

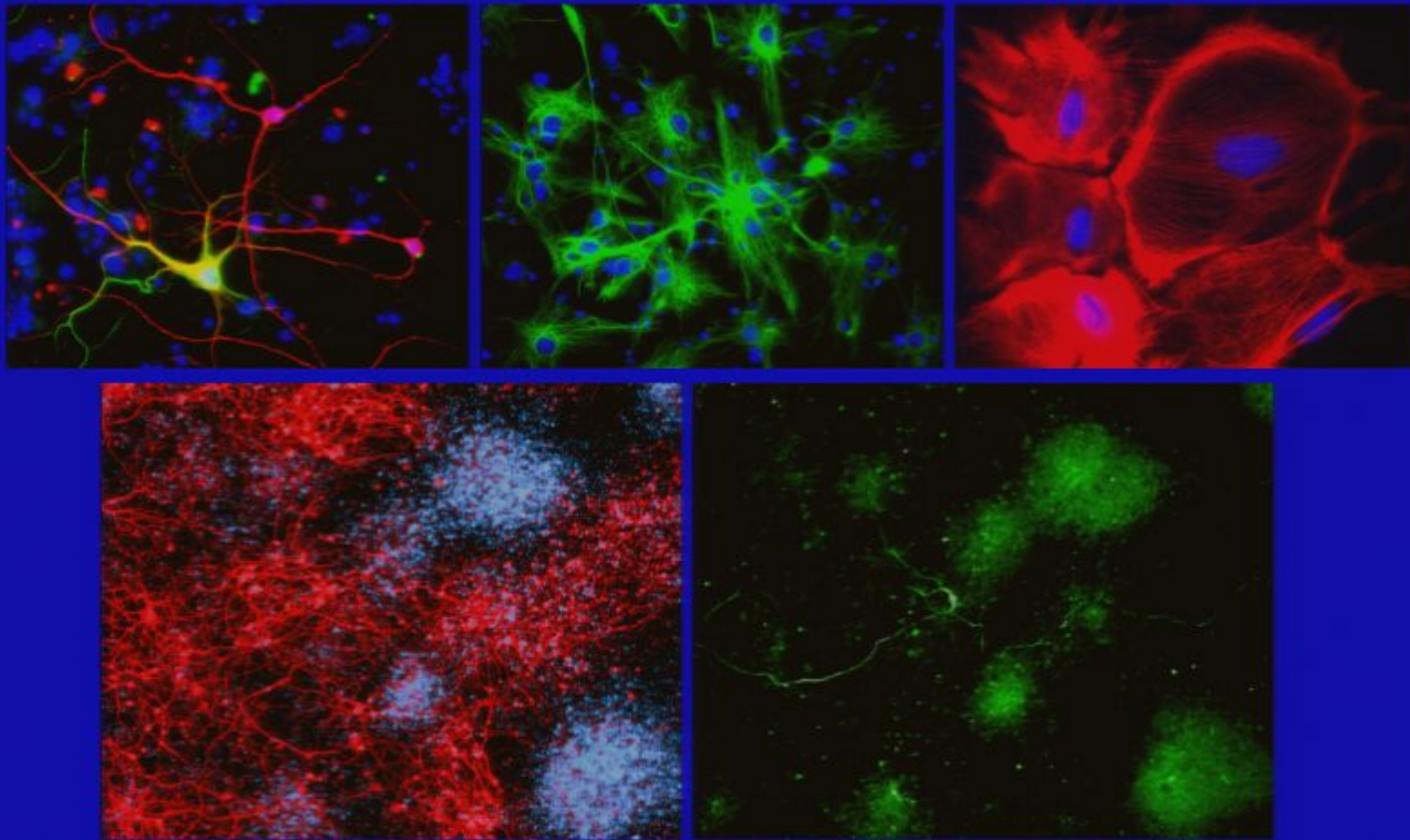
Title: Accessible adult stem cells from mammalian skin – from basic biology to therapeutic utility

