A cautionary tale with a distinct message about not letting new technology go to your head; as relevant today as it was then 150 years ago!

Comment

Both poems were written by eminent scientists (both held professorial posts at the time) and yet the treatment of the subject is quite different. Maxwell's treatment is more descriptive whereas Holmes' treatment is more satirical. However, both display a depth of knowledge only available to those who are well versed in their use and both express sentiments that should be understandable to both scientists and non-scientists alike. So, why not an 'Ode to a Mass Spectrometer' or 'The Rhyme of the Raman Microscope'? The possibilities are endless – a challenge to the readers of *Drug Discovery Today*!

References

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Raymond C. Rowe
Pharmaceutical and Analytical R&D
AstraZeneca
Alderley Park
Macclesfield, Cheshire
UK SK10 2NA
tel: +44 1625 513112
fax: +44 1625 512381
e-mail: Ray.Rowe@astrazeneca.com

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Stem cells: hype *and* hope ▼

A recent short review article by Paul *et al.* in *Drug Discovery Today* [1] provided an update on the possible use of two types of stem cell in regenerative medicine. The first is the embryonic stem (ES) cell derived from the inner mass of the developing blastula, and the second is the adult stem cell derived from specific regions of differentiated tissues. Several possible clinical applications for these cells are also highlighted in the review, including diabetes and Parkinson's disease (PD). The review title poses the question of whether there is 'hype' or 'hope' in this field. I would like to suggest that there is both.

First, there are the master cells from the blastocyst. This whole field is, of course, shrouded in the ethical controversy regarding derivation of ES cells from living human embryos. Because the moral status of the embryo is determined largely by one's own religious and ethical persuasions, there will never be a simple answer as to whether society should have harvested such cells to begin with. However, the reality is that there are now several cell lines available. These ES cells cannot form a new human alone, they exist as an artefact of tissue culture. As such, there is little ethical argument over the growth of these isolated cells. This is perhaps why President Bush has allowed National Institutes of Health (NIH) funding to be used for all ES cell lines already generated and logged with NIH, but not the derivation of new ones (http://grants.nih.gov/grants/stem_cells.htm). The challenge now is to prove that these cells can actually provide important information on human development, and possibly restore function in various diseases.

The sequence of events begins with extensive tissue culture experiments to show that different cell lineages can be isolated from the starting ES cell population. Ideally, these lineages (neural, muscle, blood) will be devoid of ES cells that, by definition, will form a teratoma following transplantation. Once specific lineages have been isolated, the next challenge will be to prove they can function as well as sister cells that are normally resident in adult tissues. This is an important point, because simply deriving a differentiated cell from an ES cell might not recapitulate normal development (which occurs over a much longer time period and within the complex environment of the developing organism).

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The final challenge will be to transplant these delicate cells into animal models of disease, and prove they can integrate and repair damaged tissues. This alone is an enormous feat given the immune rejection problems, particularly following grafts into tissues outside the CNS.

Perhaps the best example highlighted by Paul *et al.* where stem cells could first be used is PD. Of particular interest is a recent paper, which has been published since the review was completed, where neurons derived from mouse ES cells were shown to mature into dopamine neurons and restore function following transplantation into a rat model of PD [2]. This is encouraging, but a large number of animals also developed teratoma-like tumors and had to be excluded from the study. This elegantly reveals both the excitement and necessary caution that needs to be exerted before taking ES cells to the clinic.

Adult stem cells are of course ethically acceptable, and there is an impressive clinical history already available for haematopoietic stem cells being used to treat a wide range of diseases [3]. The excitement over new plasticity of adult stem cells is warranted, given the range of new papers suggesting such events might occur. However, this is tempered by the rarity of such events and in nearly all cases (particularly with regard to neural replacement) there is little evidence that the cells are functional. This has prompted several cautionary commentaries [4,5]. Furthermore, despite more than 30 years of research, blood stem cells cannot be easily expanded to large numbers in the tissue culture dish, a feature shared by most other adult stem cells.

One missing type of stem cell from the review by Paul *et al.* is the fetal stem cell. This is an interesting type of stem cell, and falls between the two extremes of ES cells (totally non committed cells that need entire programming to become differentiated tissue) and adult stem cells (highly committed and perhaps require some de-programming). Fetal stem cells can be isolated from a range of developing organs but a particularly interesting example is the human neural stem cell, which can be derived from the late embryonic or early fetal brain between six and 20 weeks. These cells are less likely to form tumors, and are already committed to a neural lineage – two useful attributes that are still difficult to achieve from ES cells [6]. However, it is also possible that the developmental power present within ES cells will ultimately be required to generate the range of different neuronal phenotypes required for different diseases. In particular, large dopamine neurons that are lost in PD are difficult to generate from expanded populations of fetal derived neural stem cells, but can be produced from ES cells, as mentioned previously.

Clearly, future studies need to focus on comparisons between these various types of stem cells. Hype *and* hope will permeate the field during these early stages. The onus is on authors, journal editors and the media to be responsible. The data should be presented in a way that, while not distracting from the excitement of this field, does not raise false hopes.

References

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Clive Svendsen
Professor, Anatomy and Neurology
Stem Cell Research Program
The Waisman Center
University of Wisconsin-Madison
1500 Highland Avenue
Madison, WI 53705, USA
tel: +1 608 265 8668
fax: +1 608 265 4103
URL: http://www.waisman.wisc.edu/scrp/index.htmlx

Osteoprotegerin and bone loss associated with spaceflight ▼

In a recently published article [1], Grimaud *et al.* gave an excellent overview of significant advances in the understanding of bone biology since the discovery of osteoprotegerin (OPG) approximately five years ago [2]. The roles that OPG, RANK (receptor activator of nuclear factor κB) and RANK ligand (RANKL) play in the differentiation, activation and eventual death of osteoclasts is one of the most fundamental discoveries related to the maintenance of bone health in recent decades.

In addition to describing the interacting mechanisms of these three cytokines, Grimaud *et al.* describe initial research activities in the development of OPG as a potential drug. Preclinical studies have indicated that OPG could effectively treat both osteoporosis and the bone loss associated with metastatic bone cancer. It is our understanding that Amgen (Thousand Oaks, CA, USA) is proceeding with FDA clinical trials for these two indications.

As investigators who work with the National Aeronautics and Space Administration (NASA) to promote a commercial interest and exploitation of the spaceflight environment to help discover, develop and test new drugs, we would suggest that OPG might also be an appropriate treatment for the bone loss that is caused by extended

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