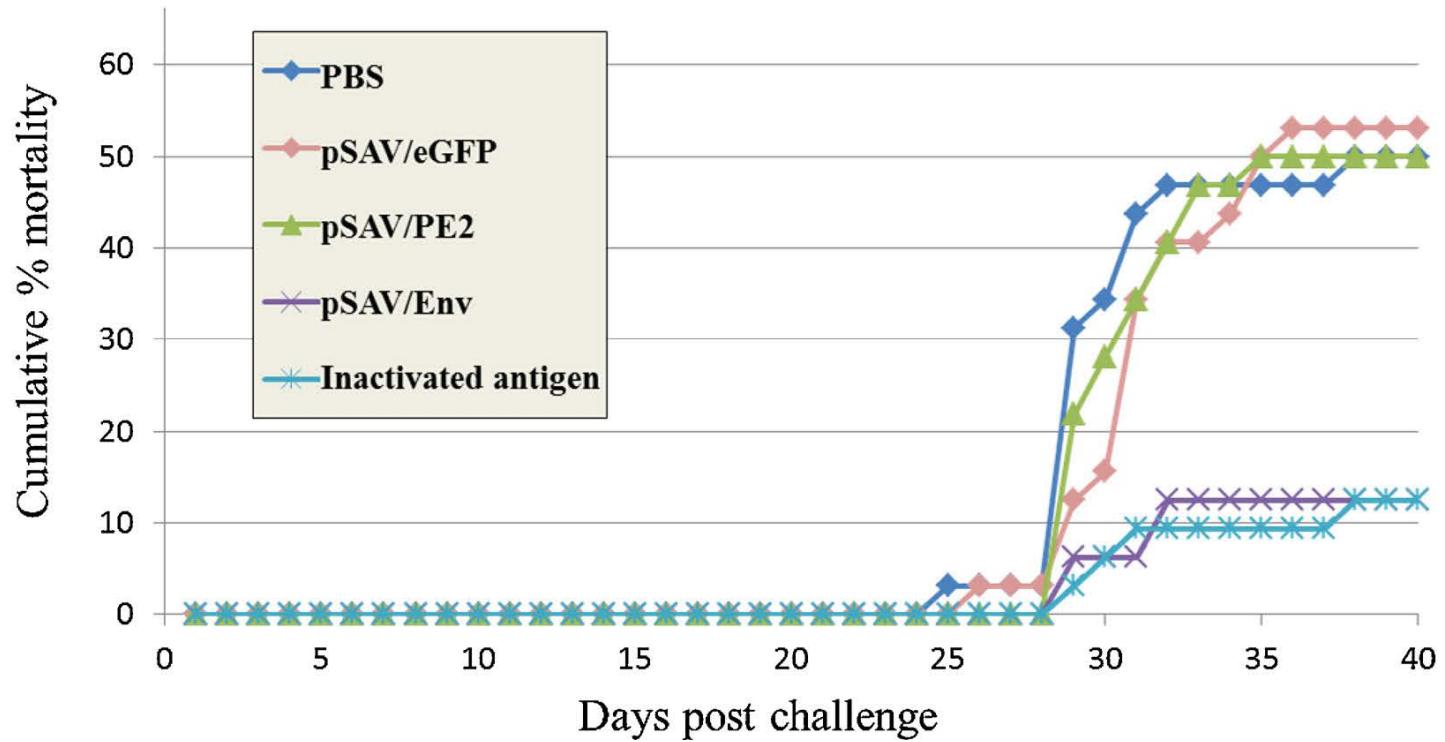






Infeksiøs lakseanemi - ILA

Wolf et al 2013, 2014

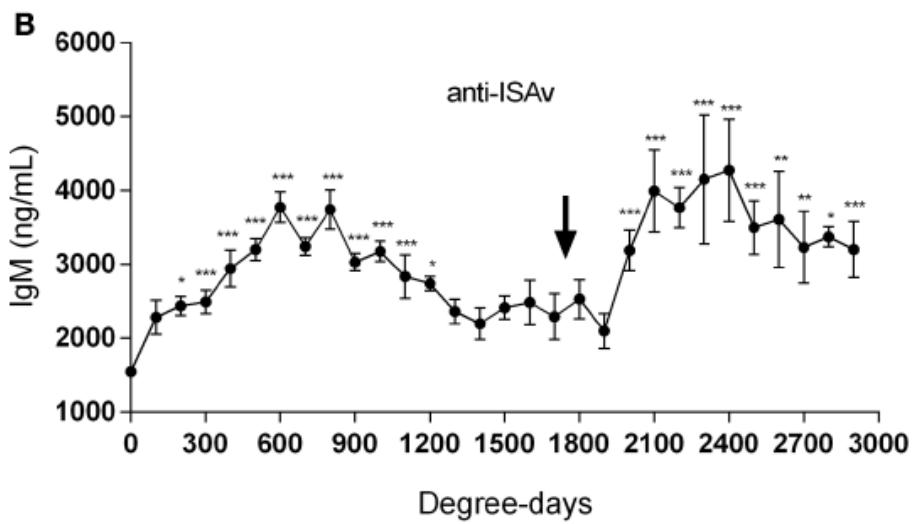


Pankreas sykdom - PD

Hikke et al 2014

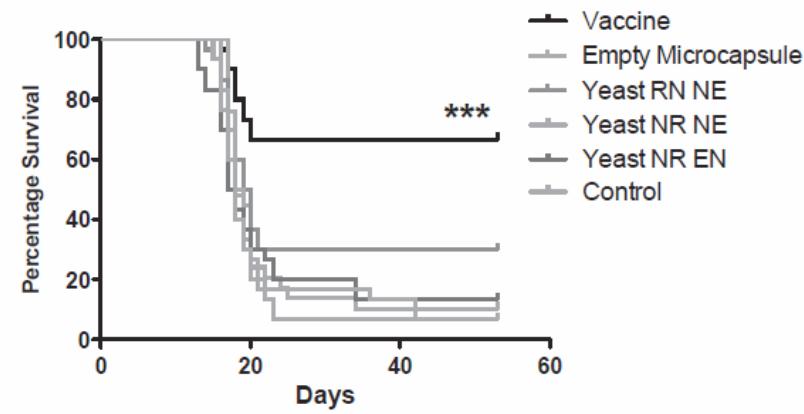


# Oral vaccines



Tobar et al 2015 –CentroVet (Chile)

Oral booster etter injeksjonsvaksiner gir økt mengde spesifikk IgM



Caruffo et al 2016,–CentroVet (Chile)

Oral vaksine alene gir en viss beskyttelse dersom den er pakket inn i spesielle mikrocapsuler.



# ISA as a model?



AMERICAN  
SOCIETY FOR  
MICROBIOLOGY



RESEARCH ARTICLE



## Characterization of a Novel Orthomyxo-like Virus Causing Mass Die-Offs of Tilapia

Eran Bacharach,<sup>a</sup> Nischay Mishra,<sup>b</sup> Thomas Brlese,<sup>b</sup> Michael C. Zody,<sup>c</sup> Japhette Esther Kembou Tsofack,<sup>a</sup> Rachel Zamostlano,<sup>a</sup> Asaf Berkowitz,<sup>d</sup> James Ng,<sup>b</sup> Adam Nitido,<sup>b</sup> André Corvelo,<sup>c</sup> Nora C. Toussaint,<sup>c</sup> Sandra Cathrine Abel Nielsen,<sup>b\*</sup> Mady Hornig,<sup>b</sup> Jorge Del Pozo,<sup>e</sup> Toby Bloom,<sup>c</sup> Hugh Ferguson,<sup>f</sup> Avi Eldar,<sup>d</sup> W. Ian Lipkin<sup>b</sup>

Department of Cell Research and Immunology, The George S. Wise Faculty of Life Sciences, Tel Aviv University, Tel Aviv, Israel<sup>a</sup>; Center for Infection and Immunity, Mailman School of Public Health, Columbia University, New York, New York, USA<sup>b</sup>; New York Genome Center, New York, New York, USA<sup>c</sup>; Department of Poultry and Fish Diseases, The Kiriron Veterinary Institute, Bet Dagan, Israel<sup>d</sup>; Easter Bush Pathology, The Royal (Dick) School of Veterinary Studies and The Roslin Institute, University of Edinburgh, Midlothian, Scotland<sup>e</sup>; Marine Medicine Program, Pathobiology, School of Veterinary Medicine, St. George's University, Grenada, West Indies<sup>f</sup>

\* Present address: Sandra Cathrine Abel Nielsen, Department of Pathology, School of Medicine, Stanford University, Stanford, California, USA.

E.B. and N.M. contributed equally to this article.



- ISAV is a relative to Tilapia Lake virus.