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How do the vascular systems of humans and fish differ?

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ABSTRACT

Fish are often considered simple animals, but they are in fact the most diverse group among vertebrates. According to current models, the embryonic development of the vascular systems starts similarly in fish and humans. However, living in water required fish to develop different adaptations compared to land animals. Thus, there are surprising differences during later stages of vascular development between fish and humans.

INTRODUCTION

All humans have a lymphatic vascular system in addition to the cardiovascular system. Blood circulation transports oxygen and nutrients, but what does the lymphatic vascular system do? Blood vessels are permeable to small molecules, mostly water. Because our blood is subjected to the pumping pressure of the heart and the hydrostatic pressure by gravity, fluid constantly leaks from blood vessels, especially from the smallest vessels, the capillaries. This phenomenon is called capillary filtration. Some of the fluid might be reabsorbed into the bloodstream at the venous end of the capillary bed, but generally, the lymphatic system collects the excess fluid and returns it to the bloodstream. In addition, lymphatic vessels are highways and transport routes for immune cells.

By the early 20th century, the basic functioning of the human heart and the cardiovascular system was understood, and researchers assumed that other vertebrates, including fish, largely resembled humans in anatomy and function of blood and lymphatic vessels. However, when German researcher Walter Vogel tried to study fish lymphatics more closely in 1981, he found none (1). Instead, Vogel observed that fish have two parallel circulatory systems. Physiology textbooks on fish had to be revised: fish do not have a lymphatic system! The other vascular system was named the secondary vascular system (SVS). In 2006, zebrafish embryos were

