STEM-CELL NICHE

In search of shade from the sun

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Friedrich Kapp recently took a break from his residency in Germany to spend some time at Harvard with Leonard Zon and his zebrafish. Zon's lab uses zebrafish to study hematopoiesis, the production of blood cells from their stem cell progenitors. The hematopoietic niche is found in the bone marrow of terrestrial tetrapods like humans but in the kidneys of fishes. One day, Kapp found his view obscured by a layer of pigmented cells called melanocytes. "That kind of annoyed me at first," he recalls, "But Len and I were talking about well, what are they doing there?" An unplanned project was born.

To Kapp, the melanocytes resembled an umbrella over the stem cell niche—could their presence have to do with the sun? First, they took the umbrella away and found no difference in the number of stem cells or the production of blood between fish with and without the pigmented structures. Then, they let there be light. In Cambridge, they exposed larval zebrafish with and without

melanocytes to UVC light to prove the initial idea that the umbrella was protective against UV damage. UVC, however, isn't entirely biologically relevant—it's usually filtered out by the atmosphere. When he returned to Freiburg, Kapp fortunately found a UVB light source at the dermatology lab next door and went on to illuminate additional evidence of DNA damage and decreases in stem cell numbers in fish that lack melanocytes entirely, that lack the ability to produce melanin in those cells, or that were simply flipped on their backs so that their kidneys were irradiated from below. Functional melanocytes above the kidney appear to act as a sunscreen, he says.

But there's more than just zebrafish out there. To see if similar structures occur in other aquatic species, Kapp compared histological samples from a variety of other fishes and four anurans. He found evidence in each animal of melanocytes positioned above the hematopoietic niche. In frogs,

the niche shifts from the kidney to the bone marrow as the animals transition from aquatic tadpoles to amphibious adults. A closer look at the dyeing poison frog revealed that the niche moves after the tadpoles develop legs but before they leave the water as froglets. This lends additional evidence to Kapp and Zon's hypothesis that the sun, harsher above the water line, provides at least some of the selective pressure for the formation of the hematopoietic niche in different animals.

Though moving away from hematopoiesis to study pediatric vascular diseases in his own lab, Kapp isn't abandoning his new-found model. "I'm a zebrafish guy," he says, "It's a beautiful animal and you can learn a lot from it."

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