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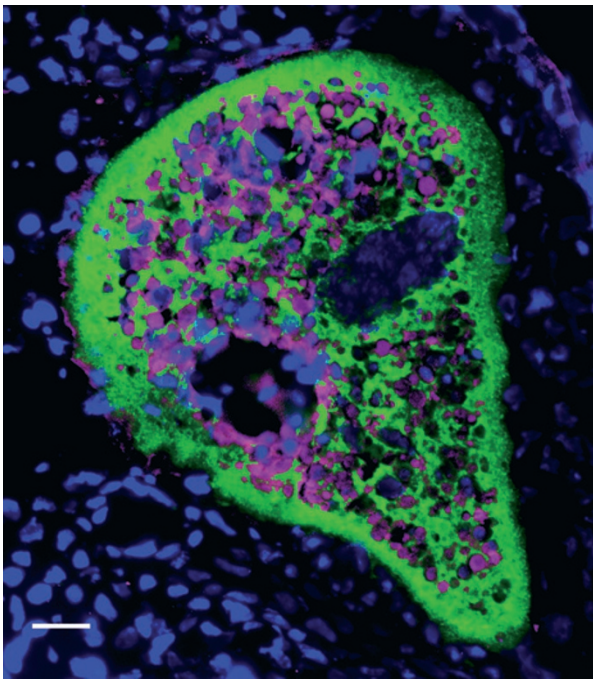
EVOLUTION

A gutsy defence of the skin

A new study from the group of J. Oriol Sunyer provides a fascinating insight into the evolutionary origins of mucosal immune defences. The authors show that the specialized adaptive immune mechanisms that are used to promote intestinal immunity in teleost fish are also used to protect their skin.

Early vertebrates — such as teleost fish — originated in aquatic environments and their skin resembles a mucosal surface, as it comprises living epithelial cells and contains many mucus-producing cells but lacks keratinization. The authors reasoned that the immune responses in the skin of teleost fish may resemble the responses seen in mucosal tissues, such as the gut.



IgT is shown surrounding an *Ichthyophtirius multifiliis* trophont on the skin epidermis of an infected rainbow trout. The *I. multifiliis* trophont is stained in magenta, IgT is stained in green and the cell nuclei are stained with DAPI (blue). Scale bar represents 20 μm. Image courtesy of D. G. Atria and J. O. Sunyer, School of Veterinary Medicine, University of Pennsylvania, USA.

A key hallmark of mucosal immunology in mammals is the production of polymeric IgA antibodies, which regulate microorganisms in a non-inflammatory manner. The authors previously found that intestinal immunity in teleost fish involves the production of IgT, which is analogous to mammalian IgA. Therefore, they examined whether IgT is associated with the skin of teleost fish. Indeed, IgT could be detected in the skin mucus of rainbow trout (*Oncorhynchus mykiss*), mainly in its polymeric form. Epithelial cells in trout skin also expressed the polymeric immunoglobulin receptor, which is needed to transport immunoglobulins to mucosal surfaces. Higher levels of IgM than IgT were detected in both trout serum and skin mucus, but the ratio of IgT to IgM was 38-fold higher in the skin mucus compared with in the serum. Furthermore, ~60% of B cells isolated from trout skin were IgT-positive, which suggests that IgT has important functions at this site.

What might these functions be? The authors found that ~38% of trout skin bacteria were coated with IgT, whereas only ~12% were coated with IgM. In fact, more than 50% of the total IgT present in the skin mucus was found to be coating bacteria (compared with 8% of total IgM). The authors suggest that this IgT is likely to be crucial for regulating the skin microbiota.

They further investigated whether IgT contributes to protective immunity by infecting trout with the skin-tropic parasite *Ichthyophtirius multifiliis*, which causes white spot disease. Fish that survived *I. multifiliis* infection had a marked accumulation of IgT-positive B cells in the skin epidermis, but no accumulation of IgM-positive B cells. The characteristic white spots of the disease are caused by *I. multifiliis* trophonts, and the authors found that trophonts on the epidermis of infected trout stained with antibodies specific for IgT but not with those specific for IgM. Finally, they showed that IgT was the main parasite-specific immunoglobulin measurable in the skin mucus of trout that survived *I. multifiliis* infection, whereas IgM was the main parasite-specific immunoglobulin found in the serum.

These data show that adaptive immune responses in the skin of teleost fish share common features with mammalian mucosal immune responses. The authors suggest that the immunoglobulin responses that protect our mucosal surfaces are based on primordially conserved principles.

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ORIGINAL RESEARCH PAPER Xu, Z. *et al.* Teleost skin, an ancient mucosal surface that elicits gut-like immune responses. *Proc. Natl Acad. Sci. USA* **110**, 13097–13102 (2013)