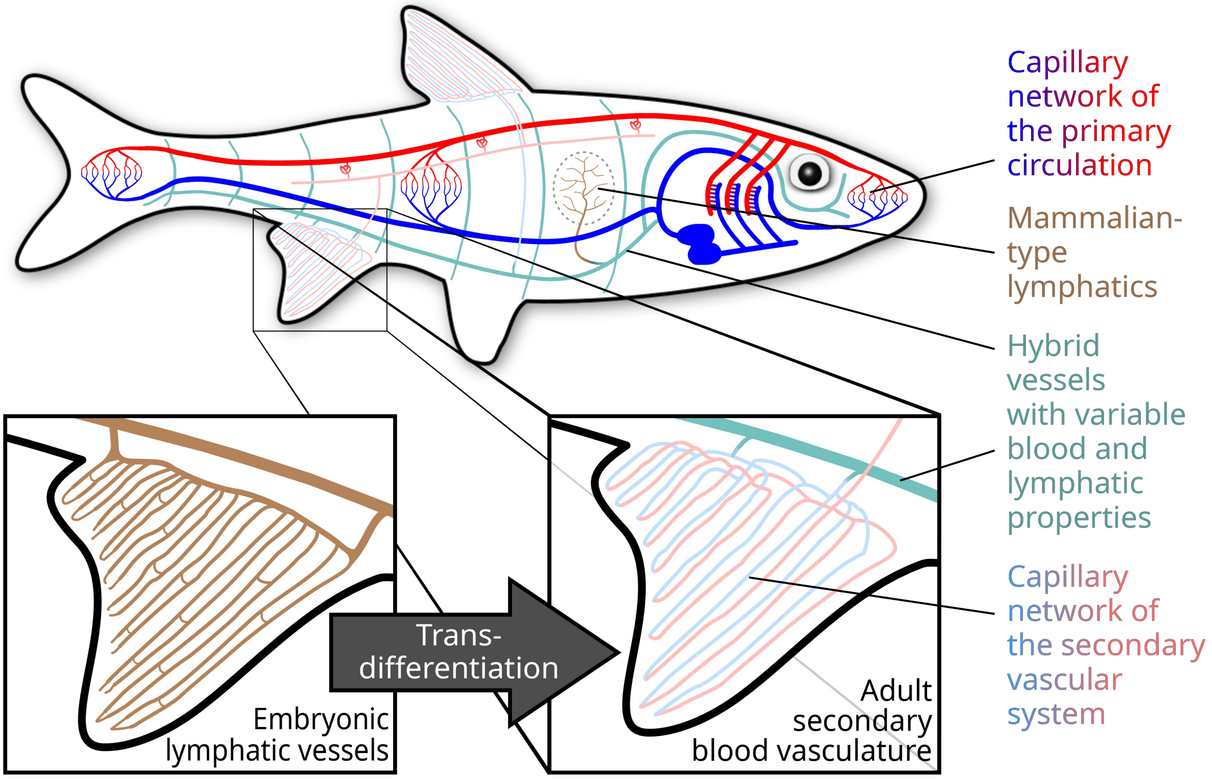

Figure 1. Fish have two types of blood vessels: primary vessels, which function similarly to human blood vessels, and secondary vessels. Secondary blood vessels are mainly located at the body surfaces, allowing fish to breathe through their skin when the oxygen content in the surrounding water is high. When the water contains little oxygen, fish conserve oxygen by preventing red blood cells from entering the secondary vessels and losing oxygen through the skin. Secondary vessels develop from the lymphatic system via transdifferentiation as fish mature into adults. Since, for example, the lymphatic vessels of internal organs do not transdifferentiate, there are hybrid vessels below the junction of secondary vessels and lymphatic vessels.

studied with better techniques, and these tiny fish did have lymphatic vessels after all (2). Since then, researchers have debated whether or not fish have a lymphatic system. In our study, we examined how the many different and often controversial experimental descriptions of the fish vasculature could fit together into a unified whole.

HOW WAS THE RESEARCH DONE?

We compiled all previous studies related to fish blood and lymphatic vessels into a review article. A review differs from experimental research, which involves detailed but limited and descriptive experiments. In our review, we also presented a model that we developed, which describes the fish vascular system, including the secondary vascular system, embryonic development, evolution, and systemic function.

Our model is consistent with experimental studies. The oldest study we found describing differences between secondary vessels and lymphatic vessels was over 145 years old. Most information was gained from experimental studies conducted in the last 20 years using advanced imaging techniques, genetic analysis, and observations of fish development and physiology. Very illuminating studies have been conducted at the Karolinska Institute in Stockholm, where researchers used transparent glass catfish for direct observation of blood vessels (3), and at the Weizmann Institute in Israel, where researchers examined blood vessel development in zebrafish fins (4). Our model explains most of the experimental results produced by hundreds of researchers over the past 250 years.

WHAT DID WE FIND?

There is broad consensus among vascular biologists that vascular system development begins in a highly similar manner in fish and humans. First, the heart and blood vessels form. Later, the lymphatic system originates from central embryonic veins as an outgrowth that connects with other cells to form the lymphatic system. In humans, development stops here, but in most fish species, some lymphatic vessels begin to transform back into blood vessels. This is called transdifferentiation, and it occurs at the juvenile stage before the fish are mature. These "new" blood vessels form a parallel secondary vascular system. Because not all lymphatic vessels revert into blood vessels, and because different fish species vary in the extent of transdifferentiation, adult fish have varying proportions of lymphatic and secondary blood vessels (see Figure 1). Some larger vessels, such as the lymphatic duct, are even shared between the lymphatic and blood vascular systems.

Oxygen uptake from water is the most limiting factor for fish life. Water contains less oxygen than air, and its oxygen content also varies greatly. Therefore, fish have had to develop mechanisms that maximize oxygen uptake and minimize oxygen loss. Fish skin is so permeable that blood vessels can absorb oxygen through the skin. However, fish can also lose oxygen through the skin if they swim in low-oxygen water. As an adaptation, they have developed the secondary vascular system. The secondary vascular system is mainly located at the body surfaces. At junctions where blood flows from the primary into the secondary vascular system, fish have the unique ability to regulate red blood cell entry. In oxygen-rich waters, red blood cells in the secondary circulation can become saturated with oxygen from the surrounding water through the skin, but when fish swim in oxygen-poor water, red blood cells cannot lose oxygen to the water because they are denied access to the secondary vascular system, i.e. to the body surfaces.

The repurposing of lymphatic vessels helps explain how fish have succeeded in developing such efficient methods to prevent oxygen loss from red blood cells when swimming in oxygen-poor waters. Fish are often considered simple animals, but in fact, they are the most diverse group among vertebrates. Fish have adaptive capabilities that other animals can only dream of. Most fish species have one heart, but some have a second heart at the base of the tail fin. Some species have lungs in addition to gills. Others can live over 400 years, while some can walk on land and even climb waterfalls. Some can produce high-voltage electricity, others can change sex. Some species' blood lacks hemoglobin entirely but contains antifreeze proteins allowing survival in freezing conditions. In some species, the male permanently fuses with the female and lives only as a sperm-producing parasite.

