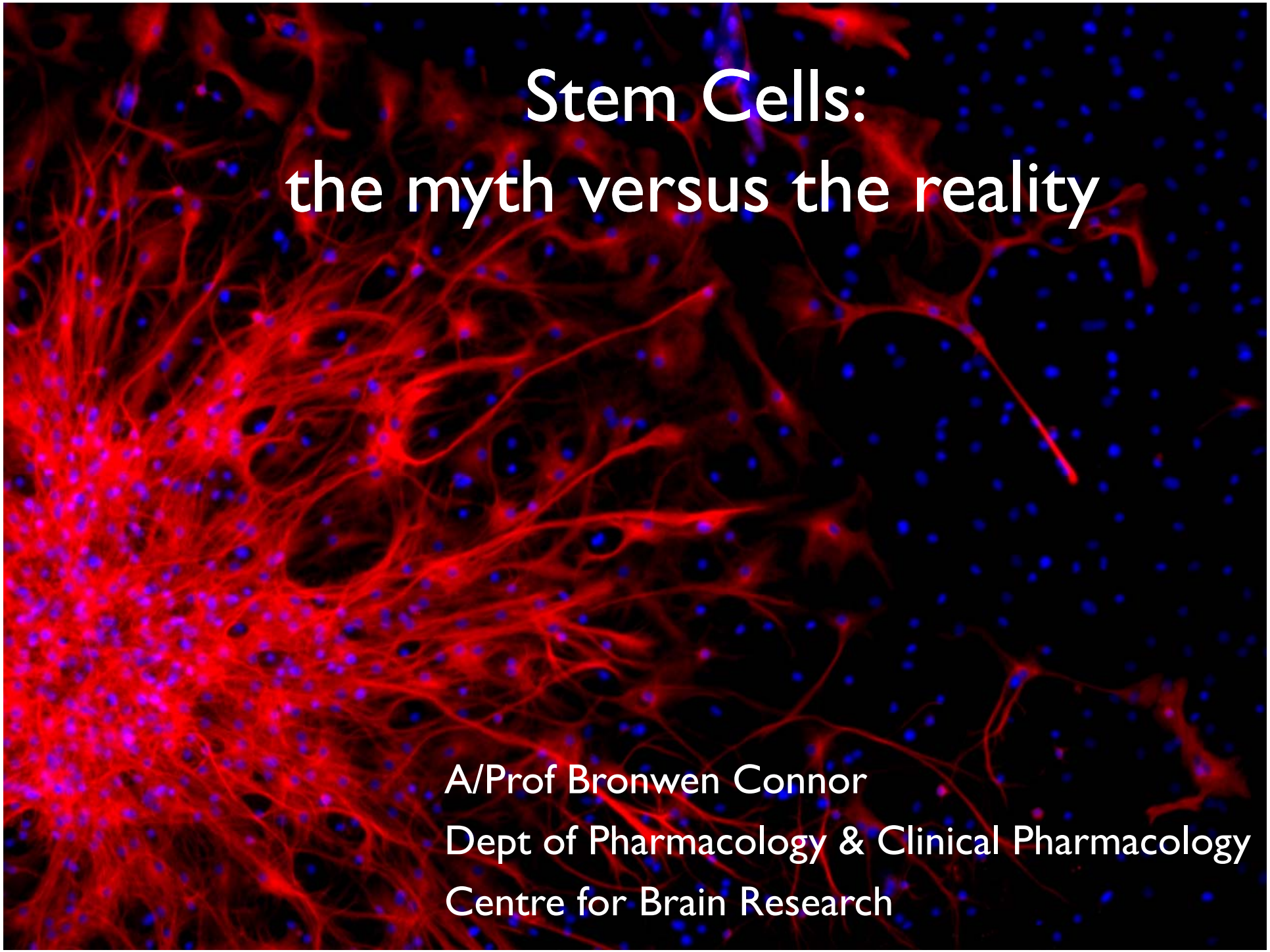

Stem Cells: the myth versus the reality