Date: Nov 22, 2006 02:00 PM

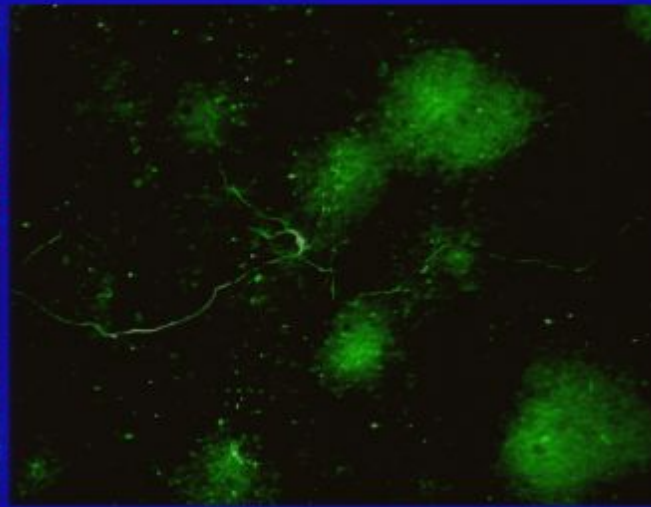
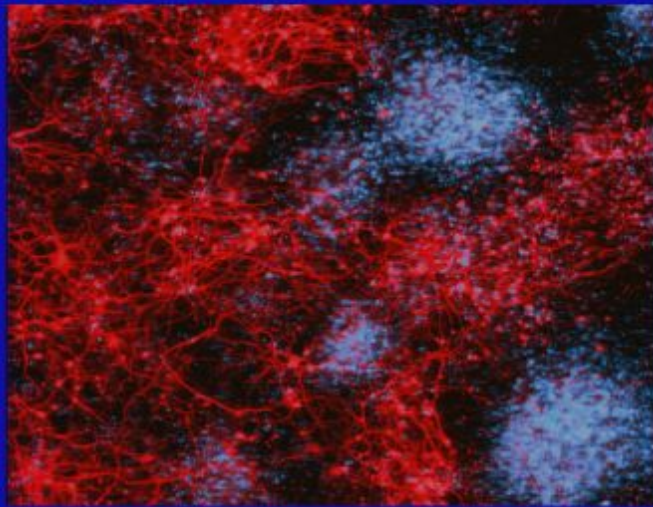
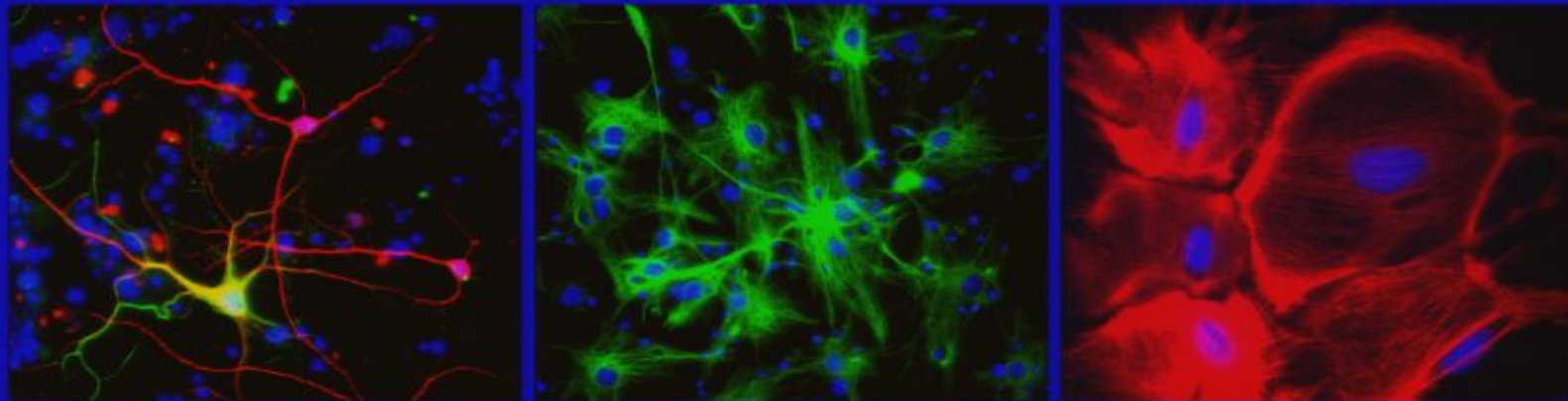
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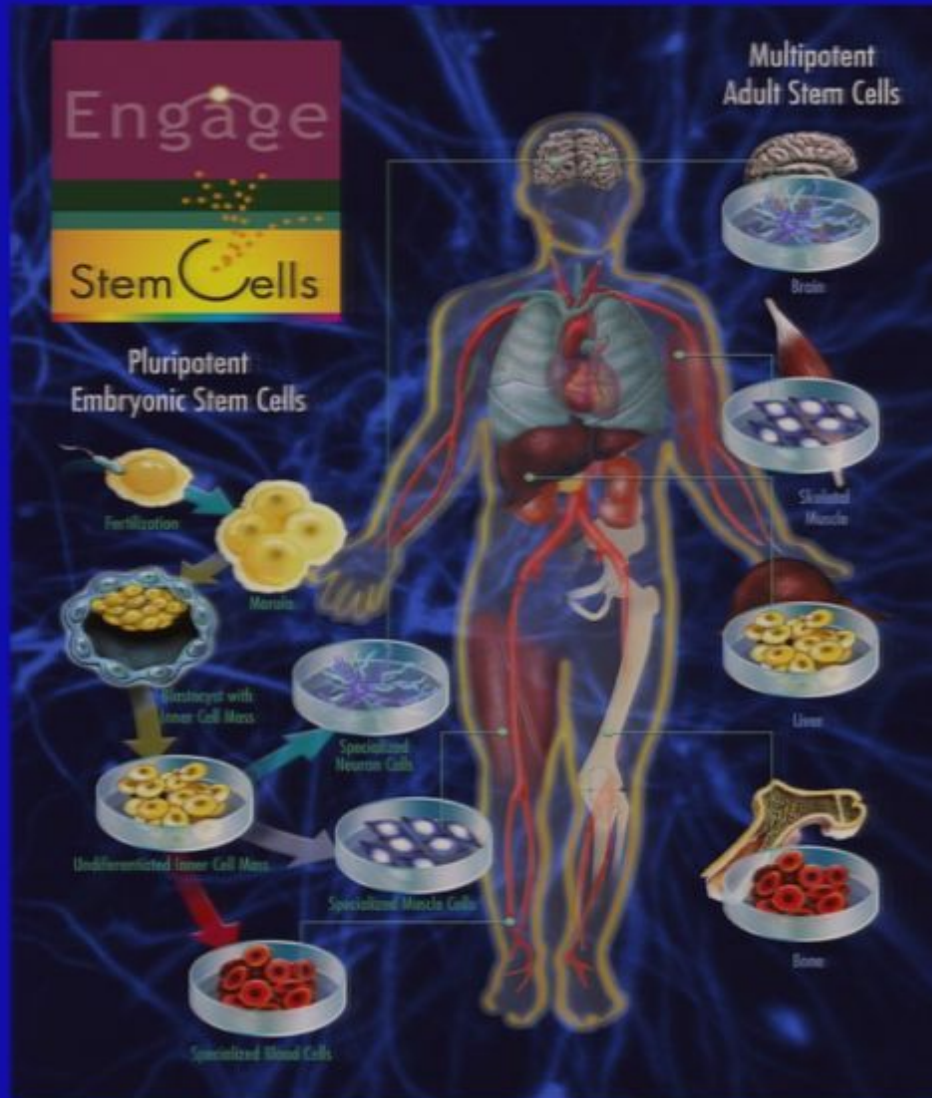
Abstract: We have previously isolated and characterized a multipotent precursor cell (termed SKPs for SKin-derived Precursors) from both rodent and human skin, and have shown that these stem cells share many characteristics with a multipotent stem cell that is found in the embryo termed a neural crest stem cell. Here I will discuss our current work with regard to the basic biology of these stem cells, with a focus on the “what, where and why”, and on their therapeutic potential with specific regard to the nervous system.

