

## Very Small Embryonic Like Stem Cells: Fact or Not?

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Stem cell based therapy, referring to both adult and embryonic stem cells, is widely used in medicine, mainly in regenerative medicine.

Adult stem cells are multipotent, while embryonic stem cells are pluripotent, they possess the potential to differentiate into derivatives of all three embryonic germ layers: endoderm, mesoderm and ectoderm.

Researchers worldwide they found stem cells isolated from umbilical cord blood that expressed early transcription factors found typically in the embryonic stem cells.

The plasticity of stem cells isolated from cord blood it is already known. In 2004 Kogler et al., found a non-haematopoietic stem cell population of umbilical cord blood called unrestricted somatic stem cells capable to differentiate into all three germ layers [1]. Recently researchers worldwide they found stem cells isolated from umbilical cord blood that expressed early transcription factors found typically in the embryonic stem cells [2]. These cells are first described by Kucia et al. 2006, in a fraction of murine bone marrow stem cells [3], and named Very Small Embryonic Like Stem cells (VSELS). VSELS are very small (2-4  $\mu\text{m}$ ) CD34 and CD45 negative stem cells that strongly express CXCR4 Sca-1<sup>+</sup> antibody and embryonic transcription factors as OCT and Nanog. These transcriptions factors are considered as markers of mouse and human embryonic stem cells playing a basic role in stem cell pluripotency [4-6]. VSELS were also described in several murine organs as brain, liver, kidney, heart, and skeletal muscles [7]. Recently some investigators found these cells in mobilized peripheral blood in patient after stroke [8] and after acute myocardial infarction [9]. The presence of very small embryonic stem cells has also been reported in adult human gonads [10]. The investigators thought that these cells represent a primitive population of stem cells that maybe plays a major role in regenerative medicine and in stem cells therapies in general.

The main value of the investigation was that the researchers have proposed very small embryonic like stem cells like an alternative source to human embryonic stem cells. The regenerative potential of VSELS is expected to be better than the HSCs and MSCs. Moreover the new promising type of stem cells didn't present the ethical issues of embryonic like stem cells.

Some of them referred that these population get lost during the isolation process for cord blood stem cell banking and bone marrow processing because of their small size but in general this study was in agreement with the literature that supports the existence of very stem cells [11]. The debate about the existence or not of very stem cells has already started as recently some others investigators doubted about the existence of this rare population of stem cells [12-15]. Especially referred, that they spent a lot of waste time failed to isolate pluripotent stem cells smaller than 7 micrometres that couldn't aggregate into spheres like the embryonic stem cells. It is very possible that the referred negative result might be due to the loss of very stem cells during the process that was followed. Furthermore is referred like a very rare small stem cell population. The supporters thinking, that all the researchers that are against lacking the technical skills for very small stem cells harvesting. And the controversies remained with the researchers to call into question claims that these stem cells are exist and can have a regenerative potential for clinical applications and repairs in human's individuals?

Recently the researcher that first described this population published

a very detailed article giving a strong response to all these investigators who managed against the existence of very small embryonic like stem cells citing positive results from other research groups worldwide [15].

I think that the question arise from all these studies must concern that if we admit that this rare population give rises to different stem cells lineages how have the ability to differentiate to specific progenitors in specific tissues. Are these stem cells having a different multiple behavior depending of the tissue environment? Is the regenerative ability of these the same in all the tissues that they have been found? It is possible these stem cells found in cord blood and bone marrow the same with these stem cells found in adult tissues? Is the mobilization that is referred capable and sufficient to support the idea of the existence of these stem in so different tissues? All these are questions that need an answer indicating that the very small stem cells population will continue to concern the research teams in the next coming years bringing new information's about the biology the origin and the regenerative potential of very small embryonic like stem cells.

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