Veterinærinstituttet
Norwegian Veterinary Institute

Salmon erythrocytes sequester active virus particles in infectious salmon anaemia

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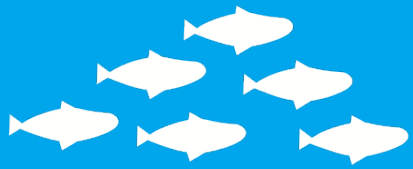
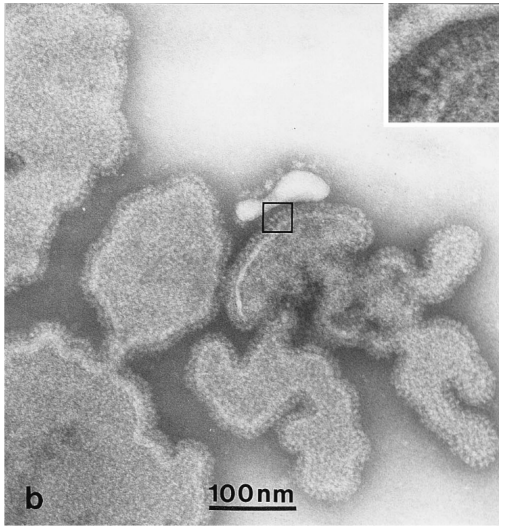


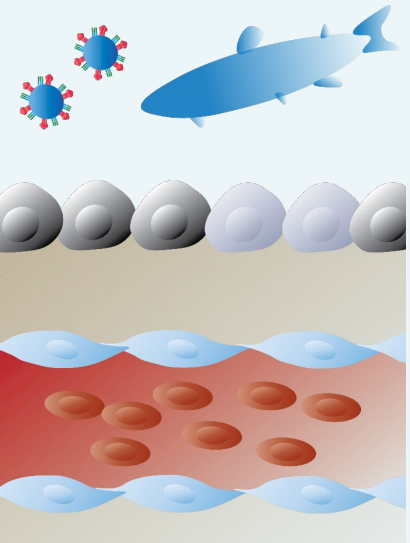
Infectious salmon anaemia virus (ISAV)

- Orthomyxovirus (enveloped, segmented, single stranded RNA virus, negative polarity)
- Exist in a non-pathogenic HPR0 variant and a pathogenic HPRΔ variant that is the causal agent of infectious salmon anaemia in farmed Atlantic salmon
- Disease is characterised by breakdown of central vascular functions, with petechial bleeding, ascites, and focal organ necrosis
- In addition, affected fish become severely anaemic
- Surge of ISA outbreaks in Norway in 2020



From Falk et al, J Vir, 1997

HPR0 and HPRΔ



Infection of surface epithelium

Rapid clearance of infection

HPR0 and HPRΔ

HPRΔ only

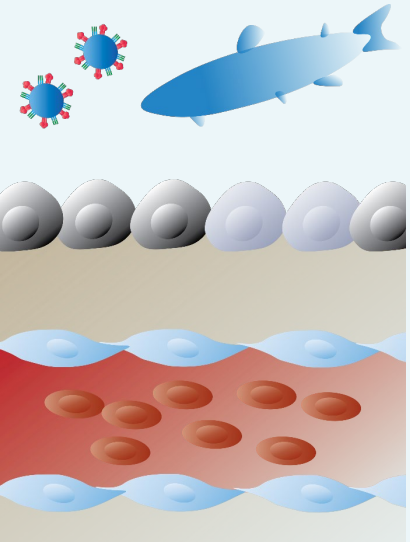
Infection of surface epithelium

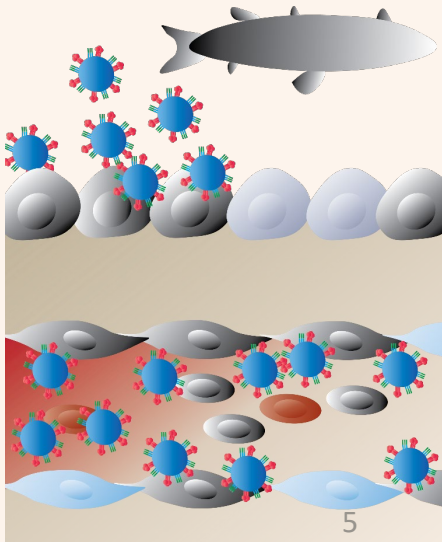
Infection spreads to the circulatory system

Disease develops

Rapid clearance of infection

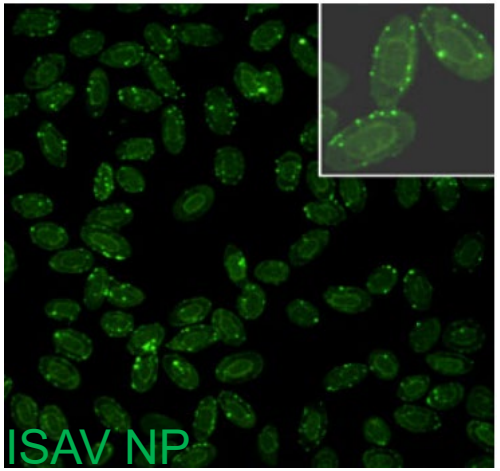
Persistent infection





ISAV and red blood cells (RBC)

