Probing the secrets of cell identity

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Dr. Ariel Gomez's research focuses on the identity and fate of renin cells, which are responsible for producing renin, an enzyme-hormone that regulates blood pressure and the composition of our body fluids and electrolytes. Credit: Dan Addison

Though organisms have drastically evolved since climbing out of the primordial soup, one scientific fact has remained the same for epochs: cells are the most basic structural units of all living things.

One researcher in the University of Virginia School of Medicine has dedicated much of his time to the study of one type of cell in particular: renin cells.

"Renin cells are part of a defense system established more than 400 million years ago," Dr. Ariel Gomez, a professor of pediatrics at UVA, said. "They appeared in nature around that time in bony fish."

Then and now, when animals, humans or otherwise, are challenged by a homeostatic threat, meaning a threat to physical equilibrium, or become injured, Gomez said they rely on that defense system to restore well-being. In particular, cells that produce the enzyme renin, which regulates blood pressure and fluid-electrolyte stability, are crucial to enabling animals to survive conditions that cause physiological distress.

"In the primitive, early days of existence, those cells became part of a defense system not limited to blood pressure homeostasis," Gomez said. "They retained multiple functions developed early in evolution."

Within the field of hypertension research, renin's role in regulating blood pressure as well as fluid and electrolyte homeostasis has long been known. What was not known – that is, until Gomez and his team of researchers discovered it – were the mechanisms that control the identity and fate of the cells that manufacture the enzyme.

In addition to discovering the main pathways that control the identity and fate of renin cells, Gomez's lab found that these cells are important in organ development, particularly kidney development. Cells that manufacture renin are present in other tissues as well, for instance in the bone marrow (where white and red blood cells originate), where they may participate in blood development and immunity.

Gomez and his colleagues discovered that a specific mutation in those renin-producing white blood cell progenitors, or parent cells, called lymphoblasts, results in a highly penetrant form of leukemia.

Understanding the origin, identity and fate of renin cells, Gomez said, has numerous medical implications. For instance, changes in cell fate are linked to the maintenance of whole body and tissue homeostasis, as well as chronic diseases like hypertensive vascular disease, kidney scarring, diabetes and cancer. Furthermore, a complete understanding of cell fate leads to knowledge that can be applied to efforts in tissue repair as well as regenerative and stem cell medicine.

Another key concept discovered by Gomez and colleagues is that renin cells are progenitors for other cells in the kidney vasculature and other

tissues outside the kidney. Descendants from renin cells retain the memory to express renin. In times of crisis, descendants of renin cells will be recruited to produce renin in order to restore homeostasis. When the crisis passes, the descendants recover their former identity, until they are needed again. Gomez found, though, that if the stressful stimulus persists, continuous recruitment of renin cells occurs, leading to thickening of kidney blood vessels. Curiously, this pathology is also seen in people with hypertension.

"In treating hypertension, a balance must be reached between blood pressure control and perivascular recruitment of renin cells," Gomez said. "Understanding these properties of renin cells may help us design better medications to prevent vascular alterations associated with hypertension or its treatment."

For his work, the American Heart Association awarded Gomez its 2016 Excellence Award for Hypertension Research, the most prestigious award it gives to an individual who has "made a meritorious discovery" in the area of hypertension research.

"On a personal level, this award recognizes the mentorship I received from my early beginnings and the outstanding group of researchers I work with every day," Gomez said.

Provided by University of Virginia

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