NEURAL STEM CELLS



NEURAL STEM CELLS





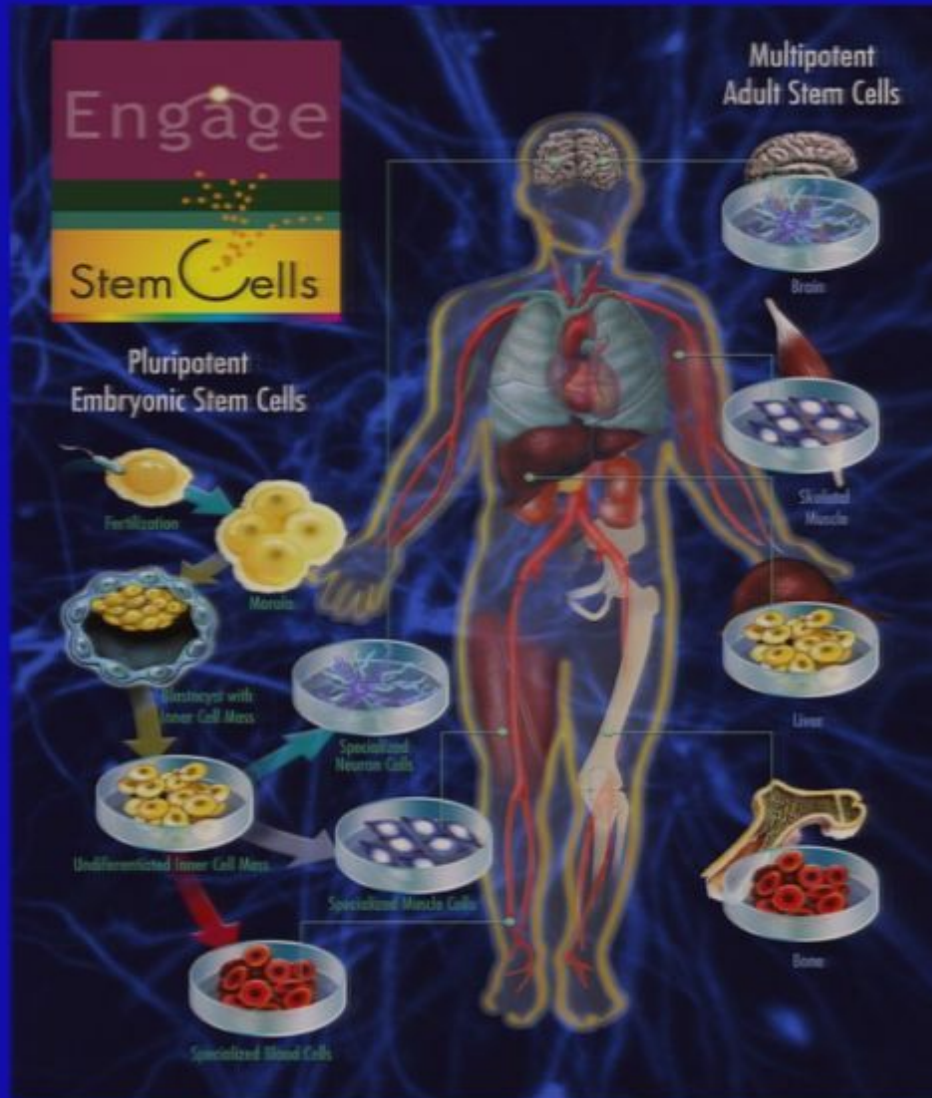
ES cells versus adult stem cells

What are the advantages of embryonic stem cells?

- - ES cells can differentiate into all of the cells of the body, while adult stem cells are largely tissue biased
- - adult stem cells, in general (the exceptions being neural stem cells and SKPs) divide poorly

What are the advantages of adult stem cells?

- - paucity of ethical issues, depending upon source
- - potential for autologous transplantation



