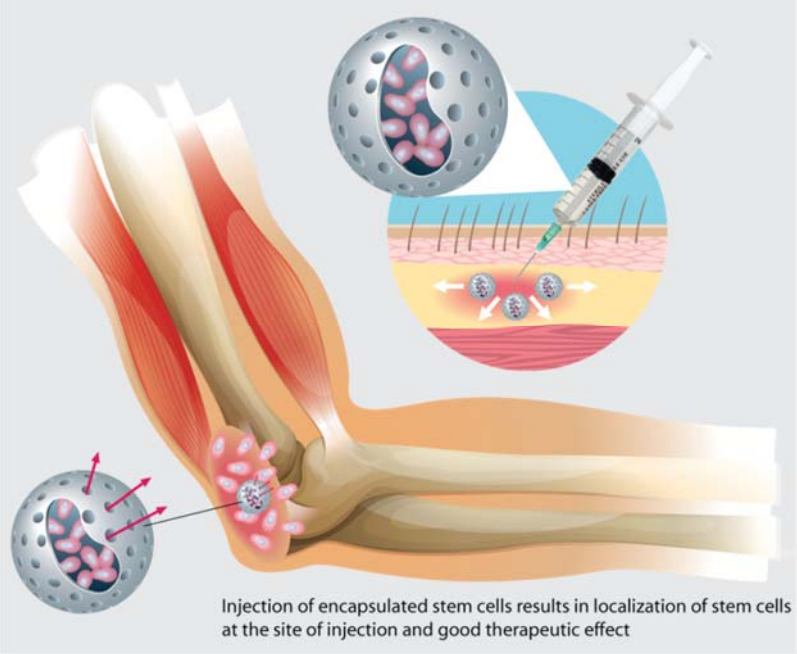
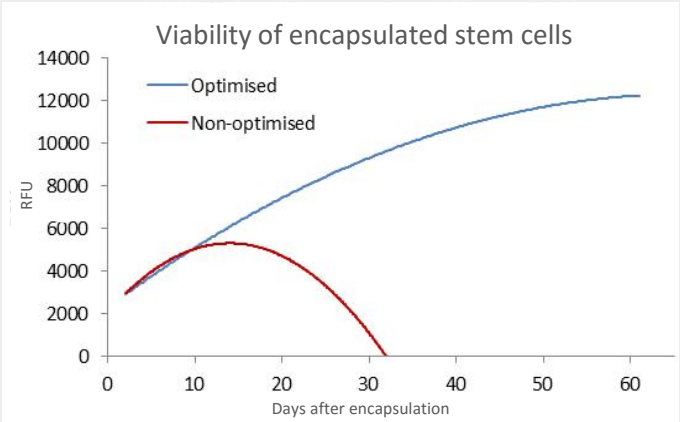
Cell-in-a-Box®: Applications for Stem Cells



Injection of encapsulated stem cells results in localization of stem cells at the site of injection and good therapeutic effect

Cell-in-a-Box® Improves Therapeutic Cell Viability



Cell-in-a-Box® enables the survival of stem cells over extended periods of time (assessed by AlamarBlue™ assay). This is believed to make the effect of stem cell therapeutics more long-lasting.

Cell-in-a-Box® Allows for Precise Placement, Protection and Removal of Therapeutic Cells

- Allows encapsulated cells to be placed precisely and restrained at the most effective location
- Prevents cells moving to unexpected locations
- Improved targeting increases efficacy of treatment
- Allows for removal of implanted cells
- Allows for increased accuracy and reduction of dosing
- Improves safety since:
  - ✓ Regulators are concerned that stem cells may migrate to non-target tissues, with hard to predict results
  - ✓ No easy method for tracking injected stem cells
  - ✓ Teratomas or stem cell tumours often documented (recently reviewed Nature Biotechnol. 30:849-57)

Cell-in-a-Box® Protects Stem Cells from the Immune System

- Protects the implanted stem cells from attack by the immune system
- Improved viability suggests that
  - ✓ Product lifespan *in vivo* will be increased
  - ✓ Less cells required for therapeutic effects

It is becoming clear that, rather than replacing damaged cells, stem cells exert their effects by a paracrine mechanism, i.e. the stem cells secrete factors and give signals to the surrounding tissue that stimulate regeneration and re-vascularisation.

