The Stem Cells of the Spleen: New Basic Research Findings from Our Lab

In 2003, our lab identified a new stem cell in the spleen of mice that could increase the speed of pancreas regeneration once the underlying autoimmune disease was removed. Knowledge about the function of this splenic stem cell has expanded in the last seven years. Other research groups have shown that this splenic stem cell: 1) can be expanded from animal samples in the lab to form sheets of insulin secreting islets (1); 2) can regenerate the islets of animals with type 2 diabetes (2); and 3) can contribute to the regeneration of bone, heart, cranial nerves and salivary glands in animals (3, 4, 5, 6).

With this information in hand, we wanted to know: what is the full regenerative potential of the splenic stem cells? That is, can we predict all of the possible tissues that these cells could help heal through regeneration?

To answer this question, we collaborated with other scientists at Harvard to examine the proteins found in splenic stem cells, which would give us information on the types of tissues these cells could possibly become. We also compared the splenic stem cells to certain closely related cancer cells, since research has shown that some stem cells (i.e. embryonic stem cells) can turn cancerous. Our findings were recently published in the International Journal of Biochemistry & Cell Biology (6).

Based on their protein expression profile, we found that human splenic stem cells appear to have the capacity to change into a wide number of different tissue types, much in the same way that embryonic stem cells and induced pluripotent stem cells (iPS cells, cells that are reprogrammed into an earlier state with embryonic qualities and these iPS cells can form whole new mice). In addition to finding the proteins we expected to see based on what we knew from animal studies (e.g. proteins associated with development of pancreas, bone, cranial nerves/central nervous system, heart, and blood tissue), we also saw that human splenic stem cells had proteins characteristic of the developing eye, testes, thymus, kidney, liver, lung, placenta, gut, tongue, and skin. In addition, our protein analysis suggests that splenic stem cells have a low likelihood of transforming into cancerous cells.

Our new work also asked another question? What happens in the spleen of an untreated autoimmune NOD mouse with active diabetic disease? Are there signs of splenic stem cells contributing to the healing process? Using some of the new stem cell proteins we identified in this study, we demonstrate the splenic stem cells are proliferating and also expressing more of the fetal proteins. Like other recent data on the splenic stem cells in cardiac repair, it is likely the expansion of stem cells in the mouse spleen is a healing response for pancreas repair.

What does this all mean? Because the splenic stem cells appear to have the capacity to become many different cell types, they have potential to be used in a wide range of applications, such as organ regeneration, new disease therapies, or disease prevention. This is exciting for future research in regenerative medicine. In terms of type 1 diabetes, while we hope that all people with longstanding autoimmunity will have their immune disease removed and insulin-secreting cells regenerate on their own in our BCG human trials, we also think it is important to have safe adult stem cells available in case the pancreas of long term diabetics does not kick in to regenerate on its own.

References:

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