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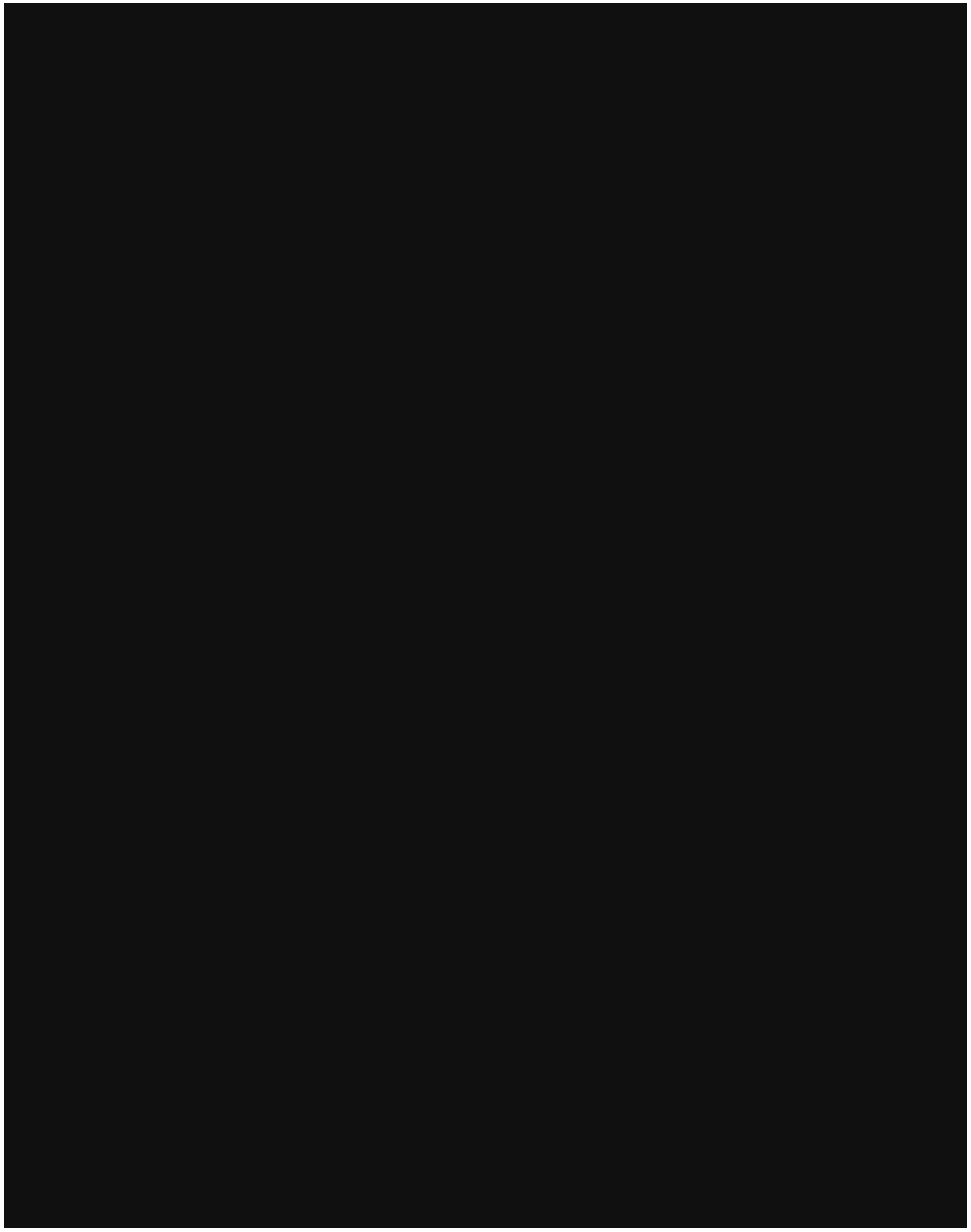
What Are Stem Cells?

