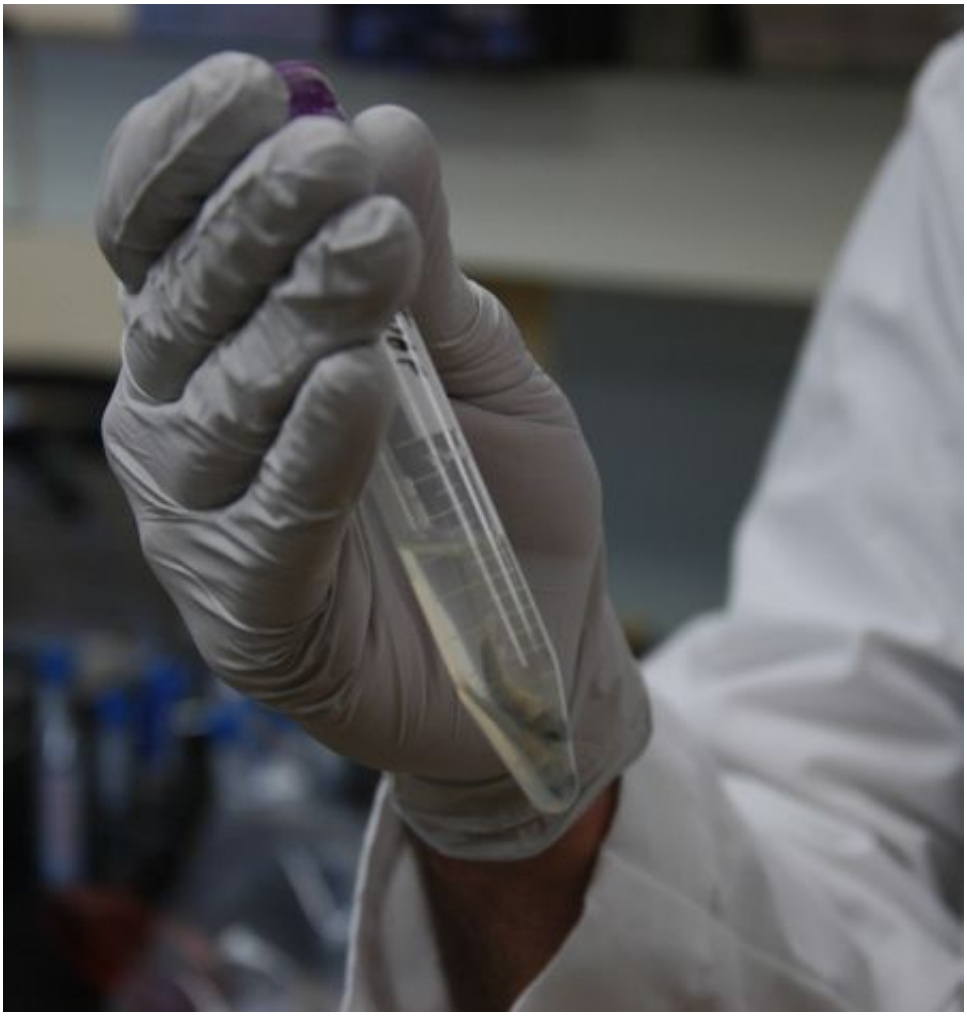
Nasal immunity is an ancient adaptation of the mucosal immune system of vertebrates

November 25 2014, by Steve Carr



UNM researchers found nasopharynx-associated lymphoid tissue, or NALT, while studying trout. NALT acts as a line of defense against pathogens similarly like other mucous membranes in terrestrial vertebrates including humans. Credit: Steve Carr

(Phys.org) —Researchers at the University of New Mexico recently discovered an olfactory immune system in fish previously thought to be associated with terrestrial vertebrates only. The results could provide a new tool for the control of infectious diseases in fish farms and hatcheries.

Olfaction is an ancient sensory system more than 350 million years old. In land-based vertebrates, the olfactory system detects low concentrations of volatile, airborne chemicals whereas aquatic vertebrates use olfactory organs to smell odorants present in the water. The olfactory system is clearly vital to both land and water-based animals.