ES cells versus adult stem cells

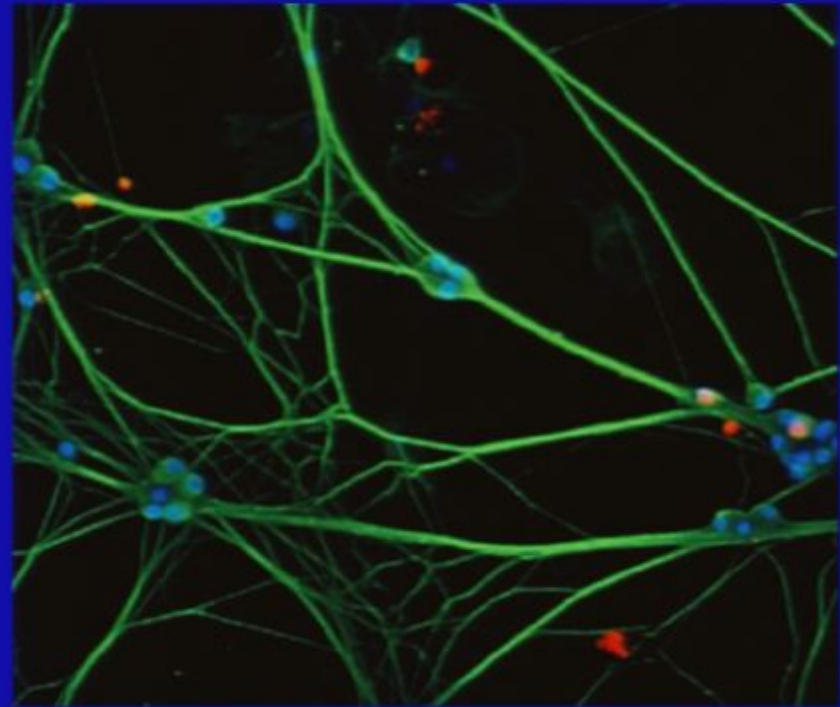
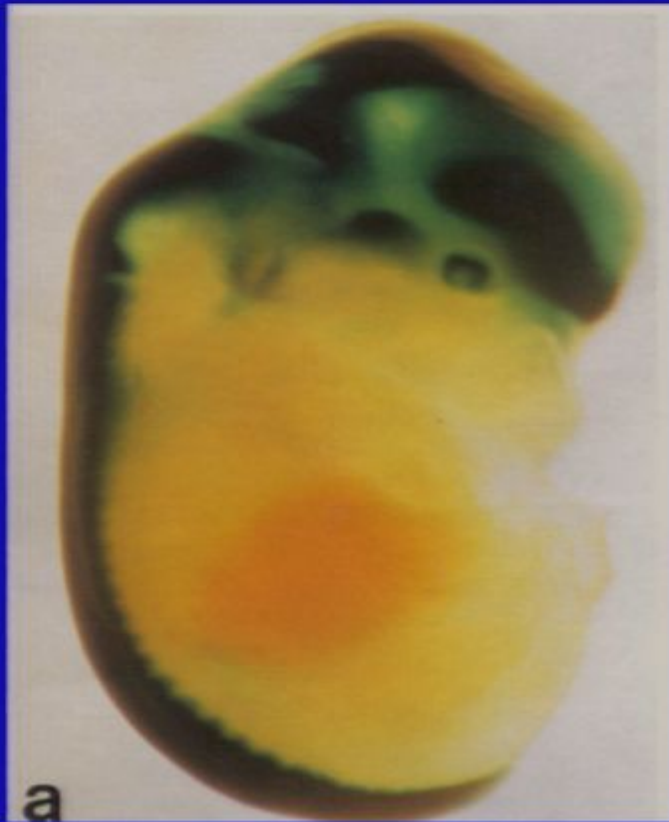
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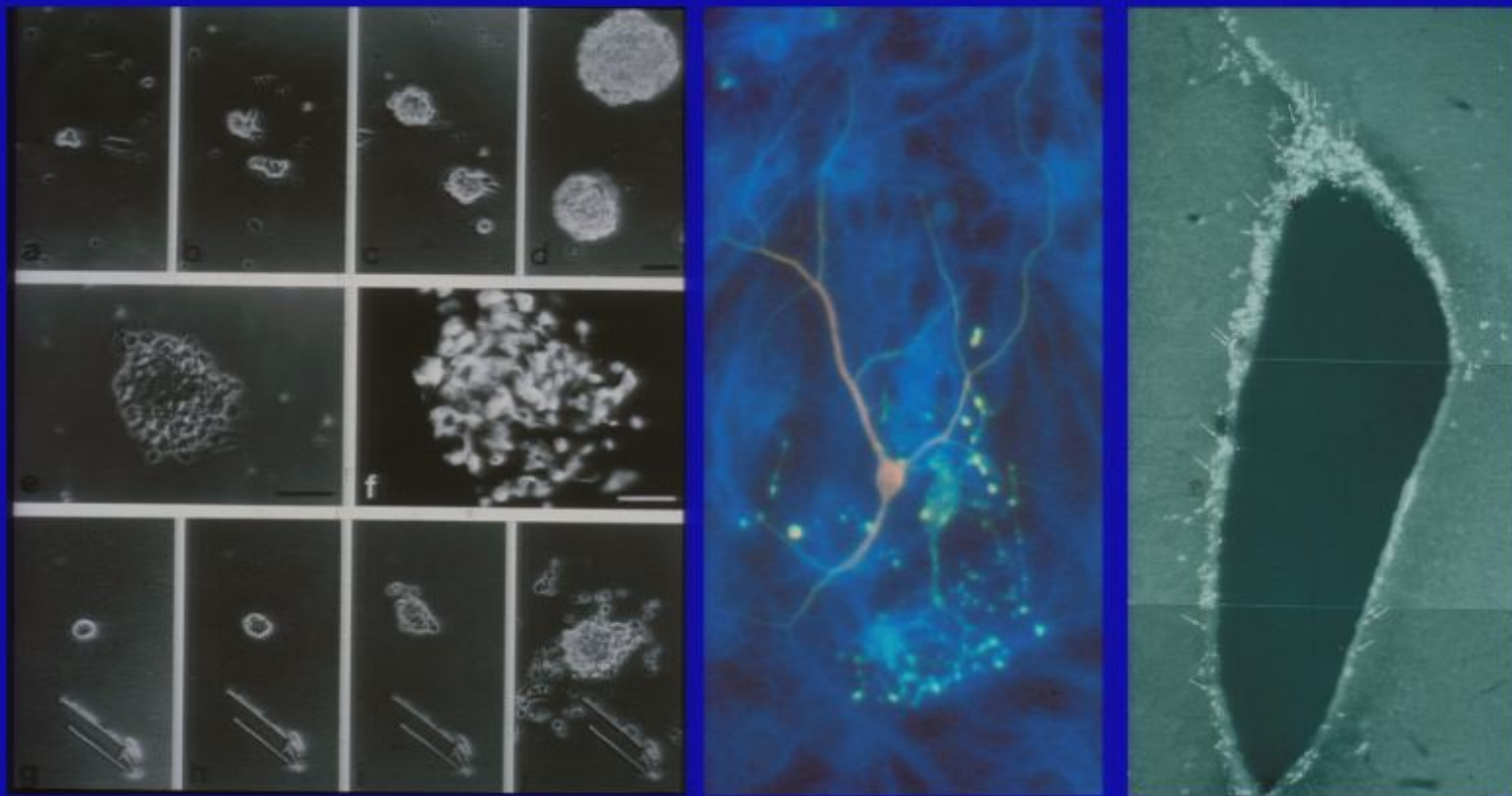
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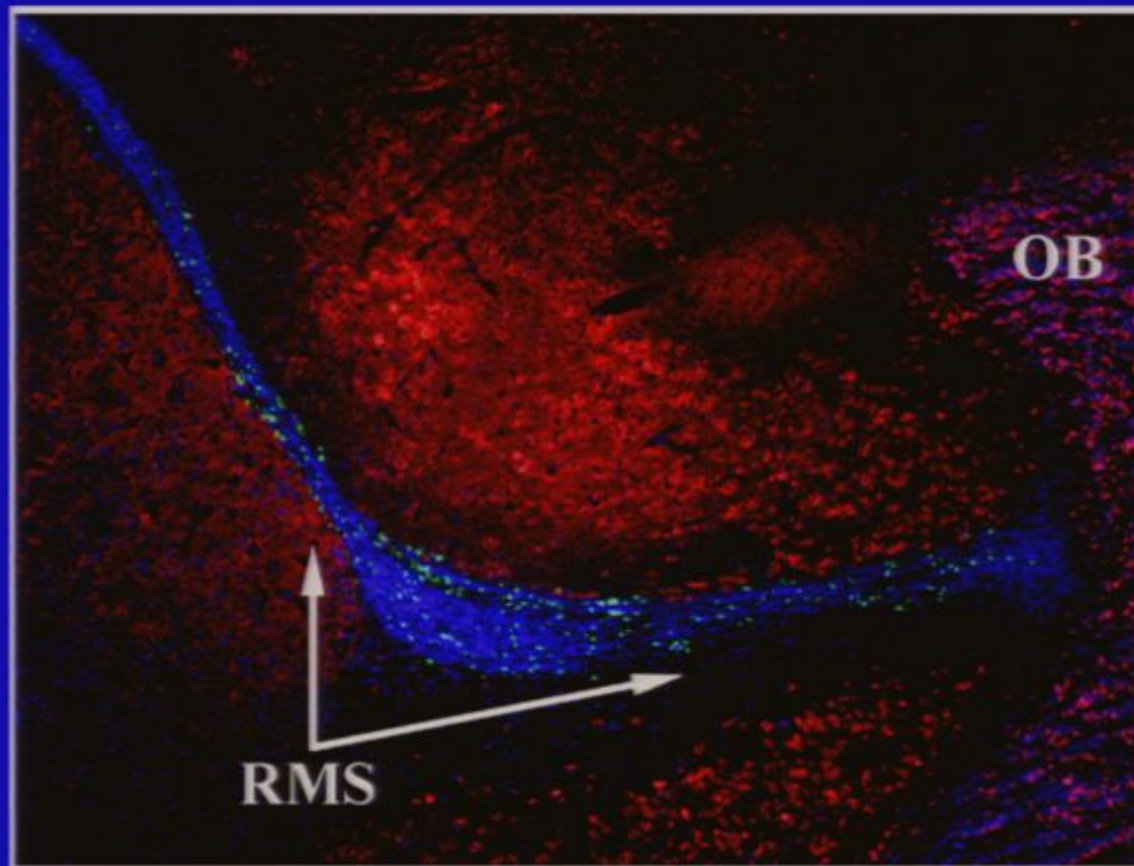
Neural Stem Cells: What are they?



