Presentation of new research projects on cardiomyopathy syndrome CMS

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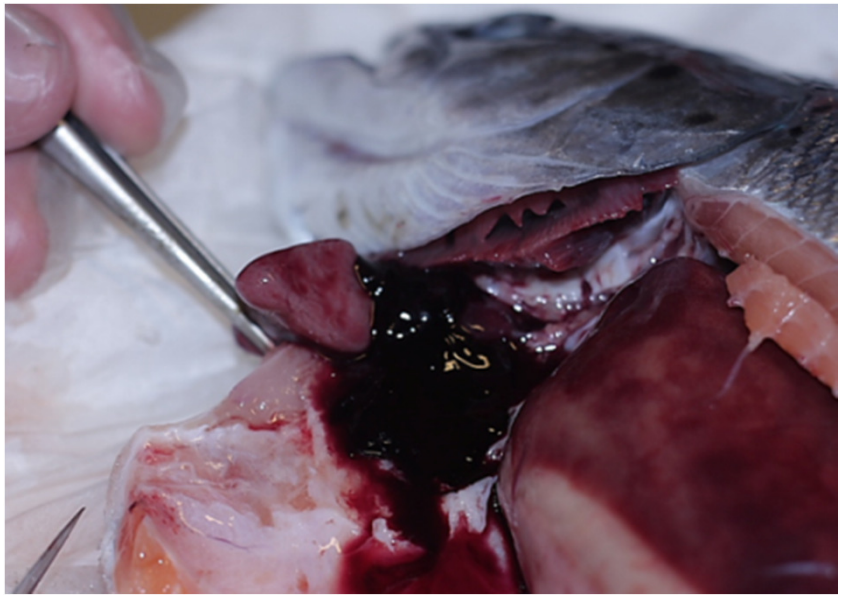

New publications from recent CMS projects

- Timmerhaus et al., BMC Genomics 2012: *Comparison individuals with different outcomes of disease*
- Wiik-Nilsen et al., J Fish Diseases 2012: *Characterisation of myocardial lesions using LC microdissection*
- Wiik-Nilsen et al., J fish Diseases 2012: *Genetic variation in Norwegian PMCV*
- PhD thesis of Gerrit Timmerhaus (2012) – *CMS: functional genomics studies of host-pathogen responses and disease markers*- limited ex available at TriNation meet

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New CMS projects 2012-2015

- Virulence mechanisms and host responses to PMCV
- Marker-assisted selection and mechanisms of disease resistance
- Development of cohabitation challenge model for salmon fry

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Studies of virulence mechanisms and host responses to infection with piscine myocarditis virus (PMCV)

Research Council of Norway project 216177: 2012-2015

- Partners:
  - Norwegian School of Veterinary Science (NSVS), Aqua Medicine – Ø. Evensen (PL), A. Mikalsen, Ø. Haugland
  - Nofima – SM. Jørgensen, H. Takle, A. Krasnov, G. Timmerhaus
  - Pasteur Institute, Paris – F. Rey
  - National Veterinary Institute – I. Skaar, E. Thoen

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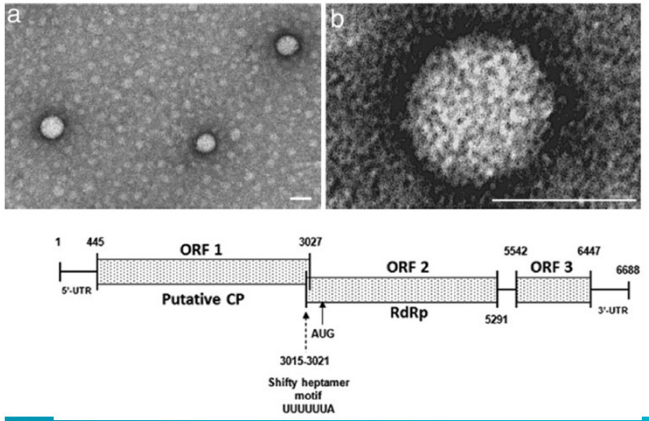
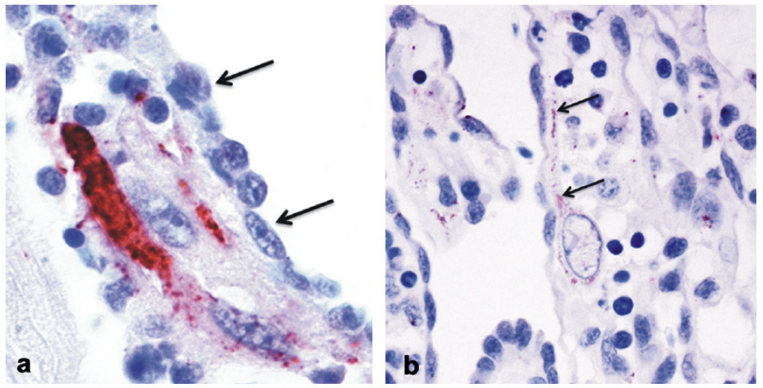
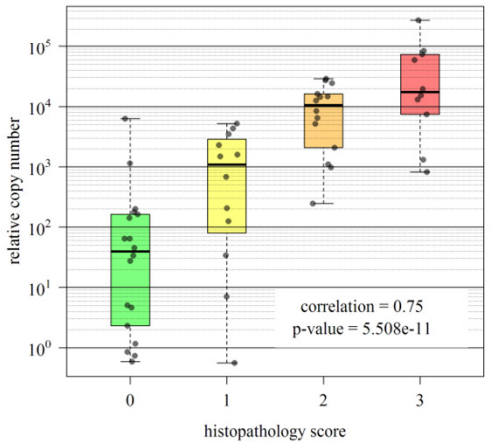
Background:

