



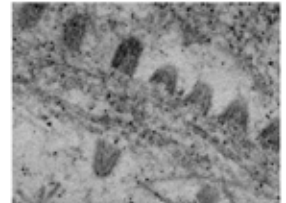
ZEBRA-VIRUS

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BIOLOGIE & SANTE 2011



INSTITUT PASTEUR



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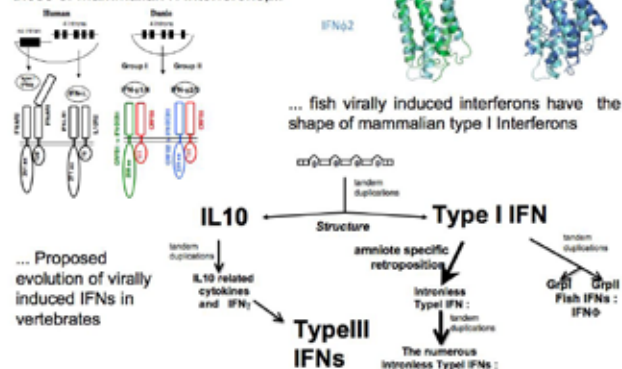
Objectives of the project: development of tools to study host-virus interactions in the zebrafish

Main approaches: functional genetics, genetic engineering, bioinformatics, whole-body imaging

The zebrafish virally induced interferon system : ligands and receptors

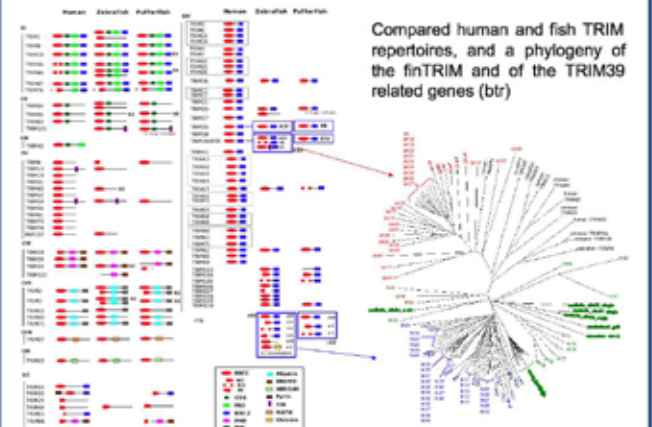
The zebrafish virally induced interferon genes were identified using in silico screens in the assembled genome. Their induction in larvae and adults were measured in the course of different infections. Their biological activity in terms of protection of the larvae against viral infections were checked. Using loss of function and gain of function genetic analysis, their receptors were identified. 3D structure of ligands were established by X-ray crystallography.

Despite genes and receptors like those of mammalian λ interferons,...



The highly diversified TRIMs of teleosts

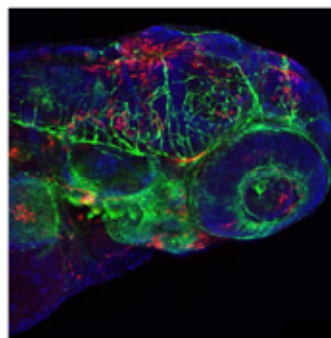
The tripartite motif (TRIM) proteins are involved in various cellular processes including innate immunity against viral infection. Starting from a TRIM-encoding transcript found among virus-induced fish genes, we have described the entire TRIM repertoire of the zebrafish, that contains 197 genes (vs 79 in humans). The increase is mostly due to three highly diversified subfamilies with C-terminal B30.2 domains: the fish-specific finTRIMs (the biggest with 84 members), and orthologues of TRIM35 and TRIM39. These genes show evidence of positive selection at residues of the B30.2 domains that correspond to viral capsid binding in human TRIM5. These diversified families are likely to play a role in viral restriction.



Whole-body imaging of a viral infection

The progression of viral infections is notoriously difficult to follow in whole organisms. The small, transparent zebrafish larva constitutes a valuable system to study how pathogens spread. We have described the course of infection of zebrafish larvae with Infectious Hematopoietic Necrosis Virus (IHNV), a fish rhabdovirus. This virus primarily targets endothelial cells, causing a hemorrhagic disease. This tractable system allows the in vivo dissection of host-virus interactions at the whole organism scale. Live imaging of the infection is also possible with a fluorescent recombinant virus.

Destruction of blood vessels by IHNV and spread to adjacent tissues.



This *fl1:GFP* transgenic zebrafish larva has been inoculated with Infectious Hematopoietic Necrosis Virus (IHNV), fixed 24 hours later, processed for whole-mount immunohistochemistry, and imaged with a confocal microscope to reveal virus-infected cells (anti-G-IHNV antibody, red), endothelial cells (GFP, green), and nuclei (blue). Infection of several vessels can be observed, especially at the top of the head, where loss of GFP expression has occurred, as well as infection of neighboring tissue. Although at this stage the larva does not display obvious macroscopic signs of disease, it is already doomed.

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Publications :

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