ParaFishControl

Working towards a vaccine against *Sphaerospora molnari*

ParaFishControl Final Conference

"Innovative Strategies to Control Parasites in Aquaculture Farms"

Brussels, 11th March 2020

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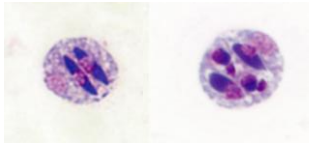
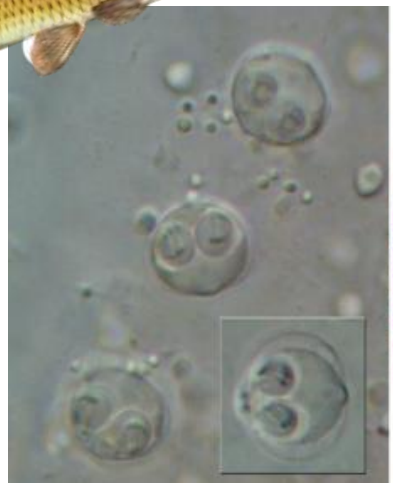
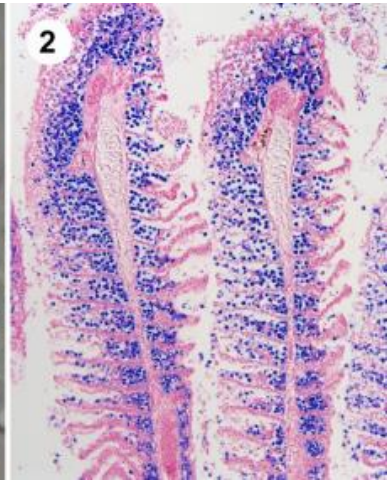
Who is *S. molnari*?

- Myxozoan (cnidarian)
- Agent of skin and gill disease of common carp (CC)
- Model for myxozoan proliferation research
- Transferability







Eszterbauer et al. *Dis. Aquat. Org.* 104: 509-607 (2013)

ParaFishControl: How can we develop a vaccine against *S. molnari*?

Search for & verification of good vaccine candidates:

- Antigenic surface proteins that cause immunity and protection to re-infection in fish
- Host-parasite interaction proteins: secreted proteases and their inhibitors

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S. molnari infection & immunity

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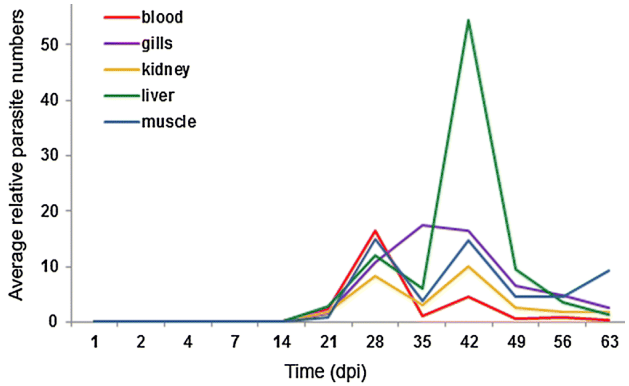
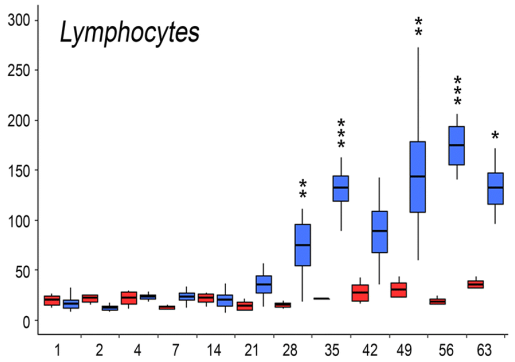
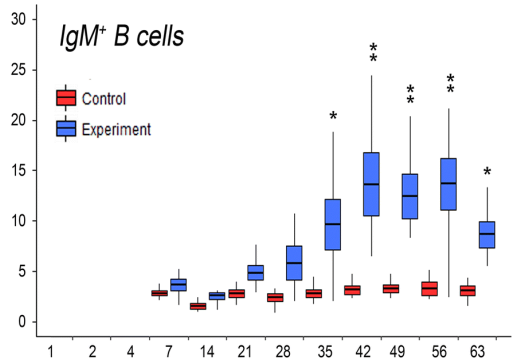
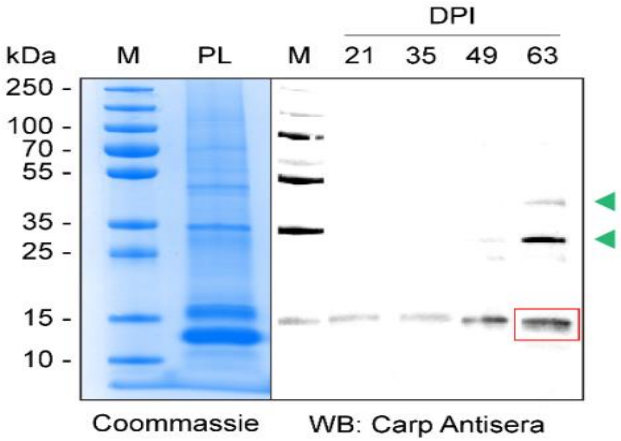
- **Does carp produce specific antibodies to *S. molnari* antigens?**