- Unspecialised cells
- Stem cells have the unique ability to grow into many different cell types in the body.
- Involved in development (embryonic stem cells)
- In adult, they are found in many tissues and serve as an internal repair system
- Two important characteristics:
  - Capable of dividing and renewing themselves for long periods.
  - Can be directed to turn into specialised cells.

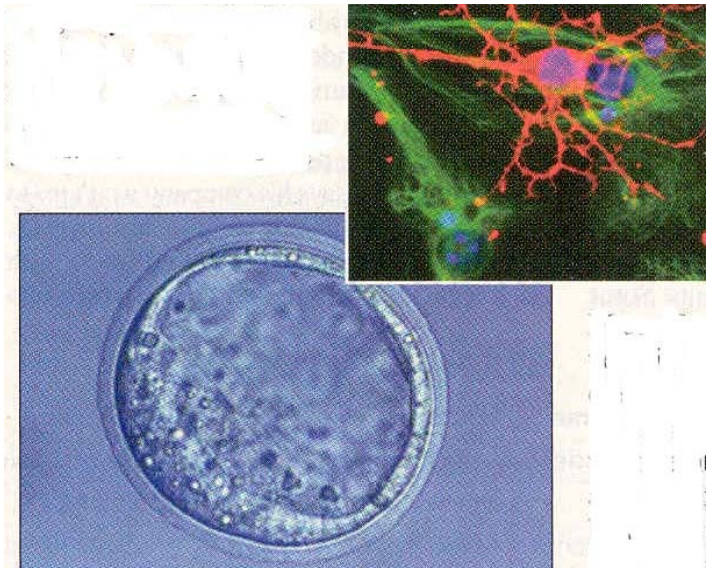


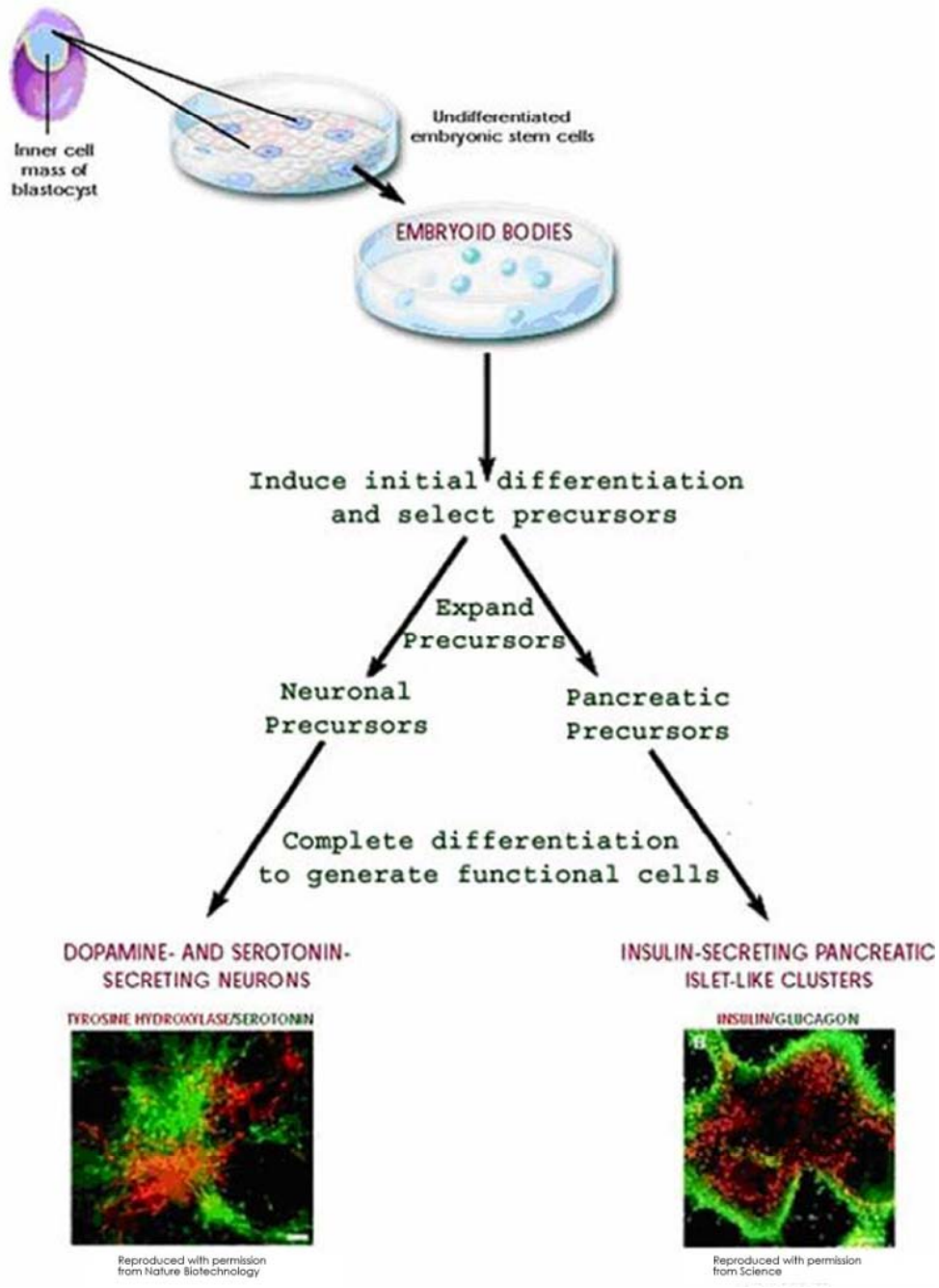
What is Exciting About Stem Cells?

