

A Commentary on Stem cells: Much Confusion

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Abstract

Stem cells and embryonic stem cells, presently, are two of the most popular terms in scientific journals and in lay publications. They are two different types of cells, but are often confused so as to imply they are the same cell. However, their origins are different and their courses of action are different. Claims have also been made that early human blastomeres, for example, cells of the inner cell mass, are, in fact, stem cells. They are not. In this review it will be argued that 1. embryonic stem cells and stem cells are not the same, and 2. human embryonic blastomeres are not stem cells.

Introduction

There are **stem cells** (derived from adult tissue), and then there are **embryonic stem cells**. The two are not the same. In fact, they are quite different. The former have always been a natural part of the body tissues; the latter term was contrived.

The term **embryonic stem cell** (esc) has been ingrained in the present day scientific jargon and has become the most advertised scientific research area cited by the mainstream media, politicians and pundits. This popularity has been strengthened even more so since Martin Evans was awarded the 2007 Nobel prize in medicine for the successful culture of mouse embryonic cells into pluripotent cell lines in 1981 (1).

The purpose of this review is to show that “embryonic stem cells” are not true stem cells, and that human embryonic blastomeres are not stem cells, contrary to popularly published statements.

Embryonic Stem Cells

Gail R. Martin has been given credit for coining the term **embryonic stem cells**, also in 1981 (2). In fact, she states “Such cells were termed ‘*embryonic stem cells*’ to denote their origin directly from embryos. . .” and puts the term in italics. The cells she cultured are identified as pluripotent cell lines derived from the inner cell mass (ICM) in the mouse.

Thomson et al. were the first to report pluripotent cell lines derived from the ICM in human blastocysts. When kept in culture for 4 to 5 months they could be directed to differentiate into several definitive tissue type cells (3).

The distinction is not usually made between embryonic stem cells and stem cells. This has led to the claim that the ICM, or even earlier blastomeres, are actually “stem cells” or “embryonic stem cells” (4). A New York Times issue on Health from 28 March, 2008 declares: “Stem cells are how we all begin, undifferentiated cells that go on to develop into any of the more than 200

types of cells the adult human body holds.” Clearly, the Times is equating early blastomeres with stem cells.

Condic has recently posted the following statement on the website: Life Issues.net: “The earliest stem cells are found in the human embryo during the first few days of life. These embryonic stem cells (or ESCs) can reproduce themselves indefinitely and are very flexible: they normally give rise to all of the tissues of the mature body” (5). She is equating embryonic blastomeres with stem cells and does not distinguish between “embryonic stem cells” and “stem cells”. She is wrong.

The recently published compendium, “Encyclopedia of Stem Cell Research” (6), states: “Embryonic stem cells, the original building blocks of life, are the body’s founder cells. They are isolated from the developing embryo. . . . After isolation, the embryonic stem cells are cultured in the laboratory”.

Not only are such definitions confusing, but they are incorrect. Embryonic blastomeres are not stem cells. The international nomenclature committee, known as FICAT, concurs with this conclusion (7). Their entry on the definition of a stem cell is: “A stem cell is either unipotent or multipotent and is a constituent of a population that is capable of maintaining its own size while exporting an appropriate output of progeny to one or more cell lineages.” Thus, it is clear, an embryonic blastomere is not a stem cell. The misinformation about stem cells and, in particular, the inner cell mass, has become pervasive. It has seriously compromised a true understanding of stem cells. This terminology conflicts with what is known about stem cells and what has previously been known about the early human embryo.

Basil Cole exemplifies the confusion of terms when citing William May’s book on bioethics (8). He states: “Perhaps one could argue that killing embryos to get their **stem cells** could have been part of the chapter on abortion. The use of adult and even pediatric **stem cells** are producing the best results so far in terms of healing certain diseases and illnesses, and there is also a new way to get **embryonic stem cells** without harming these innocent human beings.”

Since no one has yet identified true stem cells within the early embryo, it is clear that Cole is referring to embryonic blastomeres as stem cells, which they are not.

Origin Of The Term: Stem Cell

The term **stem cell** may first have appeared in a French publication as early as 1901(9). The term is found in a text of Developmental Anatomy by Leslie Arey in 1954 in a subheading entitled: “Stem cell of the neural wall” (10). Later, it appeared indexed in histology texts (11, 12). Prior to this time they were known as reparative, or, regenerative cells. The term first appeared in Citation Index in published research in the 1960s (13).

In actuality stem cells are very specific types of cells and many can be readily identified morphologically, either by light microscopy or electron microscopy. For example: the satellite cell in human skeletal muscle, mucous neck cells in the human stomach, and basal cells of the epidermis in the human, not to mention the oogonia and spermatogonia, are clear examples of morphologically defined stem cells. Their purpose is to replenish the stem cell pool with one daughter cell, while the other daughter cell differentiates and replaces lost or damaged definitive cells in the resident tissue (see, again, reference no. 7).

Stem cells are derived sometime during development (or maybe after birth) partially differentiate, then are arrested in their resident, definitive tissue, available to be stimulated under

appropriate means to undergo further differentiation to their definitive tissue type. Even though they would probably be produced during embryogenesis, or in the fetal period, they would be, *de facto*, adult stem cells. They would not be the same as embryonic stem cells, because the two different types have different courses of differentiation. Furthermore, there is no evidence, to date, that cultures of embryonic stem cells derive any true stem cells.

Clearly, human embryonic blastomeres are not stem cells. By definition they do not qualify as such. Further, no stem cells have been identified in human embryos, as yet (14).

Gurdon and Melton (15) have written an excellent review of nuclear reprogramming during early differentiation. The question is: are the gene expressions, transcriptions and inhibitions the same as for the true stem cells, especially in arrest? This has not been determined. However, it is essential that stem cells be characterized in their early and partially differentiated state, and also the controls which put them into temporary arrest.

Renewed Ethics Debate

With the advent of federal funding for research using “spare embryos” from IVF laboratories, the ethical debate on the use of those embryos will be renewed and will intensify. The question should be asked: just what are those cells (blastomeres) of the inner cell mass of the embryo?

Martin, Evans and Thomson each identify their derivatives from cultures as “pluripotent stem cells” (1, 2, 3). This is in error because true stem cells do not normally derive pluripotent cells, only if manipulated chemically. Further, each states their source for cultures as the inner cell mass of the embryo. The inner cell mass has been identified as 58 to 107 cells (16) or, by at least one author, as 12 to 16 cells (17).

The question is: are all the cells of the human inner cell mass totipotent, pluripotent or a mix of both? Most human embryology textbooks state that the majority of monozygotic twins occur prior to early blastocyst; but they also occur by division of the inner cell mass at a late stage, up to 14 days post-fertilization (18), and certainly by the 8th day, after formation of the amnion (19). This is evidenced by twins enveloped in a single amnion. This speaks to the likelihood that at least some of the cells in the inner cell mass are totipotent. Thus, the next question becomes: are at least some of the cultured cells likely to be totipotent? It appears they would be. This is likely to initiate a renewed debate on the ethics of the use of cultured early human blastomeres.

Thus, a better and truer understanding of stem cells is paramount in all forms of communications. This includes the scientific world, which has been rather careless in its use of the term “stem cell”.

Unfortunately, the term “embryonic stem cell” is probably here to stay. However, those who use this term should be obligated to distinguish these cells from true “stem cells”. Further, it is advised that the term “stem cells” be not applied to human embryonic blastomeres.

References

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