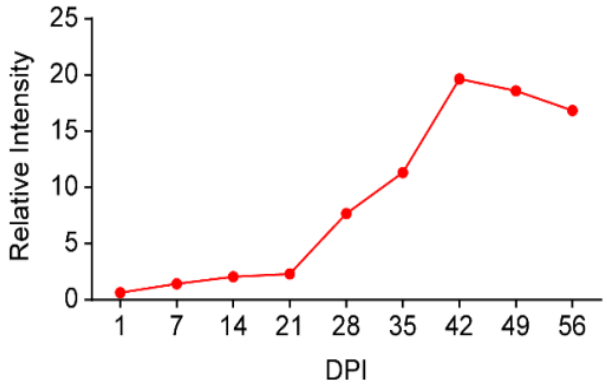






Korytar et al. *Parasit. Vect.* 12: 208 (2019)





Yes. But *S. molnari* likely uses immune evasion strategies.

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S. molnari protective immunity

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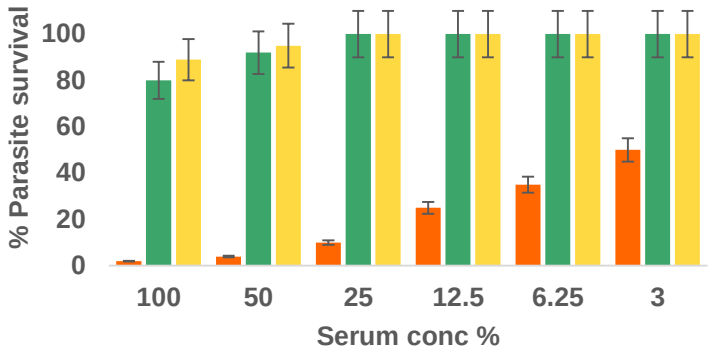
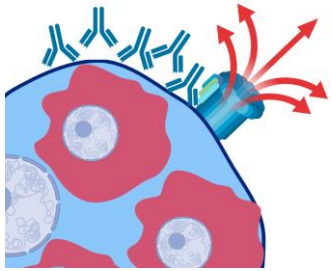
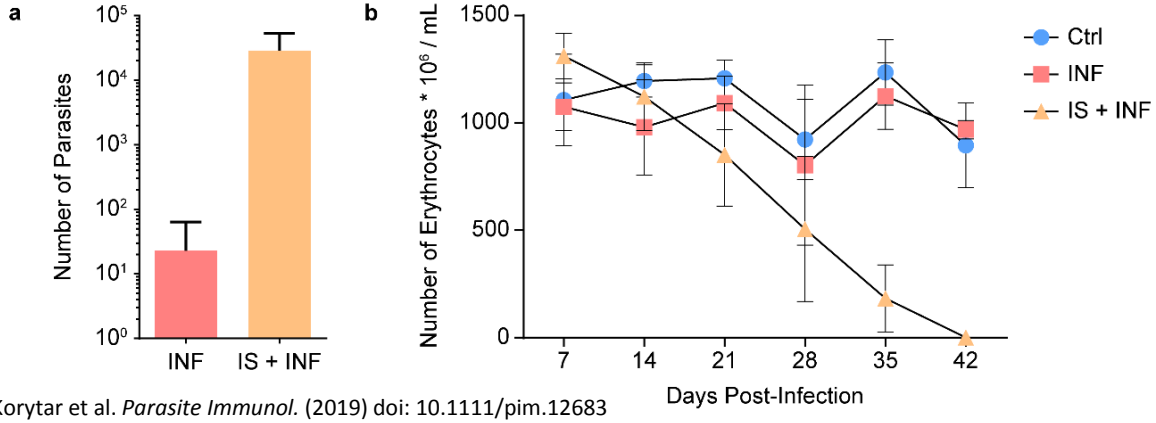
- **Do the antibodies have *S. molnari* killing capacity?**