UNM researchers in the Department of Biology, led by Assistant Professor Irene Salinas and including, Postdoctoral Fellow Luca Tacchi and undergraduate student Rami Musharrafieh, discovered that fish noses are not just "smelling organs." Over the past three years, the team discovered the presence of a nasopharynx-associated lymphoid tissue, or NALT, while studying trout and found that it acts as a line of defense against pathogens similarly like other mucous membranes in terrestrial vertebrates including humans.

Previously, it was believed that NALT was restricted only to terrestrial vertebrates, including birds and mammals. Having a nasal immune function was something that everyone thought only happened in birds and mammals because if you breathe something that is dangerous, you react by mounting an immune response through the airways or lungs. Since NALT represents a first line of defense against inhaled antigens, humans can receive spray vaccines such as the flu vaccine via the nose. However, for millions of years, the mucosal surfaces of all vertebrates, terrestrial and aquatic, were exposed to similar evolutionary processes. This idea prompted the team to hypothesize that aquatic vertebrates also have the need to protect their olfactory organs from infectious agents.

"Everyone thought the NALT was restricted to terrestrial vertebrates and no one thought that aquatic vertebrates, like fish, respond to dangerous particles present in the water that come in contact with their nose," Salinas said. When the team found NALT in trout, they quickly realized the potential of exploiting nasal vaccines in aquaculture settings. "Our results open up a new tool for the control of aquatic infectious diseases via nasal vaccination."

UNM undergrad Erin Larragoite (l.) and Assistnat Professor Irene Salinas prepare a test sample to study under the microscope. Credit: Steve Carr

This novel research shows that intranasal vaccination protects fish both against viruses and bacteria as well or better than traditional injection

vaccination. Intramuscular injection vaccinations are generally used in the fish farming industry and are similar to humans receiving a flu shot with a needle. By looking at intranasal delivery, which has also been done in humans as well as a few other terrestrial species and is known to offer a good level of protection, the researchers can determine if there is an immune response occurring in the olfactory system of these individual fish.

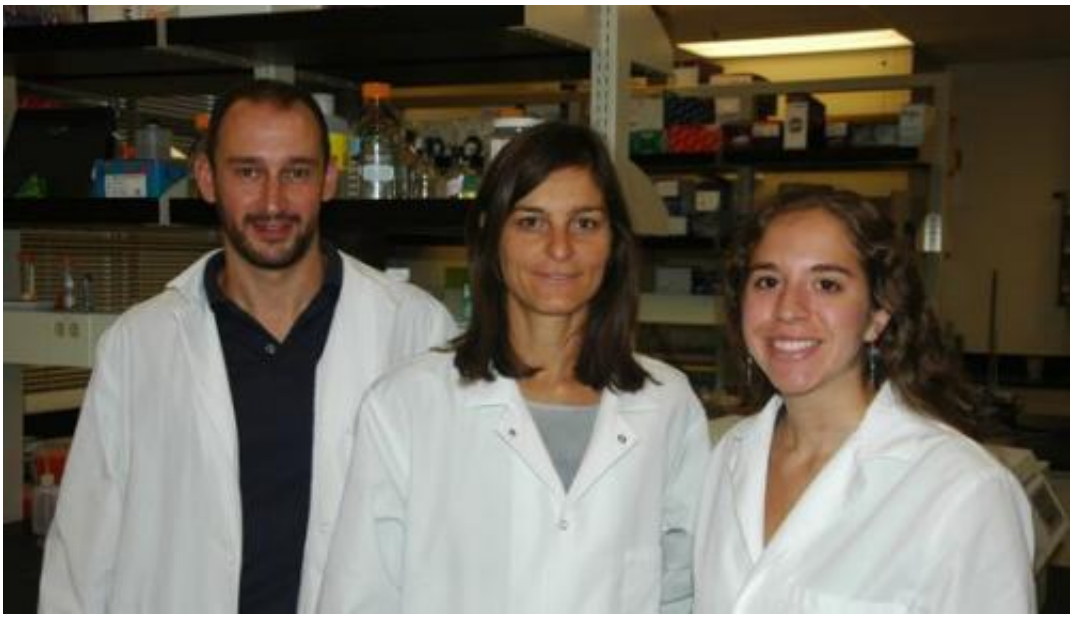
The selection of the infection model was made based on previous research showing the importance of the olfactory organ to fish during a disease called infectious hematopoietic necrosis (IHN) caused by IHN virus (IHNV), a fatal virus that threatens salmonid species including rainbow trout. "IHNV can spread through the nervous system into the brain and other organs, and quickly kills the fish," Tacchi said. "The idea was to discover a new method to vaccinate fish using these novel, needle-free nasal vaccinates. The fish were vaccinated using a thin pipette and a very small volume of the vaccine delivered into one nostril was enough to protect young fish."