Adult neural stem cells are also present in the adult brain (from Sam Weiss)



New neurons for learning and memory,
maternal behavior and maybe even repair

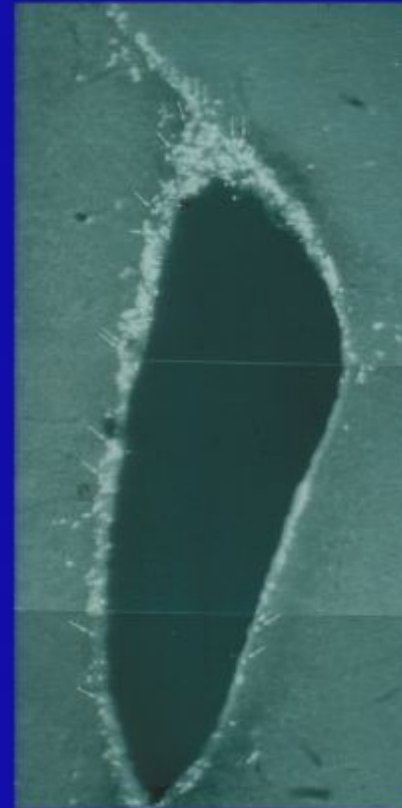
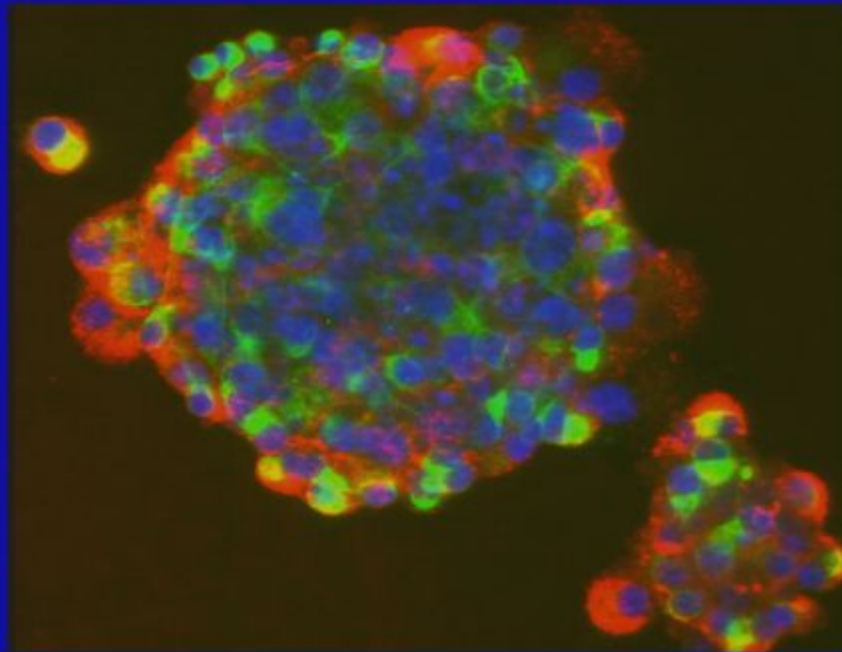


Stem Cells and Therapy

Transplantation

or

Recruitment



What kinds of conditions could we treat?