Yes. But killing capacity depends on parasite lot.

- **Are the antibodies important/is specific immunity important?**



Korytar et al. *Parasite Immunol.* (2019) doi: 10.1111/pim.12683

Yes! Without it the parasites take over and kills its host.

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S. molnari immunity & antigens

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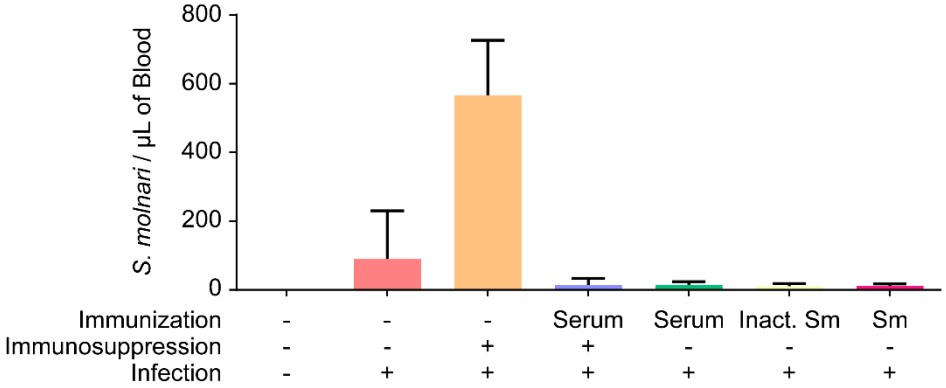
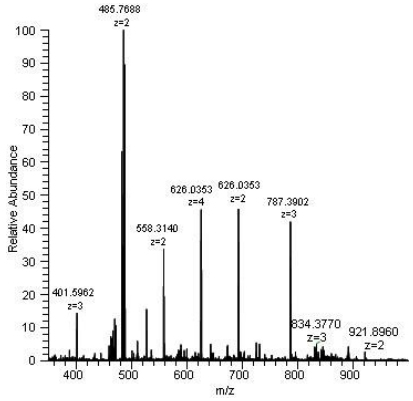
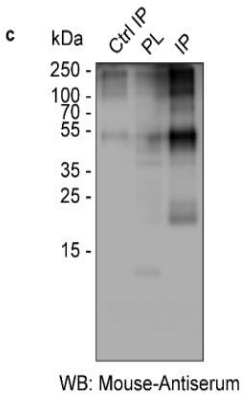
- Can we immunize carp against *S. molnari* with these antibodies?



Yes. Both, parasite extracts and immune sera provide protection against infection with *S. molnari*.

- Identification of antigenic proteins of *S. molnari* and vaccination trials





- **Mass spec of relevant proteins**
- **Immunoprecipitation**
- **Parasite membrane proteome**

We're on it.

Join forces.

