The quest for the almighty cell

ZUBA-SURMA (Jagiellonian University in Krakow): Has the perfect stem cell been found at last?

From the time of the ancient Greeks people have always dreamed about ambrosia – the food of the gods, bestowing immortality. Today, we still ask whether any of our inventions, medicines or the benefits of civilization have become such a blessing and fulfilled the dream. I don’t think so, unfortunately…

The 20th and 21st centuries have brought us several outstanding discoveries which significantly extend human life. I will only mention two of them, representing distinct and important groups of inventions: those directly restoring healthy homeostasis, or stability (such as antibiotics applied in standard therapies); and those leading indirectly to the development of novel therapeutic approaches. The latter group includes the identification and characterization of both the structure and role of nucleic acids. This became the cornerstone of a multitude of scientific and medical inventions, and eventually enabled us to decipher the complete human genome. However, despite the knowledge emerging from the identification of genes responsible for several disorders, we are still unable to prevent and treat them: in other words, we are still pursuing our quest for the best therapeutic approaches.

Recent decades have also been called the “golden ages” of cellular therapies, leading us in new directions and holding out the prospect of being able to treat multiple chronic and acute conditions. The quest for the “almighty cell” – therapeutically the most suitable stem cell capable of replacing injured or dysfunctional tissues – has recently speeded up, and the past few years have seen ground-breaking discoveries in the field of stem cell research.

Embryonic stem cells (ESCs), derived from developing blastocysts, were initially felt to offer great hope for organ repair and tissue replacement. Despite the fact that ESCs are able to develop into all cell types – which means they are pluripotent – the therapeutic usage of these cells was limited, mostly because of ethical controversies. However, such obstacles may be overcome following the recent discovery of inducible pluripotent stem cells (iPSs), initially created by the two independent scientific groups run by professors Shinya Yamanaka from Kyoto University and James Thomson from the University of Wisconsin-Madison. These “miracle cells” can mimic ESC characteristics following genetic reprogramming of any selected mature cell in vitro – that is, in “out-of-tissue” conditions. Importantly, such reprogramming, which leads to the forced expression of selected genes crucial for pluripotency, could become a successful approach in regenerative medicine, providing a population of pluripotent stem cells that are autologous – in other words, derived from the individual being treated.

Excitement about iPS cells and their potential medical applications continues, and looks as if it is growing; however, some major problems are appearing too, and must be addressed before these cells are successfully introduced into the clinic. Top of the list is the potential of iPS cells to promote tumor development after transplantation, the same obstacle previously faced by ESCs and their therapeutical applications. Thus, the most potent and “omnipotent” stem cells are still on their way from “benchside to bedside”; all the same, they are unquestionably on a well-defined path to clinical use. So, are there any alternative pluripotent stem cells suitable for regenerative therapies? A unique stem cell population with pluripotent characteristics has indeed been found to be present in adult animal and human tissues. In 2006, scientists led by Professor Mariusz Ratajczak from the Stem Cell Institute at the University of Louisville, USA, discovered a rare population of stem cells in the bone marrow of adult rodents. These cells looked and functioned in a way that was similar to ESCs, and hence became known as very small embryonic-like stem cells (VSELs). This unexpected discovery completely destroyed the belief that primitive pluripotent stem cells exist exclusively in embryonic tissues, and never in the mature organism!

Today, we know that VSELs are present not only in adult bone marrow, but also in other mature tissues, and may be harvested from human as well as animal specimens. Moreover, there is growing evidence that they may efficiently participate in tissue repair, as we have shown by treating heart attack patients with VSEL transplantation. What is even more important is that because of their unique gene expression, VSELs do not form primitive tumors (teratomas) after transplantation. Their ability to give rise to several cell types, lack of tumorigenicity, and the possibility of harvesting from the bone marrow tissue of the patient concerned make VSELs attractive candidates for treating various disorders with cellular therapies.

Dozens of scientists are on the quest for the “almighty cell” that would be suitable for clinical applications in regenerative medicine, and which would open up new opportunities for longer and healthier life in human society. The hunt for ambrosia continues, and it might be that our ancient dream will soon come true.

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