Parkinsons disease

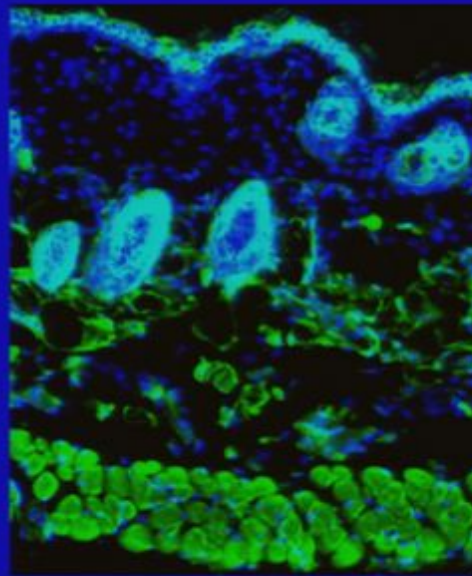
Demyelinating diseases

Spinal cord injury

So what are the issues?

- Supply - the current source of adult neural and ES cells are human embryos, raising concerns about ethics and about quantity
- Problems with heterologous transplantation
- Little knowledge of how to control the cell fate decisions made by stem cells

The Search for an Accessible Stem Cell

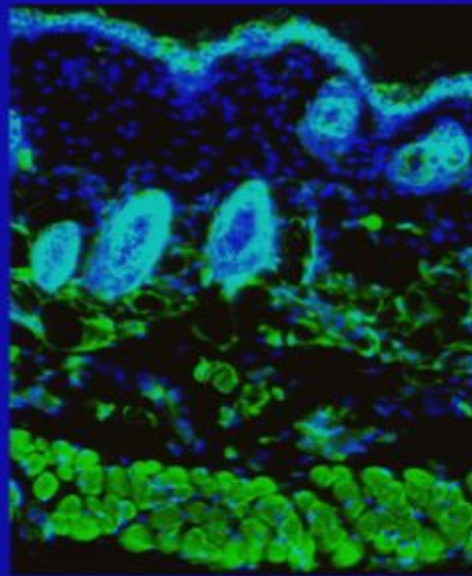


skin

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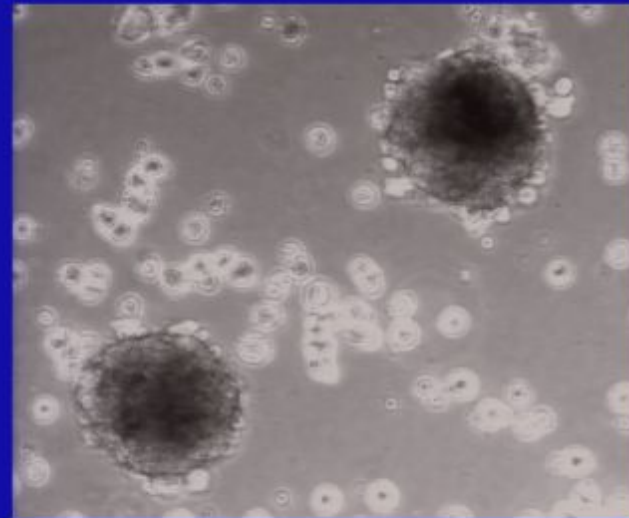
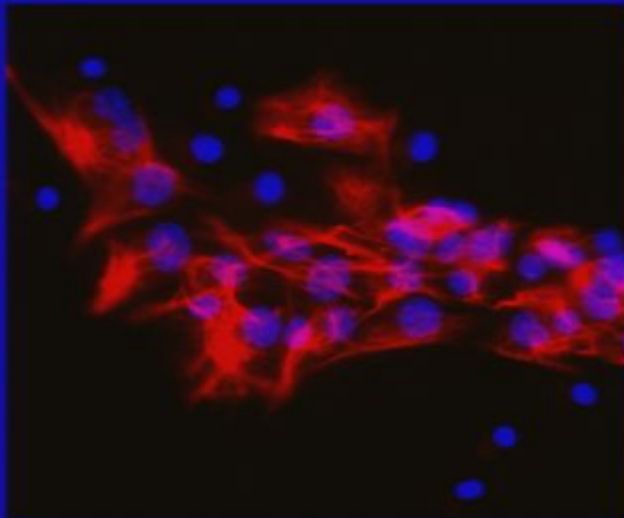
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The Search for an Accessible Stem Cell

