



**ParaFishControl**

# **Towards the development of a vaccine for proliferative kidney disease (PKD)**

**ParaFishControl Workshop “North European Fish Parasite Management Strategies in Aquaculture Farms”**

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# Challenge and Impact

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## ➤ Challenge

- PKD: A chronic infection caused by the myxozoan, *Tetracapsuloides bryosalmonae*
- Abnormal kidney swelling compromises kidney function
- Disease emergence & spread linked to climate change processes
- High mortalities in naive infected fish
- Parasite is neither culturable nor purifiable from fish tissues

## ➤ Impact

- Economically damaging disease for trout aquaculture in Europe and USA
- Pre-exposure programs only form of control (only in EU)
- Pre-exposure prevents mass mortalities, but causes production bottlenecks
- Success of pre-exposure provides impetus for vaccine studies
- **No current fail-safe for exposure programs!!**

# Our approach and our team

## Brief description of the proposed solution

- Develop bioinformatic pipeline and RT-qPCR assay to shortlist antigens for vaccine testing.
- Focus on both known vaccine candidates & genes encoding unknown intrinsically disordered secretory proteins (IDPs) highly expressed during fish infection
- Utility of DNA vaccination and development of functional tools (recombinant proteins / antibodies) to:
  - 1) Test and validate vaccination approaches
  - 2) Test for antigen-specific antibody responses
  - 3) To understand the biological function of vaccine candidates
  - 4) To promote the development of non-invasive diagnostic tests for PKD

## Team involved in the development

- University of Aberdeen (Marc Faber, Chris Secombes, Pieter van West, Jason Holland)
- Vertebrate Antibodies Ltd (Ayham Alnabulsi); Eurofins Ingenasa (Paloma Rueda)
- Carolina Tafalla (INIA, Madrid)

# Our proposed solution (I & II)

## Comparative Transcriptomics of *T. bryosalmonae*

### Host-specific dominance indicative of biological importance

Annotatable vaccine candidates  
(eg. proteases, lipases, tetraspanins)

Predicted secretory unknown  
proteins, especially IDPs



Gene selection and characterisation by RTqPCR

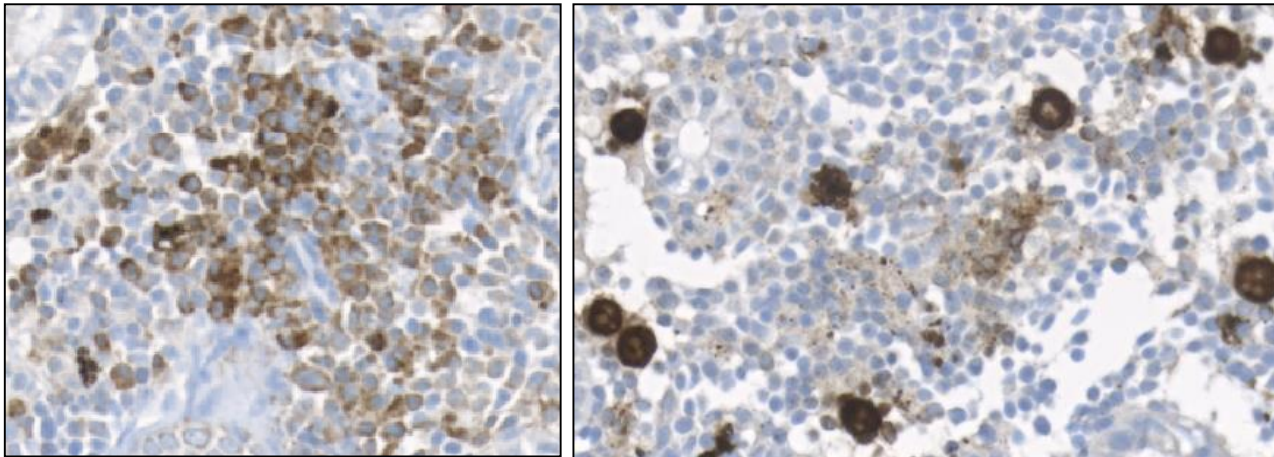
**Fish-specific annotatable  
candidates**

**Fish-specific unknown  
candidates**

# Our proposed solution (III)

## Vaccine validation & interpretation of biological function using new tools

***Tb*MEG-1 Mab to visualise Protein expression:**



**In kidney tissue to visualise parasites and affected host cells**

# Positioning of our solution vs currently available or future expected solutions

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- No current long-term solutions of controlling PKD, only restrictive pre-exposure programmes.
- Vaccination protocols need to be further developed to improve efficacy & test against different parasite populations, especially in combination with other leading fish-specific secretory unknowns / IDPs.
- Therefore, we need further investment in R&D to test more suitable vaccine candidates & other therapeutic approaches.
- Future commercial solutions (vaccine and / or non-vaccine based) are expected to sufficiently reduce PKD pathology to prevent mortalities.

# Expected benefits for the industry

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- Combined transcriptomics & host-specific expression profiling; a very effective way to shortlist further antigens for vaccine studies and identify new drug targets (eg. parasite's dependence on scavenging fish lipids)
- An ideal platform to build towards a commercially exploitable control strategy for PKD
- Functional studies open up other possibilities (eg. blocking host-*Tb*MEG-1 interaction)
- Provision & validation of *Tb*MEG-1 functional tools enables the development of future non-invasive diagnostics for PKD monitoring.

# Current status and next steps

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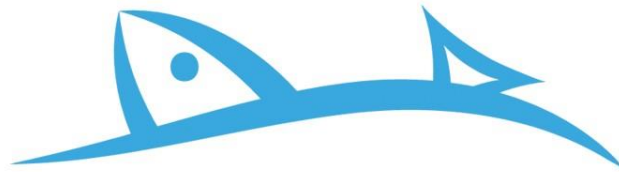
- Most field-based vaccine trials, to date, conducted using DNA vaccines
- Current most promising antigens also tested as protein vaccines
- Need to improve vaccination approach with current lead antigens
- Select additional secretory unknowns / IDPs for testing alone & in combination with current lead antigens.
- Exploit *TbMEG-1* functional tools to develop new non-invasive PKD diagnostics. Working with VAL and Eurofins Ingenasa to develop sandwich ELISA to detect endogenous *TbMEG-1*
- Future planned uptake to be discussed with VAL, Eurofins Ingenasa, (& others?)

# Conclusions

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- Combining comparative parasite transcriptomics with functional approaches provides a solid foundation for antigen selection for vaccine studies and identification of other targets for drug intervention
- DNA and protein-based vaccination protocols require further optimization to improve current efficacy levels
- A need to exploit PKD functional tools to develop a rapid non-invasive diagnostic test to facilitate disease monitoring / epidemiological studies.

# Thank You



## ParaFishControl

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