Red blood cells derived from stem cells could offer a limitless supply for transfusions

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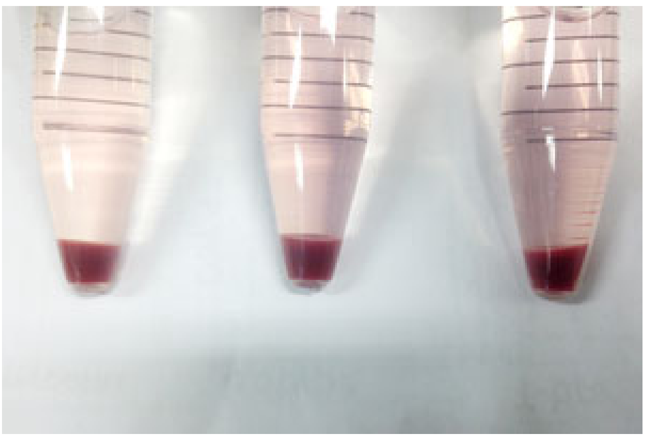

Red blood cells grown from stem cells using a microcarrier-based suspension culture platform developed at A*STAR. Credit: A*STAR Bioprocessing Technology Institute

As the Singapore Red Cross says, the need for blood never stops. But the demand for blood from living donors could become a thing of the past, as A*STAR researchers make red blood cells (RBCs) from stem cells in an efficient and reliable way.

"What's lacking in the field of RBC generation is the ability to manufacture high-quality cells in a large-scale and cost-effective manner," says Jaichandran Sivalingam, a research scientist at the A*STAR Bioprocessing Technology Institute. "Our approach provides a first step in that direction."

Every year, at hospitals across Singapore, people undergoing surgery, cancer patients, accident survivors and even newborns with medical complications collectively receive more than 100,000 units of blood. Donor-derived supplies can generally meet current demands, but as the population ages, the need for blood will increase at the same time that the pool of willing donors dwindles.

Lab-grown blood offers a potentially limitless solution, but existing methods for manufacturing blood from stem cells are not appropriate for clinical use.

Take the systems for making RBCs, for example. Researchers typically culture embryonic or reprogrammed stem cells in flat lab dishes so they can form three-dimensional aggregates called embryoid bodies before the cells develop into blood. But the large surface area required for this method makes it impractical for scaling up. Alternatively, scientists can grow the stem cells alongside mouse cells that secrete differentiating factors. However, these non-human cells can carry animal pathogens and can't be used for human transfusion.

Jaichandran and his colleagues got around these problems by using tiny plastic spheres known as microcarriers. These spheres float in suspension, providing large amounts of surface area. And covering them in a human protein called laminin-521 eliminates the need for any animal material.

By culturing the stem cells on these microcarriers and adjusting the media, the A*STAR team could generate at least six times as many RBC precursor cells and 80 times as many differentiated RBCs as the standard method involving embryoid bodies in a dish. Since reporting the method last year, the researchers have boosted the yields even further.

Terminal maturation of the blood cells is still difficult, stringent quality checks have yet to be done, and the process is still too costly to be commercially viable. But Jaichandran's team is making progress. "We are looking at different approaches and systems to address some of these challenges," he says.

More information: Jaichandran Sivalingam et al. Superior Red Blood Cell Generation from Human Pluripotent Stem Cells Through a Novel Microcarrier-Based Embryoid Body Platform, *Tissue Engineering Part C: Methods* (2016). DOI: 10.1089/ten.tec.2015.0579

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