- Naturally infected fish suffer from regenerative anaemia, with increased fragility of RBC
- ISAV haemagglutinates salmon RBC
- The ISAV receptor (4-O-acetylated sialic acid) is found on salmon endothelial cells and RBC, in addition to epithelial cells in gills, skin, and gut
- ISAV coats RBC during experimental infection



From Aamelfot et al, 2012

Thorud, phd thesis, 1991; *Falk et al, J Vir, 1997; Hellebo, J Vir, 2004; Aamelfot et al, J Vir, 2012*

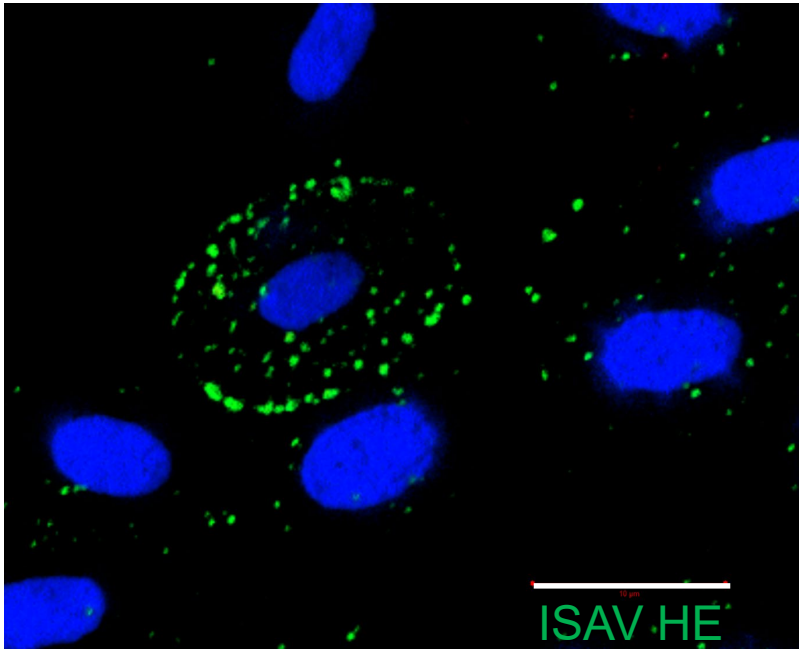
Mapping the extent of ISAV-RBC interactions in experimental infection and natural infection

- Three trials with similar design (2012, 2018, 2020)
  - –Mortality 20-100% (starting d12-18)
  - –Variable anaemia (mild-severe)
- Two natural outbreaks in the North of Norway, october 2020

Experimental design, trials

- Immersion challenge
  - 2 hours, 10^4 tcid50/mL
  - Glesvær/2/90 strain
- Atlantic salmon presmolt
  - 50-150 g
- Regular sampling of fish
  - every 1-3 days around peak

ISAV-coated RBC in blood smear



Please note

- Data have been removed from the presentation, as they are preliminary and not yet published
- If you are interested in discussing results, please contact principal investigator johanna.hol.fosse@vetinst.no

Possible consequences of RBC targeting

To the virus

- Circulation half-life
  - Neutralising antibodies
  - Scavenging
- Distribution
- Trans-infection
- Replication in RBC not likely to be of general importance

To the host

- Anaemia
  - Virus particles and virus-targeted antibodies or complement shorten RBC halflife
  - Damage to cell membranes shorten RBC halflife
- Modulation of host response

Summary

- ISAV coating of RBC is a persistent feature of experimental and natural infection, involving up to 100% of the RBC population at its peak
- ISAV remains infectious when bound to RBC. We are investigating if this may promote systemic spread of infection, e.g. by prolonging the halflife of virus particles in the blood stream
- In ISA, RBC show increased osmotic fragility. Membrane modulations could contribute to removal from circulation, as could viral antigen on RBC surfaces
- Under some circumstances, RBC also produce ISAV proteins. This is a rare feature and not required for disease and mortality.

Thanks to everyone involved

Norwegian Veterinary Institute
Knut Falk
Maria Aamelfot
Tonje Sønstervold
Simon Weli
Anita Solhaug
Torfinn Moldal

EURL, Technical University of Denmark
Niccolò Vendramin
Argelia Cuenca

Faeroese Food and Veterinary Authority
Debes Christiansen
Maria Marjunadóttir Dahl
Petra E Petersen

Main funding body
Norwegian Research Council

Faglig ambisiøs, fremtidsrettet og samspillende - for Én helse!

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