- New potentials for treating many diseases and injuries including neurological diseases and injuries.
- Provide new replacement cells for those lost through disease or injury.
- Provide supporting chemicals to enhance axon regrowth, prevent cell death and inflammation.
- Information about how brain cells develop and are affected by disease process
  - Cell models of neurological disease
- Platform for testing new drugs

What Are Embryonic Stem Cells?

- Derived from embryos
  - Blastocyte 3-5 after fertilisation (IVF)
- Pluripotent
  - Able to generate any cell type in the body
- Can be directed by scientists to form specialized cell types = brain cells




Inner cell mass of blastocyst
Undifferentiated embryonic stem cells
EMBRYOID BODIES
Induce initial differentiation and select precursors
Expand Precursors
Neuronal Precursors
Pancreatic Precursors
Complete differentiation to generate functional cells
DOPAMINE- AND SERONTONIN-SECRETING NEURONS
TYROSINE HYDROXYLASE/SEROTONIN
Reproduced with permission from Nature Biotechnology
INSULIN-SECRETING PANCREATIC ISLET-LIKE CLUSTERS
INSULIN/GLUCAGON
Reproduced with permission from Science

What Are Adult Stem Cells?

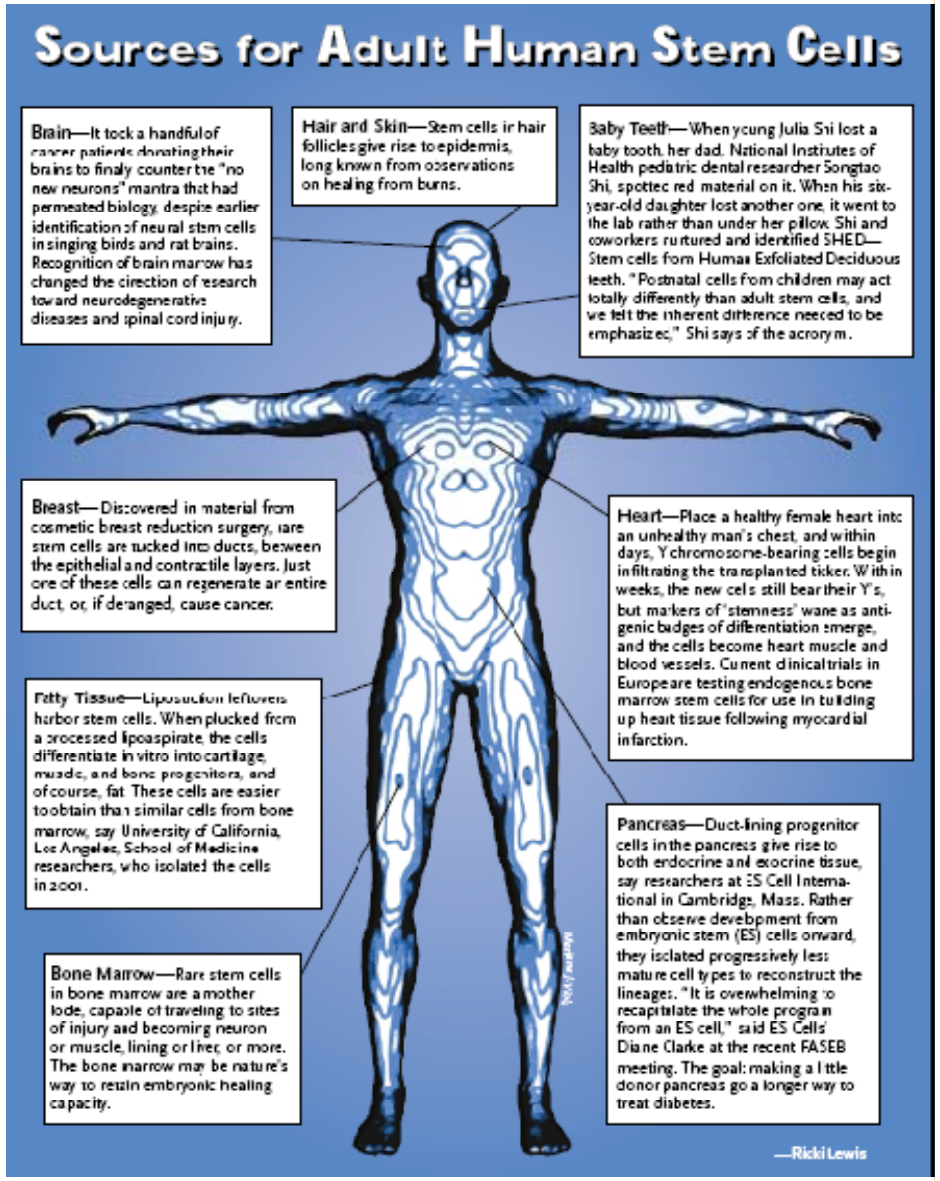
- Uncommitted cells found among mature cells in a tissue or organ
- Can self-renew and generate the specialised cells found in mature tissue / organ
- Involved in maintenance and repair
- Exciting use in cell replacement therapy as provides potential to use patients own stem cells!

