

An Epidemiological study of CMS: Transmission, risk factors and disease development in Norwegian salmon farming

Funded by the Norwegian Seafood Research Fund













### Project goal

To increase knowledge on spread of PMCV and factors influencing development of CMS

### Specific aims:

- Is PMCV transmitted from broodstock to ongrowing fish under normal production?
- Map the course of PMCV infection in the sea
- Identify risk factors for infection with PMCV
- Identify risk factors for development of CMS
- Literature review
- Advise farmers on best practise for prevention and control



# Cardiomyopathy Syndrome (CMS) in Atlantic salmon

Litterature review

### Overview of presentation

- ▶ The CMS-Epi project
- CMS Cardiomyopathy syndrome
- ▶ PMCV piscine myocarditisvirus
- Epidemiology
  - Occurrence
  - Reservoirs
  - Transmission
  - Risk factors
- Prevention and control
- Economy
- Knowledge gaps



### CMS - cardiomyopathy syndrome

- Disease in Atlantic salmon
- Occurrence
  - Norway (100 + cases/year)
  - Scotland
  - Ireland
  - Faroe Islands
- Onset and course of disease:
  - Typically second year in sea, but also earlier
  - Sudden high mortality or prolonged period of raised mortality
- Considerable welfare issue
- Significant economic impact



### CMS – clinical signs

- None or signs of lethargy
- Signs of circulatory failure
  - Protruding eyes (Exophthalmia)
  - Ventral skin bleedings
  - Raised scales
- Internal findings
  - Ascites
  - Blood clots in the pericardial cavity.
  - Enlarged or ruptured atrium and/or sinus venosus = «Hjertesprekk»
  - Discoloured liver with fibrinous casts



Photo: Per Anton Sæther, MarinHelse AS

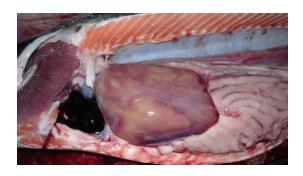
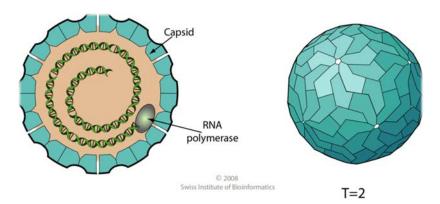


Photo: Brit Tørud, Norwegian Veterinary Institute



### PMCV – piscine myocarditis virus

- RNA-virus
- Similarities with Totiviridae family
  - A family that:
  - Infects protozoan parasites and fungi
  - Are transmitted with cell division, sporogenesis or cell fusion
- ▶ Size: ~50nm
- Structure:
  - Non-enveloped («naked»)→ likely very resistant
  - Spherical
- Biophysical proporties:
  - Unknown



**Totiviridae** 

Illustration: Swiss Institute of Bioinformatics (SIB) used with permission



### PMCV – genome

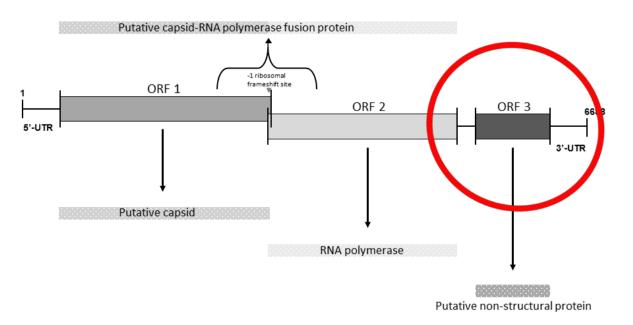


Illustration: Aase B. Mikaelsen NMBU

- ▶ 6.688bp
- ▶ Three open reading frames (ORFI, ORF2 and ORF3)
- ▶ ORF3: Exclusive for viruses infecting vertebrate hosts
  - Research is focused on the ORF3



### PMCV – genetic variation

- Homogenous population in Norway (one genogroup)
- Most divergent:98.6% nucleotide identity
- PMCV from Atlantic argentine had 86% nucleotide identity
- Virulence factors:
  - Three positions on the ORF3 has been suggested

Illustration: Åse Helen Garseth Norwegian Veterinary Institute



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Illustration: Åse Helen Garsethe, NVI



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69 gi|430133428|gb|JQ728712.1|:946-2586 Møre og Romsdal 2009
                                  gi|430133430|gb|JQ728713.1|:946-2586 Møre og Romsdal 2009
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      36 gi|430133474|gb|JQ728735.1|:946-2586 Vest Agder 2010
                                    /ir806 PMCV ORF1 Wild salmon from River Årøy, Sogn og Fjordane 2012
gi|430133438|gb|JQ728717.1|:952-2586 Møre og Romsdal 2010
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gi|430133462|gb|JQ728729.1|:949-2586 Rogaland 2009
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         gi|310877909|gb|HQ139954.1|:1393-3113 Piscine myocarditis virus AL V-708 complete genome
         gi|388460553|gb|JQ745675.1|:1-798 Wild salmon from Fiver Nausta, Sognog Fjordane 2008
                  gi|388460555|db|JQ745676.1|:1-798 Wild salmon from River Åroy, Sognog Fordane 2007
 gi|430133408|gb|JQ728702.1|:949-2586 Sør Trøndelag 2010
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                                         69 gi|430133384|gb|JQ728690.1|:946-2586 Nordland 2010
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### CMS & PMCV – diagnostic tools