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S. molnari proteases and inhibitors

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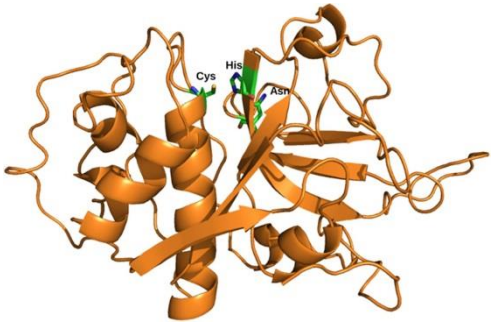
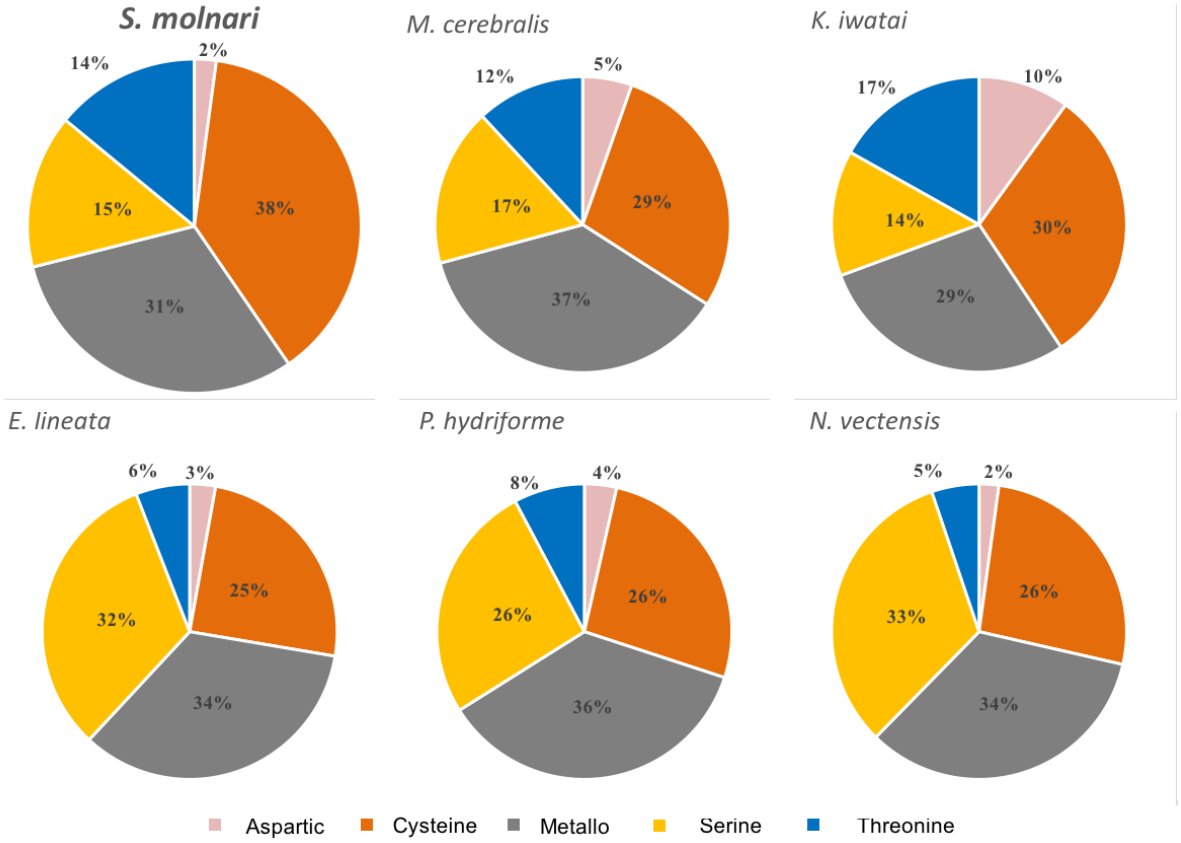
- **Protease household of *S. molnari* blood stages - transcriptome**

- 235 proteases and protease inhibitors
- 2.5% of proteins in the transcriptome
- Cysteine proteases 38% vs. 25-30%
- Candidates that are secreted (signal pep)





Hartigan et al. *BMC Genomics* in press

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S. molnari proteases and inhibitors