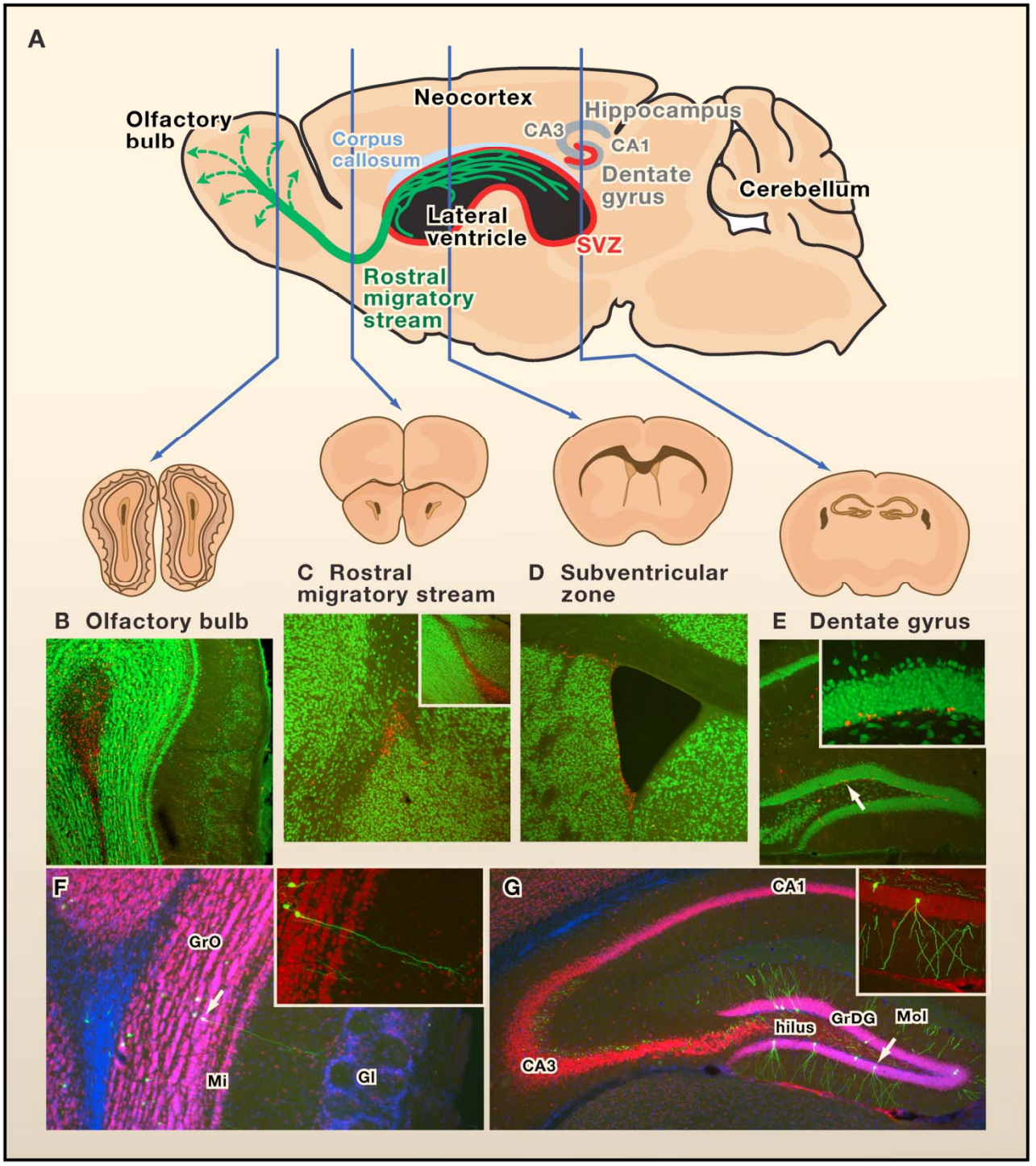
Range of Adult Stem Cells

- Brain → neurons, astrocytes, oligodendrocytes

- Bone marrow / umbilical cord:
  - Mesenchymal stem cells → bone, cartilage, fat, connective tissue
  - Hematopoietic stem cells → blood cells

→ brain cells???




A
Olfactory bulb
Neocortex
Corpus callosum
CA3
Hippocampus
CA1
Dentate gyrus
Cerebellum
Lateral ventricle
SVZ
Rostral migratory stream
B Olfactory bulb
C Rostral migratory stream
D Subventricular zone
E Dentate gyrus
F
GrO
Mi
Gl
G
CA1
hilus
GrDG
Mol
CA3

What Are the Similarities and Differences Between Embryonic and Adult Stem Cells?

- Each have advantages and disadvantages for cell replacement therapy

- Embryonic stem cells can become any cell type (pluripotent)
  - but can form teratomas
- Adult stem cells limited to become cells from tissue of origin
  - don't form teratomas

- Adult stem cells rare and more difficult to grow in lab
- Embryonic stem cells grow easily but ethical issues regarding source

- Adult stem cells can obtained from patient
  - Removes issues of rejection

The Truth - Current Clinical Trials

- Stem cell therapy MUST obtain US FDA approval.
- An approved clinical treatment is a medical practice that has been shown through a formal process of clinical trials to be reasonably safe and effective for treating a particular disease or condition.
- An experimental intervention is new, untested, or different from the usual medical treatment. It has not yet been proven that it is safe or that it will work in treating the particular disease.