Cell-in-the-Box® Technology allows:

- Cells to be restrained at the site of placement thus preventing them rapidly moving to other locations and increasing efficacy whilst reducing the number of stemcells required to be used.
- Cells to survive in a protected and favourable microenvironment inside or outside the body
- Cells to be tracked and if necessary removed from the patient
- Cells to be stored for long periods and easily transported worldwide
- Cells to be expanded without loss of "stemness"

Cell-in-a-Box® Allows Freezing, Transport and Long Term Storage of Stem Cells

- We have successfully resuscitated HEK293 cells up to 5 years post-freezing and current data indicate long term frozen storage of stem cells should also be feasible

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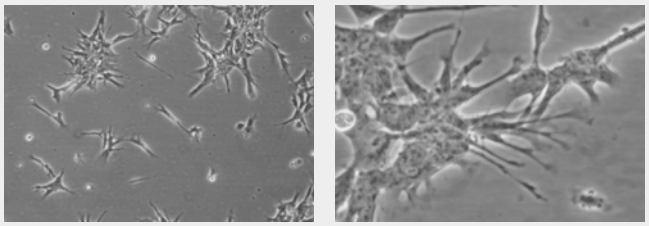
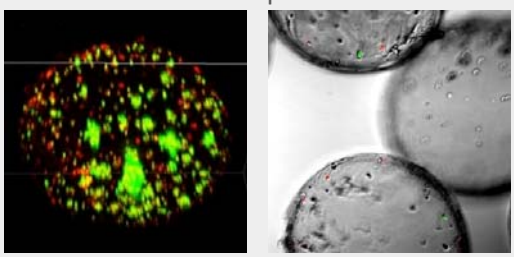
Cell-in-a-Box® Preserves "Stemness" of Stem Cells

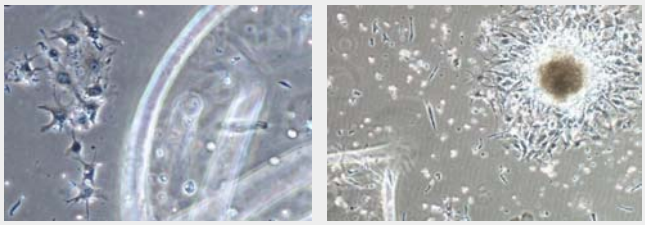
Stem cells before encapsulation



Once encapsulated

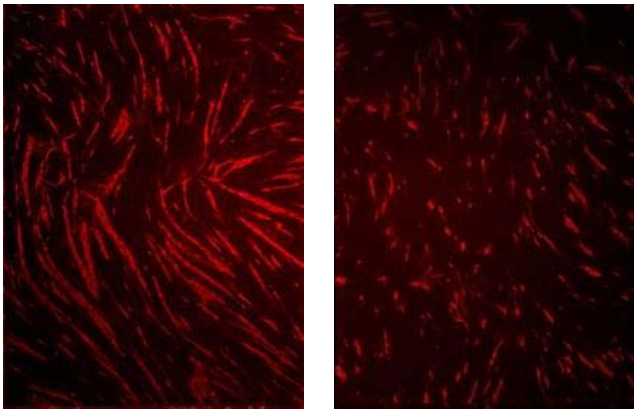


After release from capsules



Improved stability: Maintenance of stemness

- Maintaining the identity of stem cells is key to their therapeutic effect



Stem cells retain their functional properties after encapsulation as assessed by angiogenesis assays.
Left: angiogenesis surrounding encapsulated stem cells.
Right: angiogenesis surrounding empty capsules.

- Encapsulation does not affect the identity of the cells during encapsulation, maintaining their therapeutic effect (see images left and above)
- Cells can be released from capsules if required to analyse any changes (see images left)

Figures Left: Stem cells re-gain their original morphology when released form Cell-in-a-Box®.
Upper panels: Stem cells before encapsulation.
Middle panels: Stem cells inside the capsules.
Lower panels: stem cells 18h after being released from the capsules.

Summary of Benefits for Cell-in-a-Box® for Stem Cells

The use of therapeutic stem cells offers huge potential for the treatment of a wide range of human diseases. However, there are many hurdles to overcome before stem cell use becomes widespread.

Cell-in-a-Box® offers solutions to many of these problems:

- Allows well targeted restraint, dosing and subsequent removal of stem cells, alleviating concerns over cell migration and tumour formation, as well as reducing the number of cells required
- Offers improved viability and protection of stem cells, enhancing therapeutic efficacy
- Provides physical protection, widening the range of biotechnological applications for stem cells
- Ease of freeze/thawing, long term storage and transport
- Several types of stem cell successfully encapsulated already including iPS and adult stem cell lines

For more information on our **Cell-in-a-Box®** technology and potential applications:

Dangerfield JA, Salmons B, Corteling R, Abastado J-P, Sinden J, Gunzburg WH, Brandtner, EM. (2013) Chapter 3: "The diversity of uses for cellulose sulphate encapsulation". E-Book "Bioencapsulation of Living Cells for Diverse Medical Applications", Bentham Science Publishers. Eds. EM Brandtner and JA Dangerfield

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