### ▶ The CMS diagnosis is based on:

- Clinical observations and autopsy
- Histopathology
- Differential diagnosis: PD and HSMI

### ▶ PMCV specific real-time PCR:

- High correlation between virus load and pathological changes
- Widely used for screening
- Patent by Pharmaq Analytiq

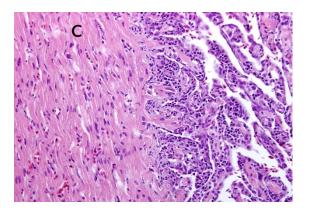


Photo:Trygve Poppe

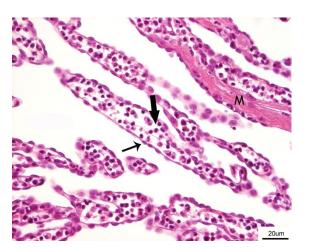


Photo: Camilla Fritsvold, Norwegian Veterinary Institute



### CMS & PMCV – diagnostic tools

### In situ hybridization:

Detects virus specific nucleic acids in fish tissue with histopathological changes

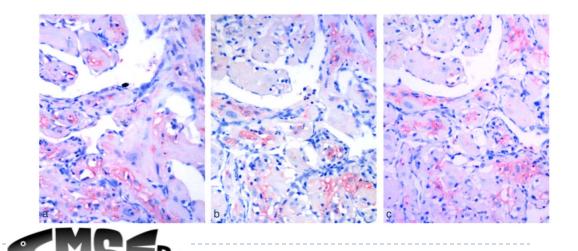
### Immunhisto chemistry (IHC):

- Detects PMCV specific proteins
- Not available for routine use due to lack of antibodies

#### Cell culture:

PMCV replicates in fish cell lines, but at too low levels, and too weak CPE.

Immunhisto chemistry detects PMCV specific proteins by the use of labelled antibodies Photo: Gulla et al. 2012



### CMS & PMCV - epidemiology

#### Reservoir:

- Farmed Atlantic salmon
- Diagnosed in a few wild salmon
- Found in escapees
- Recently found in cleaner fish in Ireland
- Not found in environmental samples, but in mucus, faeces and salmon lice in infected cage

#### Transmission routes:

- Horizontal transmission
- Vertical transmission is under investigation

#### Risk factors:

- Time in sea
- Size of population
- Infection pressure (CMS in neighbouring farms and distance)
- CMS in previous cohorts
- HSMI



A virus sharing 86 % nucleotide identity with PMCV has been found in Atlantic Argentine Photo: Wikipedia



## < MSEP

### CMS - prevention and control

### Biosecurity

All-in all-out, disease free stock, cleaning and disinfection

### Screening

For early detection, before movement of fish

### Husbandry

Reduce stress, early slaughter

#### Vaccination

Pharmaq is working on a vaccine

### Breeding

▶ High heritability for resistance. QTL-selected eggs are available

#### Feed

- Lower lipid content and higher  $\Omega$ -3/ $\Omega$ -6 ratio (PUFAs)
- Effect demonstrated in trials





### CMS - economic impact

- > 100 cases per year
- Direct loss ~4.5-8.8 million € in 2002
- Estimated loss in 2007: ~25 million €

(Not including costs for prevention and extra labour)



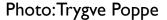




Photo: Per Anton Sæther, MarinHelse



### Knowledge gaps

#### PMCV:

- Characterize proteins that are coded for by the virus RNA
- Understand mechanisms for infection and replication in the host
- Develop cell culture technique

#### ► CMS:

- Pathogenesis
- Factors that trigger disease development in infected fish
- Can infected fish get rid of virus?

### Transmission, prevention and control

- Can PMCV be transmitted vertically?
- Virus reservoir (beyond the farmed salmon)
- Does transmission with smolt from freshwater phase have any importance?



### Read more about CMS and the project

http://www.fhf.no/prosjektdetaljer/?projectNumber=901118 https://www.vetinst.no/rapporter-og-Rapport 1 - 2017 publikasjoner/rapporter/2017/kardiomyopatisyndrom-cms-hos-laks Kardiomyopatisyndrom (CMS) hos laks Sykdomsutvikling - Agens - Epidemiologi eterinærinstituttet/

### Thank you for the attention!



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