

## ROHER'S LAB BACKGROUND



We are a young group starting its independent activity in 2010, with a solid formation in fish immunology and with the capacity to start new collaborative and multidisciplinary projects. Over the past decade the PI have focused her work in the study of pro-inflammatory responses of fish macrophages with special emphasis on LPS-TNF $\alpha$  pathway (Roher et al., 2008; Roher et al., 2011). These studies provide insight into the specific features of trout TNF $\alpha$  system and shed light on how fish immune system could be modulated after bacterial or viral challenge (Mackenzie et al., 2008). By dissecting the LPS response we have described different molecules that take part in this response in different fish species such as eel, seabass, seabream or trout (Callol et al., 2013; Mauri et al., 2011; Ribas et al., 2008; Doñate et al., 2007). Other input signals such as viral (Poly I:C) and bacterial (peptidoglycan) have been also studied during the last years and importantly, we have demonstrated that peptidoglycan is a central stimulus in the fish innate immune response (Mackenzie et al., 2010).

Using wide genome analysis and zebrafish as a model, we have recently completed an analysis (Boltaña et al., 2013) showing for the first time in fish the importance of behavioural fever in zebrafish and how fever is a synergic signal that improves the immune system efficiency. This project is the main research line of Dr. Mackenzie and the PI has been collaborating in his research line mainly performing the genome wide analysis (microarrays) and the experimental design.

Our research background has allowed us to design a nanovaccine composed of a lipid bilayer encapsulating LPS and Poly I:C. The rationale behind this vaccine is that all the fish species are able to respond to LPS and Poly I:C and we can use this formulation to achieve high levels of protection for virtually all fish species (Ruyra et al., 2013 and Ruyra et al., 2013 manuscript in preparation).

The major challenge now is to take the data from basic research and translate it to obtain better vaccines. To achieve this, we need to develop novel approaches in a multidisciplinary environment and also we need a better understanding of how fish immune system works to integrate the data within the vaccine design.

Selected publications (2008-2013; see PI Resume for an extended publication record):

Ruyra A., Cano MA., Mackenzie SA., Maspoch D., Roher N. (2013) In vivo dynamics and functionality of LPS/dsRNA encapsulating liposomes. Manuscript in preparation.

Rey, S., Boltana, S., Vargas, R., Roher, N. and MacKenzie, S. (2013) Combining animal personalities with transcriptomics resolves individual variation within a wild-type zebrafish population and identifies underpinning molecular differences in brain function. Accepted in Mol. Ecology

Ruyra A., Cano MA., Mackenzie SA., Maspoch D., Roher N. A novel liposome-based nanocarrier loaded with an LPS-dsRNA cocktail for fish innate immune system stimulation. Accepted in PlosOne (2013).

Callol A, Roher N., Amaro C., Mackenzie, SA. Characterization of PAMP/PRR interactions in European eel (*Anguilla anguilla*) macrophage-like primary cell cultures. Fish and Shellfish Immunology doi:pii: /j.fsi.2013.07.037 (2013).

Boltaña S., Rey S., Roher N., Vargas R., Huerta M., Huntingford FA., Goetz FW., Moore J., Garcia-Valtanen P., Estepa A. and MacKenzie S. Behavioural fever is a synergic signal amplifying the innate immune response. Proceedings of the Royal Society B Sep 7;280(1766):20131381 (2013)

Ferrer-Navarro M., Planell R., Yero D., Mongiardini E., Torrent G., Huedo P., Martínez P., Roher N., Mackenzie S., Gibert I., Daura X.. Abundance of the Quorum-Sensing Factor Ax21 in Four Strains of *Stenotrophomonas maltophilia* Correlates with Mortality Rate in a New Zebrafish Model of Infection. PlosOne;8(6):e67207 (2013).

Crespo, D., Mañanos, EL., Roher, N., MacKenzie, SA., and Planas, JV. Tumor necrosis factor  $\alpha$  may act as an intra-ovarian mediator of luteinizing hormone-induced oocyte maturation in trout. Biol Reprod. 86(1):1-12 (2012).

Morera D, Roher N, Ribas L, Balasch JC, Doñate C, Callol A, Boltaña S, Roberts S, Goetz G, Goetz FW, MacKenzie S. RNA-Seq reveals an integrated immune response in nucleated erythrocytes. PLoS One. 6(10):e26998 (2011).

Boltaña S, Roher N, Goetz FW, Mackenzie SA. PAMPs, PRRs and the genomics of gram negative bacterial recognition in fish. Dev Comp Immunol. 35(12):1195-203 (2011).

Mauri I, Roher N, MacKenzie S, Romero A, Manchado M, Balasch JC, Béjar J, Alvarez MC, Tort L. Molecular cloning and characterization of European seabass (*Dicentrarchus labrax*) and Gilthead seabream (*Sparus aurata*) complement component C3. Fish Shellfish Immunol. 30(6):1310-22 (2011).

Vraskou Y, Roher N, Díaz M, Antonescu CN, MacKenzie SA, Planas JV. Direct involvement of tumor necrosis factor  $\alpha$  in the regulation of glucose uptake in rainbow trout muscle cells. Am J Physiol Regul Integr Comp Physiol. 300(3):R716-23 (2011).

Roher N., Callol A., Planas JV., Goetz FW. and MacKenzie SA. Shedding of TNF $\alpha$  by TACE/ADAM17-like activity in fish is conserved throughout evolution and regulation of TNF $\alpha$  secretion does not contribute to LPS tolerance. Innate Immun. 17(1):16-28 (2011).

Mackenzie S.\*, Roher N.\*, Boltaña S., Goetz FW. Peptidoglycan, not endotoxin, is the key mediator of cytokine gene expression induced in trout macrophages by crude LPS. Mol Immunol. 47(7-8):1450-7 (2010). \* both authors contributed equally.

MacKenzie S, Balasch JC, Novoa B, Ribas L, Roher N, Krasnov A, Figueras A. Comparative analysis of the acute response of the trout, *O. mykiss*, head kidney to in vivo challenge with virulent and attenuated infectious hematopoietic necrosis virus and LPS-induced inflammation. BMC Genomics 26, 9:141 (2008).

Roher N, Samokhvalov V, Díaz M, Mackenzie S, Klip A, Planas JV. The proinflammatory cytokine TNF $\alpha$  increases the amount of GLUT4 at the surface of muscle cells independently of changes in IL-6. Endocrinology 149, 1880-9 (2008).