The Truth - Current Clinical Trials

- A clinical trial is a research study designed to answer specific questions about a new treatment or a new way of using current treatments.
- Clinical trials are used to establish whether new treatments are safe and effective.
- It is very important to understand that the new treatment being tested is *unproven*. It may not be better than, or even as good as, existing treatments.
- Some research studies are not trials. In some cases, new experimental treatments might be tried on a very small number of people before a clinical trial is started. Again, the new treatment being tested is *unproven*.
  - Must have approval from an institutional authority / ethical approval
- The fact that a procedure is experimental does not automatically mean that it is part of a research study or clinical trial.

The Truth - Current Clinical Trials

- Bone marrow / umbilical cord stem cells
  - Undergoing clinical trials for a range of disorders
    - Heart disease; vascular repair; bone and cartilage repair etc
  - Autologus; easily accessed; currently approved for leukemias and rare blood disorders

- Clinical trials in CNS:
  - Multiple sclerosis; motorneuron disease; stroke; cerebral palsy etc.

- Experimental intervention
  - Dr Joanne Kurtzberg Duke University
    - Ceberal palsy; Stroke

- Generate new brain cells??
  - Probably not.
  - Provide chemicals to protect cells, support regrowth of connections, stimulate resident stem cells, reduce inflammation

The Truth - Current Clinical Trials

- Human embryonic stem cells
  - Currently only 1 approved clinical trial
    - Geron
      - Spinal cord injury - hES-derived oligodendrocytes
  - Currently on hold at start of Phase 1 to resolve issues of tumour formation.
- Olfactory ensheathing cells
  - Alan MacKay-Sims Griffith University, Brisbane
  - Phase 1/2a clinical trial
    - No significant functional improvement. No adverse effects.
  - Spinal Cord Society of NZ undertaking similar trial University of Otago

The Myths – Stem Cell "Clinics"

- **Claims based on patient testimonials.** Clinical trials are based on extensive preclinical research or Phase 1/2 clinical trial data.
- **Multiple diseases treated with the same cells.**
- **The source of the cells or how the treatment will be done is not clearly documented.** Purity of harvested cells?
- **Claims there is no risk.**
- **High cost of treatment or hidden costs.** It is not customary for someone to pay to be in a clinical trial (other than perhaps travel and other personal expenses). Consider whether you should pay for a treatment that is unproven. Furthermore, ask about the costs of emergency medical care if something goes wrong, particularly if you are outside your own country.
- **No follow-up after procedure**. No assessment of improvement. No reporting of the outcomes of the procedure to the international community.

The Myths – Stem Cell "Pills"

- "Stimulating the release of adult stem cells from bone marrow into the circulation to slow aging process and repair areas of the body suffering from degeneration / injury."

- ColoStem
  - Colostrum product
  - Colostrum has no effect on bone marrow stem cell release.

- StemEnhance®
  - Blend of two compounds extracted from the aquatic botanical Aphanizomenon flos-aquae (AFA).
  - No scientific evidence that AFA effects bone marrow stem cell release or migration
  - Suggestions that chronic ingestion of AFA may cause liver toxicity.

- These are food supplements so do not require FDA approval – be careful!

In Conclusion

- Stem cell therapy for neurological disease and injury is an exciting possibility.
- We still have much to learn about stem cells.
- We need to be sure of the long-term safety and effectiveness of stem cell therapies before clinical use
  - Approved clinical trials are the only way to do this.
- Stem cell "clinics" do not assist with further development of stem cell therapy and many offer empty promises.
- There is no "over-the-counter" stem cell "pill"

Supporting Information

- http://stemcells.nih.gov/info/basics
- www.isscr.org
  - Patient guideline to stem cell therapy
- www.clinicaltrials.gov/ct2/info/resources/
- Please feel free to contact the Centre for Brain Research for support and information.