Extensive collaborations with industry partners in Idaho spearheaded by Dr. Scott LaPatra have been instrumental at revealing the power of these vaccines. "We have now tested three other fish vaccines using this method and they all work very well," Salinas said.

The research, titled "Nasal immunity is an ancient arm of the mucosal immune system of vertebrates," was published recently in *Nature Communications*. The researchers found NALT present in trout and that it resembled other mucosa-associated lymphoid tissues such as the skin, gills and gut.

NALT in trout consists of diffuse lymphoid cells, but lacks organized structures such as tonsils and adenoids found in humans. Yet, this less complex NALT found in fish is very effective and sufficient to protect

them against pathogens that reach their olfactory organs. "This study helped us increased our basic understanding of immunity, but can also be translated into human medicine," said Salinas. "This is actually a great finding since we can now use trout as a model to study nasal immunity in humans in the absence of tonsils or adenoids (many people get these removed surgically at some point of their lives)."



(l. to r.): Postdoctoral Fellow Luca Tacchi, Assistant Professor Irene Salinas and Erin Larragoite. The researchers discovered a nasal immunity defense system, NALT, in trout. Credit: Steve Carr

We all co-exist with millions of bacteria in our mucous membranes that are beneficial and help us fight pathogens. "Fluorescent probes allow us to mark different players such as the beneficial bacteria present in the trout nose. We also studied the antibodies secreted into the nasal mucus and the cells that produce these antibodies" said Erin Larragoite, who was an undergrad working in Salinas's lab and a co-author of the paper. Again, similar to humans, trout olfactory organs are the home of millions

of good bacteria that are controlled by nasal antibodies.

Initially, the researchers measured the levels of expression of several immune genes and markers for myeloid and lymphoid cell types to test whether or not the olfactory organ expressed immune relevant genes. To their surprise, they found that the trout olfactory organ expresses immune genes at levels comparable to those found in main immune organs such as the head-kidney.

"The magic happened when the nose was stimulated with the IHNV vaccine," Salinas said. "When we added a vaccine through the nose, we noticed it was taken by the olfactory rosette and quickly induced a local immune response and the activation of many, many new genes following vaccine delivery. We also saw a very strong induction of systemic immune responses leading to a fast migration of immune cells from the blood into the nose. The beauty of every nasal organ of any vertebrate is that it's very well-vascularized. We (and fish) have so many blood vessels there that the connection of the local nasal immune response with the systemic immune response in the blood is extremely fast."

The quick formation of new blood vessels and the arrival of the immune cells to the site of the vaccine amplify the immune response rapidly. Researchers were able to detect systemic responses in the head-kidney which is a main immune organ in trout similar to bone marrow in humans. Nasal vaccination appears to induce both systemic and mucosal immune responses. The research shows the widespread presence of immune functions associated with the olfactory organ of vertebrates.

More information: "Nasal immunity is an ancient arm of the mucosal immune system of vertebrates." *Nature Communications* 5, Article number: 5205 DOI: 10.1038/ncomms6205