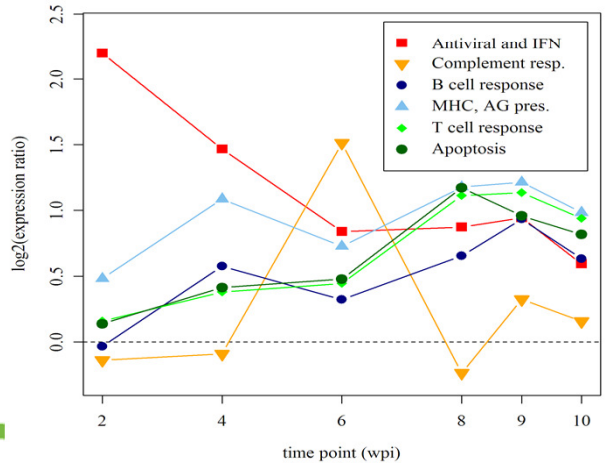
Virus:







Host:



2 wpi	4 wpi	6 wpi	8 wpi	10 wpi	
- low virus load in heart[a] - no histopathological changes (heart)[a] - activation of early antiviral and innate immune responses[a,b] - initital repression of cytoskeleton organization and cardiac muscle development[b]	- increased virus load across organs[a] - first evidence of histopathological changes (heart)[a] - activation of innate antiviral and early adaptive immune responses[a,b] - repression of cytoskeleton organization and cardiac muscle development[b]	- high virus load in heart[b] - significant histopathological changes with influx of immune cells (heart)[a] - induced innate and adaptive immune responses (heart)[a,b]	- peak of virus load in heart (and other organs)[a,b] - peak of histopathological changes, strong influx of immune cells[a] - peak of adaptive immune responses, strong expression of T cell response genes[a,b]	- sustained high virus load in heart[a,b] - sustained histopathological changes and influx of immune cells[a,b] - sustained adaptive immune reponses, strong expression of T cell respone genes[a,b]	high responders
		- high virus load in heart[b] - no/weak histopathological changes (heart)[a,b] - induced innate and adaptive immune responses (heart)[b]	- decreased virus load in heart[b] - no/weak histopathological changes (heart)[a,b] - repressed adaptive immune responses (heart)[b] - induced cardiac energy metabolism[b]	- low virus load in heart[b] - no histopathological changes (heart)[b] - repressed adaptive immune responses (heart), ablated transcription of T cell response genes[b] - induced cardiac energy metabolism[b]	low responders

Tasks (work packages)

1. **Development of reverse genetics systems for PMCV (responsible partner: NSVS)**
   - Recombinant virus, transgenes (reporter proteins), deletion mutants
2. **Protein characterisation (NSVS)**
   - Viral proteins and virions, crystal structure
3. **Viral entry and release (NSVS)**
   - Cell surface binding, entry/replication, intracellular pathways and release, ORF3 localization
4. **Virus protein functional studies (NSVS)**
   - Hemagglutination and membrane fusion
5. **Studies of host responses and risk factors (Nofima)**
   - Robustness groups and suboptimal oxygen levels
   - Challenge trial Veso Vikan week 46

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Marker-assisted selection and mechanisms of CMS resistance

- Partners:
  - Aqua Gen (N. Santi, T. Moen)
  - Nofima (S.M. Jørgensen, A. Krasnov)
  - Norwegian School of Veterinary Science (Ø. Evensen)
  - Cigene (S. Lien)

