

Very Small Embryonic-Like Stem Cells: A Scientific Debate?

Graham C. Parker

THE VAST MAJORITY OF publications in *Stem Cells and Development* are original research reports. However, we are also known for allowing discussion of issues that are not given, perhaps, the attention they deserve in more conservative journals. For example, we gave voice to a highly unpopular stand on the problems associated with induced pluripotent stem cells when no other journal was prepared to give credence to such concerns. We have given room for publications on topics that have found difficulty in finding a home with other journals. As longtime readers and authors of our journal know, we pride ourselves on reviewing and publishing data first and dogma second, if at all. If the data are novel, and the work has been well performed, the work is published. Anyone in the field knows well that sometimes those data have to be drastically re-evaluated and reinterpreted. However, it does not negate the worth of the data, nor the publication, except perhaps, the discussion section! We look to the poet Robert Frost to remind us of “truths being in and out of favor.” However, the ability to revisit existing publications is a topic for a different day.

Today, the topic is the current debate as to the significance of the body of publications concerning very small embryonic-like stem cells (VSELs). From my earliest association with the journal, we have published reports on cell populations isolated from adult tissues that share properties that we routinely associate with cells derived from the inner cell mass of the embryo. Readers interested in tracking these publications are more than welcome to do so, and indeed, the “issues in development” piece submitted by the Ratajczak group [1] will give you a helpful list of the keywords necessary to locate these pieces, including the multilineage-differentiating stress-enduring cells reported in this issue [2].

The piece submitted by the Ratajczak group is an attempt to clarify, for the field, their methods and reasoning behind their isolation and description of VSELs. The primary contention against their research appears to rest on the difficulty some groups have found in isolating these cells. I find these rather odd grounds for doubting the worth of a scientific subject. For just as I in no way would doubt the worthiness and competence of those groups that have failed or found little evidence to support the ability to isolate these cell

populations, I in turn would ask them what we are supposed to do with the claims from several groups that have managed to isolate such cells? We have all surely experienced situations where workers in the laboratory seem to share similar skill sets and competences, but yet cannot seem to achieve the same data sets. These issues of replication and standardization we have covered here previously [3,4]. Surely, this is exactly what a worthy organization like the NIH Center for Regenerative Medicine should be able to resolve for us [5]. Let them take this as a clarion call to organize a workshop to determine the veracity of the claims as to how these cells are isolated and thence, I suspect, determine the deeper truth that underlies why some researchers are achieving data sets that appear at the very least to be consistent with their claims.

I think it is fascinating that the Taichman group has managed to isolate a population of cells from both human and murine sources that they have rigorously demonstrated to have the potential to contribute to diverse tissue types, but that appears to have limited proliferative abilities [6]. If you are currently convinced of the nonexistence of the VSELs, I encourage you to review carefully the data presented by the Taichman group, which I find compelling. Taken with the further recent publication by another group concerning VSEL contribution to lung epithelial tissue [7], the question begs: how many laboratories must demonstrate a phenomenon before a field must classify it as something more than just that?

I have chided previously Dr. Ratajczak for what I believed to be an unfortunate name and acronym for these cells. I understand they are Very Small. However, are they Embryonic-Like? Well actually in their limited proliferative capacity, yes. We are far too comfortable referring to the pluripotent cells we trick into being supernumerary as being embryonic stem cells. They are not. They briefly were embryonic stem cells, thereafter, the inner cell mass-derived cells become cultural artefacts. Very useful cultural artefacts, but they are no longer the literal embryonic stem cells whose existence in that state in vivo is so very brief before they begin their developmental course. So, maybe the name VSELs is not so bad after all.

This topic has taken on a further rather unfortunate political turn as former collaborators disagree. I trust our

readers will be able to discern that there is genuine scientific concern in both the much revised Ratajczak piece and the much revised reply to it by the Dulak group published here as a letter to the editor [8]. I must express my gratitude and respect for our reviewers who have done sterling work as always in their efforts to fairly judge both pieces as well as the encouragement they showed to both parties to remember their responsibilities to maintain the collegiality of scientific disagreement. As usual, our readers are very welcome to carefully read the pieces here and make their own opinions known, but please, keep it data driven and collegiate.

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Address correspondence to:

*Graham C. Parker, PhD
Carman and Ann Adams Department of Pediatrics
Wayne State University School of Medicine
Detroit, MI 48201*

E-mail: gparker@med.wayne.edu

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