Many researchers have proposed explanations for this astonishing diversity of fish. One possible explanation is that about 96 percent of all fish belong to the so-called teleost group. The genome of this group duplicated completely about 335 million years ago. Thanks to this genome duplication, evolution could more freely experiment with different variations, for example by developing new functions for old genes. The risk of losing essential gene functions was low because a backup copy of the genome always existed. This may explain many peculiarities observed in fish, such as the secondary vascular system.

IN CONCLUSION

During evolution, the blood and lymphatic vascular systems have adapted to changing environments. They first had to adapt to increasingly leaky vessel systems as life moved from water onto land, and then again as evolution produced bipeds. The vasculature of fish that remained in water also continued to evolve. From the perspective of objective biological systematics ("cladistics"), we are all fish. Humans belong to a subgroup of fish called "lobe-finned fishes." Some fishes in this group adapted to walk on land. We call these fishes tetrapods, or four-limbed vertebrates. Some tetrapods developed hard-shelled eggs instead of gelatinous eggs that are viable only in water. We call these fishes amniotes. Some amniote fishes developed a placenta, which enabled them to give birth to live young. We call these fishes placental mammals. Some placental mammals developed large brains, abstract thought, culture, and language. We call these fishes humans. Among many other groups of fish, tetrapods are therefore just one "small" fish group with a very limited diversity.

The evolution of the vascular system in extant (i.e.

currently alive) fish that live in water has taken as long as the evolution of our human vascular system, and it is no more primitive than ours. It has only adapted to different evolutionary pressures. Fish evolution is our evolution because humans are just a highly specialized type of fish. Understanding the secondary vascular system in fish provides researchers with additional information about the development of circulatory systems and may also yield new insights into our human condition including our diseases. If researchers can determine how fish lymphatic vessels transdifferentiate into blood vessels, it may open new possibilities for treating vascular diseases, which remain the leading cause of death in humans. Other researchers have been fascinated by how fish can breathe through their skin and have asked whether other animals can do the same. They found that some turtles hibernate underwater without lung breathing, relying only on oxygen uptake through their cloaca, which is rich in blood vessels (5). Japanese researchers have gone even further and demonstrated that pigs can be kept alive solely by blood oxygenation via the rectum. They suggest that this technique could also be used to sustain life in human patients suffering from life-threatening lung failure (6).

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ABOUT THE AUTHOR

Michael Jeltsch is a German-Finnish researcher working in basic biomedical and pharmacological research. He has worked at the University of Helsinki since 1997 and became known for discovering the first growth factors specific for lymphatic vessels.

QUESTIONS FOR CONSIDERATION

1. What is the secondary vascular system in fish and why has it evolved?
2. What kind of data is the model mentioned in the text based on?
3. How can understanding the circulatory system of fish or other animals benefit medicine?
4. Can you think of other examples of how an animal species has adapted to its environment?

GLOSSARY

Physiology: The study of the life functions of organisms and their regulation.

Genome: The entire hereditary material of an organism, usually consisting of DNA.

Capillary filtration: Capillary filtration, also called capillary ultrafiltration, is the process in which small molecules – mainly water molecules – move from blood vessels into the surrounding tissue under the influence of blood pressure and osmotic pressure.

Hydrostatic pressure: Pressure caused by the fluid above. The human heart and vascular system form a roughly 1.8-meter-high, blood-filled column.

Lymphatic vessels: A system that transports clear fluid called lymph from body tissues back into the bloodstream.

Cladistics or phylogenetic systematics: A scientific classification method for organisms where classification is based not on appearance but on evolutionary history. Classification is usually done by comparing genomes of organisms.

Glass catfish: A transparent fish species whose study allows direct observation of body parts normally hidden under the skin.

Secondary vascular system: A part of the cardiovascular system found in fish, located near the body surfaces. At entry points of the secondary vascular system, specialized structures can either allow or deny access to red blood cells.

Teleost group: The largest group of bony fishes, which includes most present-day fish species.

Tetrapods: Tetrapods or four-legged animals are a group of vertebrates that include amphibians, reptiles, birds, and mammals.

Transdifferentiation: A profound change in cell identity.