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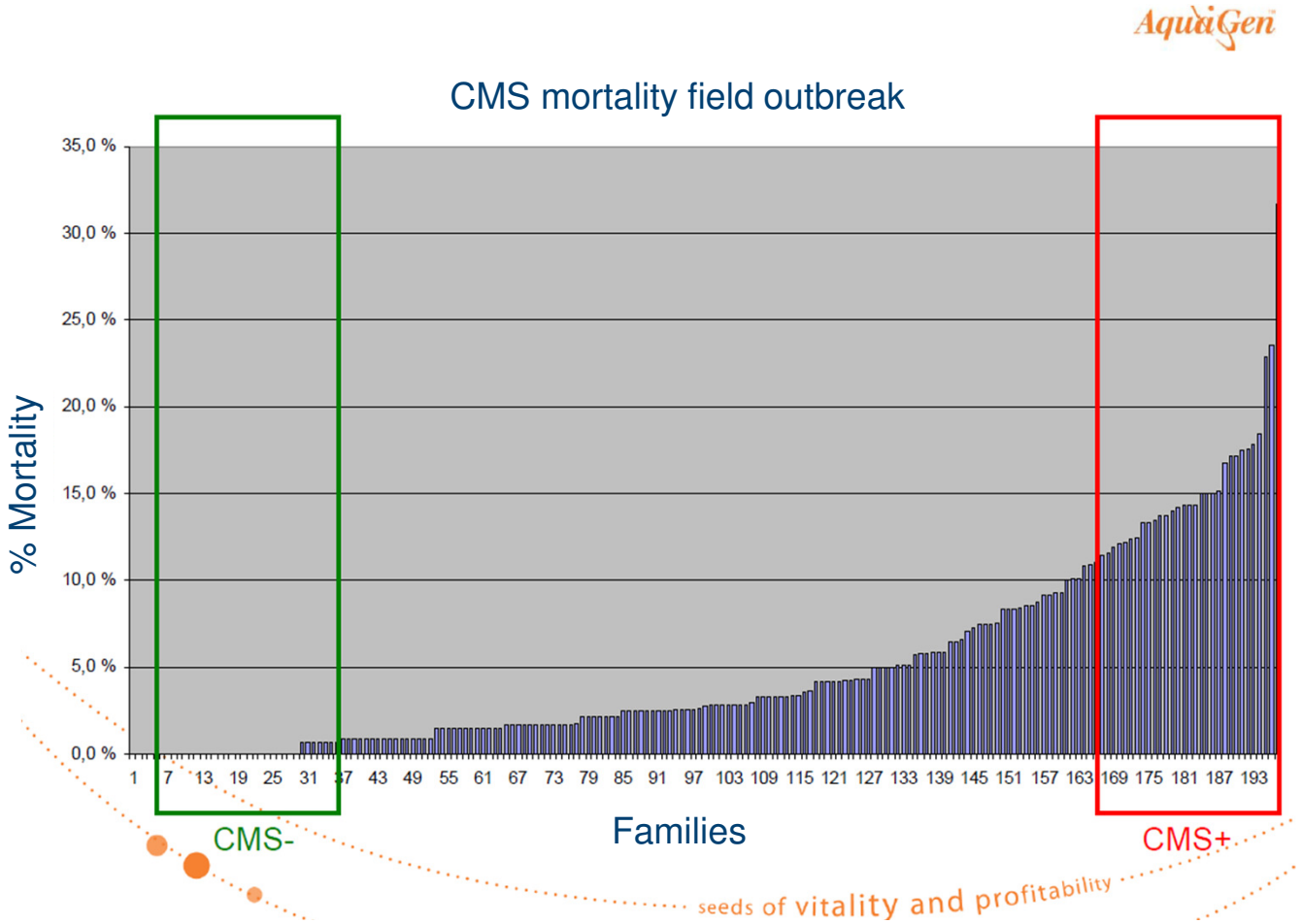
Background



- Variation between families wrt mortality & histopathology score (CMS project 187301)
- Genetic & mechanistic basis for resistance, potential for selective breeding

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Tasks

Female \male	CMS+	CMS+	CMS+	CMS+	CMS+	CMS-	CMS-	CMS-	CMS-	CMS-
CMS +	Good	Good				medium				
CMS +		Good	Good				medium			
CMS +			Good	Good				medium		
CMS +				Good	Good				medium	
CMS +	Good				Good					medium
CMS-	medium					Poor				Poor
CMS-		medium				Poor	Poor			
CMS-			medium				Poor	Poor		
CMS-				medium				Poor	Poor	
CMS-					medium				Poor	Poor

- Offspring groups from parents of extreme families
- Evaluation disease performance during experimental CMS
  - Histology, virus load
  - Host responses
  - In vitro (primary cultures of cardiomyocytes): supportive studies on functional mechanisms
  - Resistance markers, eQTLs

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CMS cohabitation challenge model for fry

Project granted 2012-2015, MABIT fund & EWOS Innovation

- Sub-task of project: 'Northern competence group: Aquaculture clinical nutrition'

- Partners:
  - EWOS Innovation (S Wadsworth)
  - Nofima (SM Jørgensen, A Krasnov, B Ruyter)
  - Norwegian School of Veterinary Science, Aquatic Medicine section (Ø Evensen)
  - Norwegian School of Veterinary Science, Nutrition section (AM Bakke, Å Krogdahl)

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Background

- Cost issues of current CMS model
  - Smolt
  - SW (contamination etc)
  - Injection
  - Long duration
- Clinical nutrition studies
  - High tank replication
  - Complex test group design
  - Large numbers of test fish

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Tasks

- Development cohabitation model (ongoing)
  - Cooperation with Havbruksstasjonen, Tromsø
  - Shedder groups: smolt vs parr
  - Cohabitation design
  - Biomass & exposure

- Disease evaluation- diagnostic tools
  - Virus load (qPCR)
  - Histopathology
  - Gene expression markers

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