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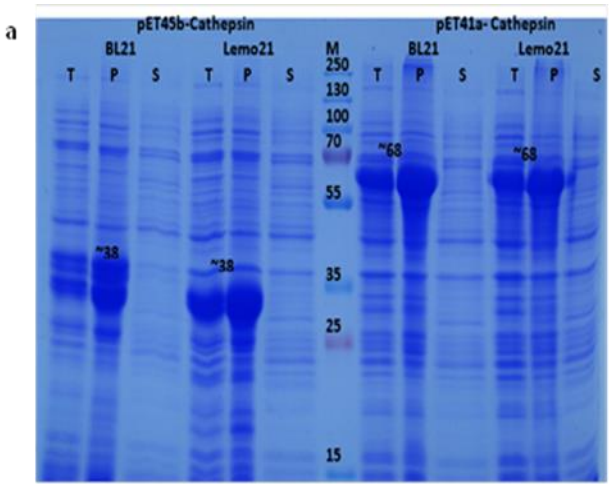
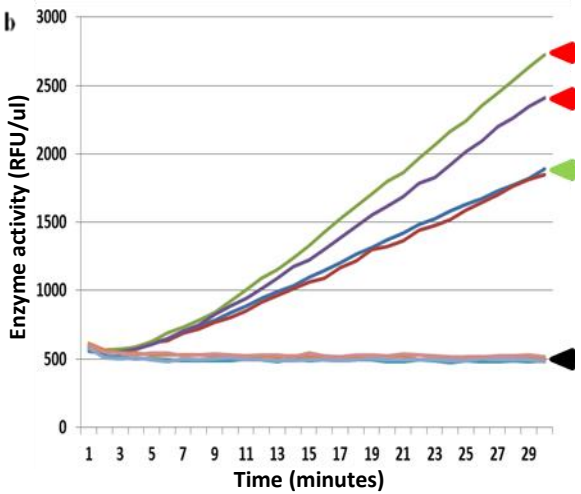
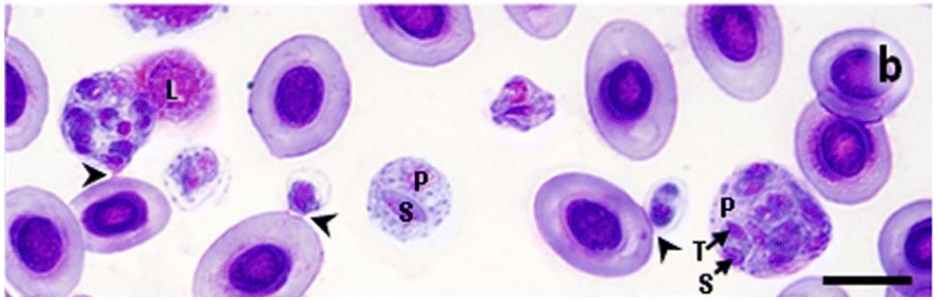
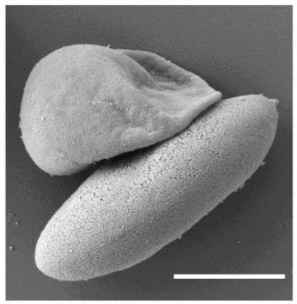
- **Smol Cathepsin L – an important parasite protease for host exploitation**

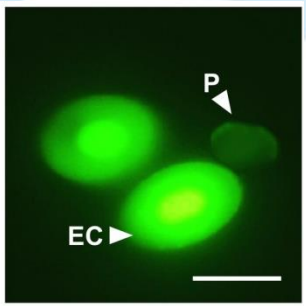




- Extremely high expression in all stages, especially blood stages
- Feeding
- Recombinant protein: Not soluble, optimal pH is low - lysosomal
- Vaccination trial ongoing







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S. molnari proteases and inhibitors

