These Dendritic Cells Are Fishy, But That's A Good Thing

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Scientists from the University of California, San Diego School of Medicine have identified dendritic antigen-presenting cells in zebrafish, opening the possibility that the tiny fish could become a new model for studying the complexities of the human immune system.

The study, reported in the online edition of the *Proceedings of the National Academy of Science*, was headed by David Traver, an associate professor in UCSD's Department of Cellular and Molecular Medicine, with colleagues in UCSD's Division of Biological Sciences and at the Brazilian National Cancer Institute.

Dendritic cells (DCs) form a crucial link between the innate and adaptive immune systems in mammals. Innate immunity is present in all organisms, providing immediate but short-lived and relatively non-specific defense against infection. Adaptive immunity is evolutionarily younger and more complex. It produces long-lasting protection against specific pathogens after initial exposure. Mammalian DCs act as sentries that bridge the innate and adaptive systems, confronting and engulfing newly discovered pathogens, then recruiting and activating antigen-specific T lymphocytes.

While DCs and the adaptive response have been well-documented in mammals, it was not clear whether these cells existed in non-mammalian vertebrates. Scientists knew that zebrafish – an increasingly popular animal model – exhibited many of the cellular elements of the adaptive system, including T and B lymphocytes, but no one had documented the presence of dendritic cells.

Traver and colleagues inventoried hematopoietic cells that could engulf labeled bacteria, looking for cells that appeared and behaved like mammalian DCs. They found multiple suspects, but finally zeroed in on one rare cell type that appears to fit all of the criteria for being a dendritic cell.

"All signs point to these cells being the fish version of dendritic cells," said Traver. "They have all of the major characteristics."

The discovery of DCs in zebrafish provides researchers with another model for investigating the mammalian immune system, particular with regard to humans. "The cool thing is that the more we learn, the more we realize that our immune systems are highly conserved," said Traver. "Of

course, there are differences. These differences, however, are variations on a theme, with the major themes of immune cell function being quite similar. Likewise, there are differences and variations in the dendritic cells of mice compared to humans, but the basics are the same."

Zebrafish do offer some practical research advantages over other models.

First, the fish are translucent. "You can track individual cells and systems directly in the whole animal," said Traver. "Very little is known about the initial immune response in mammals because we can't see it happening. In these fish, we can visualize what happens in real time."

Second, zebrafish are easy to handle and reproduce rapidly, making it easier to engineer and study mutations. "We can quickly grow generations of fish, letting the genetics tell us what's important," Traver said.

Co-authors with Traver are Geanncarlo Lugo-Villarino, Keir M. Balla and David L. Stachura of the Section of Cell and Developmental Biology, Division of Biological Sciences, UC San Diego and Miriam B.F. Werneck of the Division of Cellular Biology, Brazilian National Cancer Institute.

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