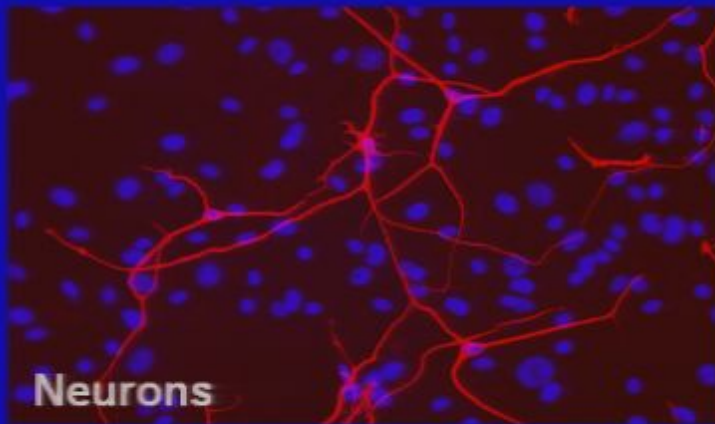


skin

SKin-derived Precursors (SKPs) "look" like neural stem cells

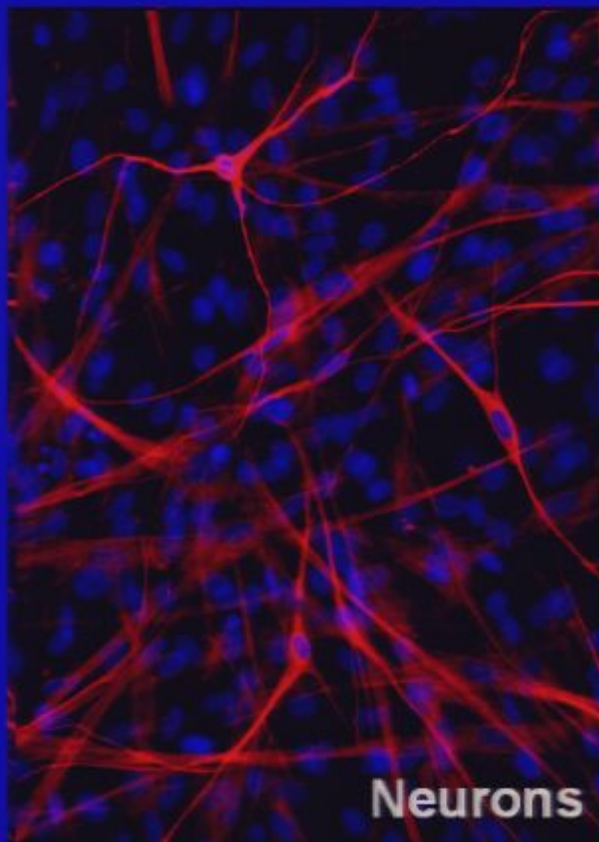
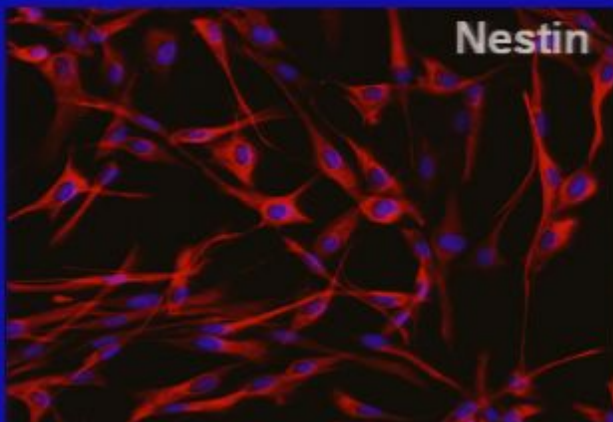
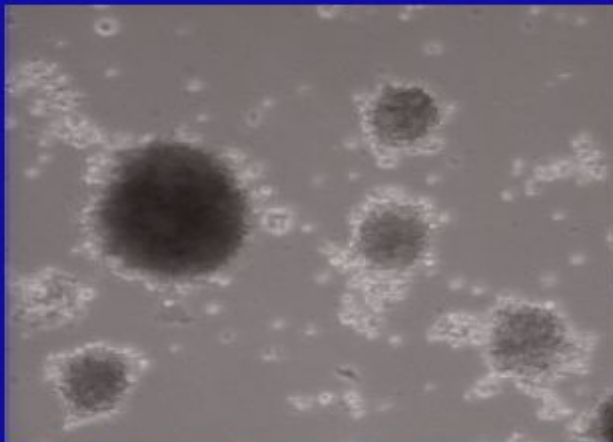


SKPs clonally generate both neural and mesodermal progeny



Jean Toma

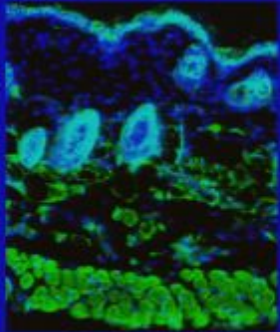
**SKPs can be routinely isolated from human foreskin,
and they too are multipotent**