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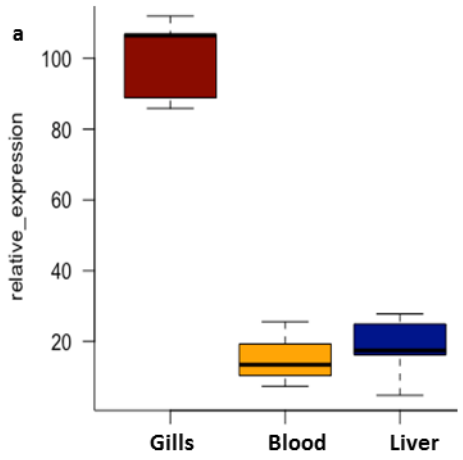
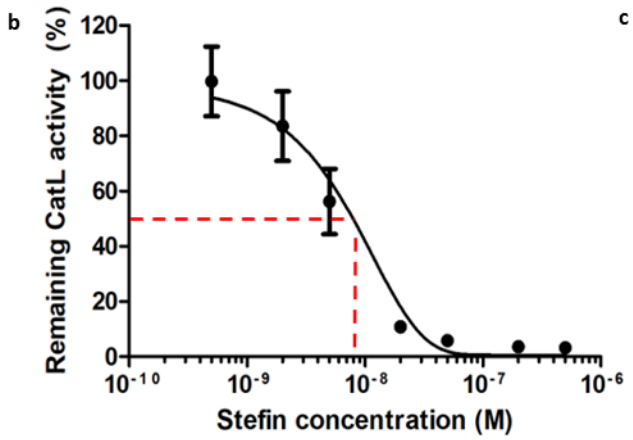
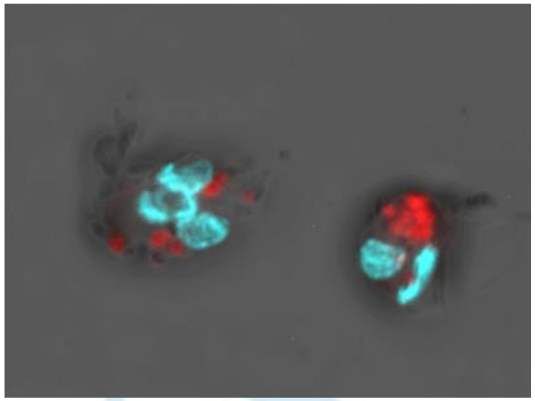
- **Smol stefin – a cysteine protease inhibitor active in the gills**







- High expression in the gills
- Inhibit host recognition of histozoic stages/spores?
- Recombinant protein: Inhibits Cathepsin L
- Antibody detection: Lysosomal? compartments in blood stages but functions at various pHes
- Function in gill stages?

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Summary & conclusions

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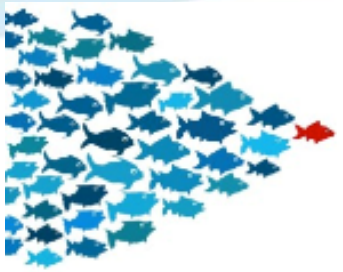
- Carp acquires specific immunity to *S. molnari* and we discovered that the parasite has several antigens with immunogenic potential
- Antibodies produced to these proteins by CC protects fish from infection and can kill the parasite
- Identification of these antigens is difficult
- We will likely need to use a combination vaccine to be able to combat immune evasion strategies of *S. molnari*
- We expect high effectivity of a vaccine based on immunogenic surface proteins and predict transferability of methods and potentially molecules to vaccine design in other myxozoans
- *S. molnari* protease and inhibitor research has improved our understanding of myxozoan host exploitation strategies. If these proteins are successful as vaccines has yet to be confirmed.
- Overall, ParaFishControl has greatly advanced functional protein analyses and vaccine discovery research in *S. molnari*



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Thank You

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Contact details

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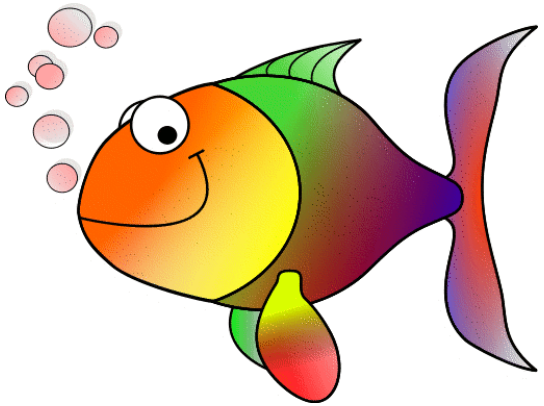

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