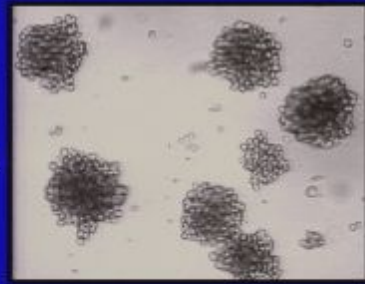
Osteoblasts



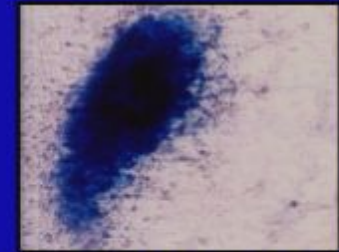
Jean Toma, Jeff Biernaskie



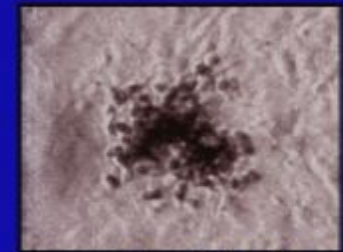
skin



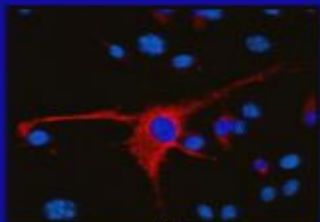
SKPs



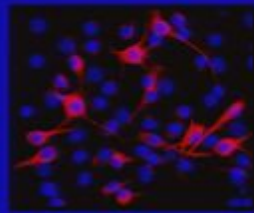
chondrocytes



osteoblasts



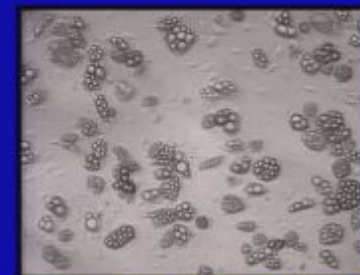
glia



neurons



smooth muscle

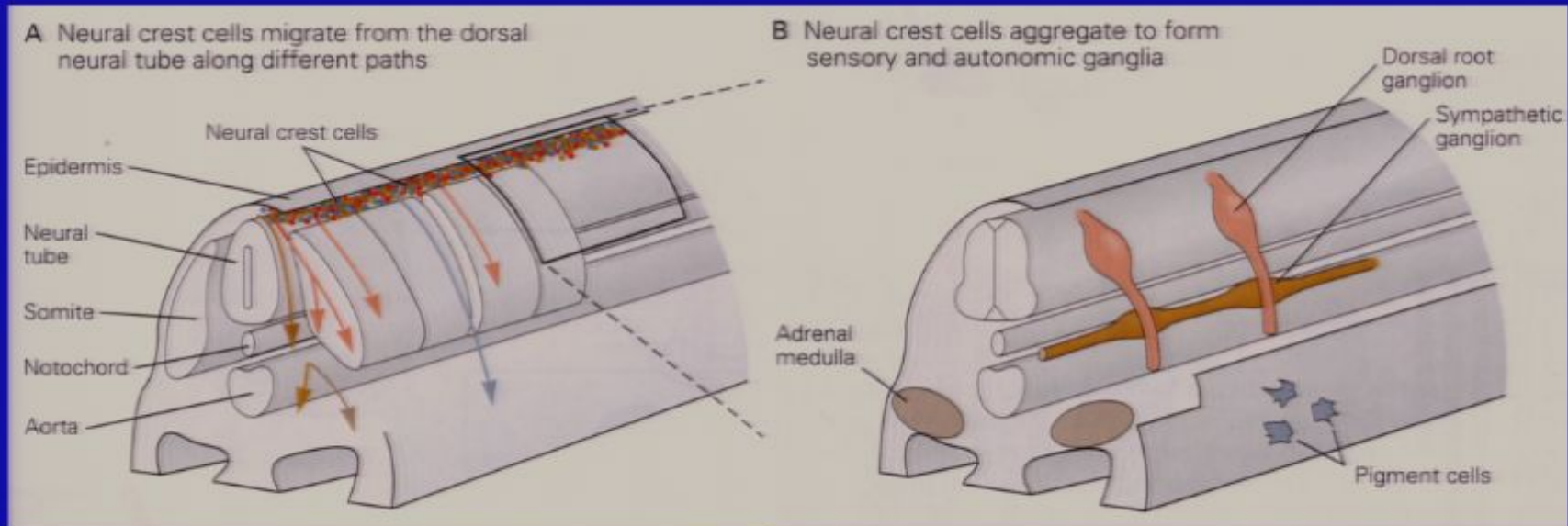


adipocytes

•SKPS: WHAT, WHERE AND WHY?

•CAN SKPS BE USED THERAPEUTICALLY?

THE NEURAL CREST

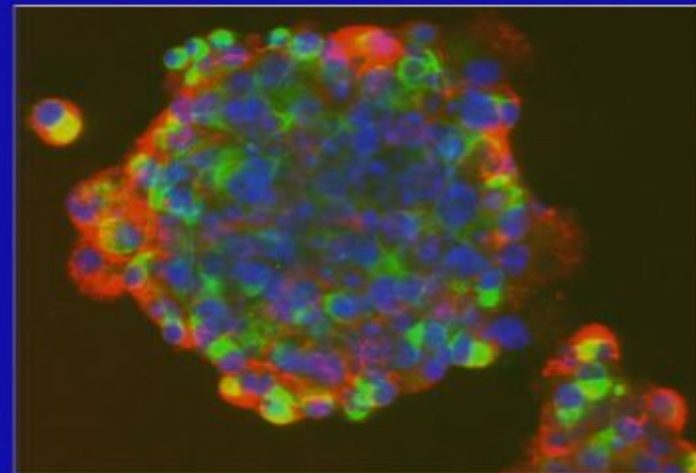


Neural crest derivatives include:

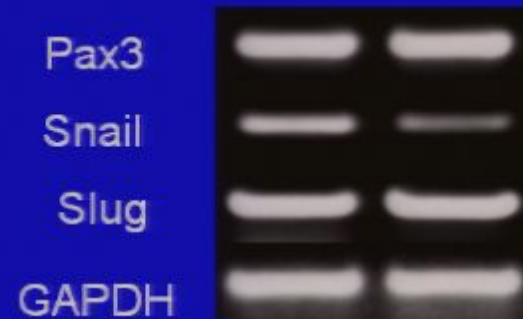
- peripheral nervous system
- smooth muscle/myofibroblasts
- adrenal cells
- melanocytes, Schwann cells, Merkel cells in skin
- bone and cartilage of the head
- dermis in the head, fibroblasts in the nerve
- adipocytes in head and parasympathetic ganglia

SKPs express transcription factors that are expressed in embryonic neural crest precursors

Mouse SKPs

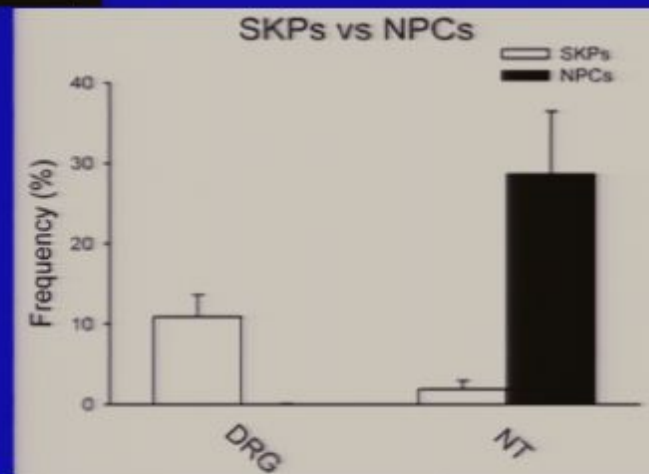
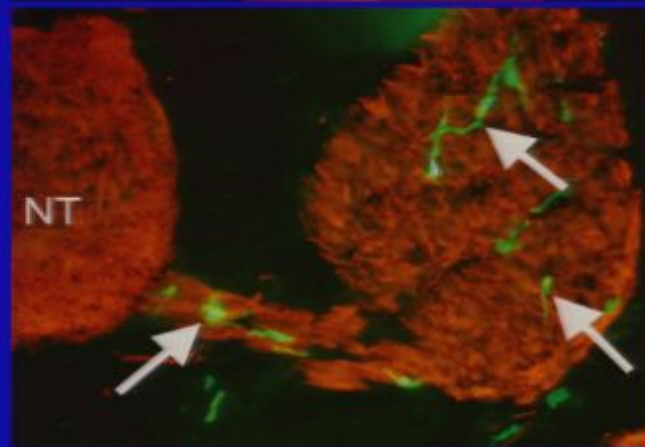
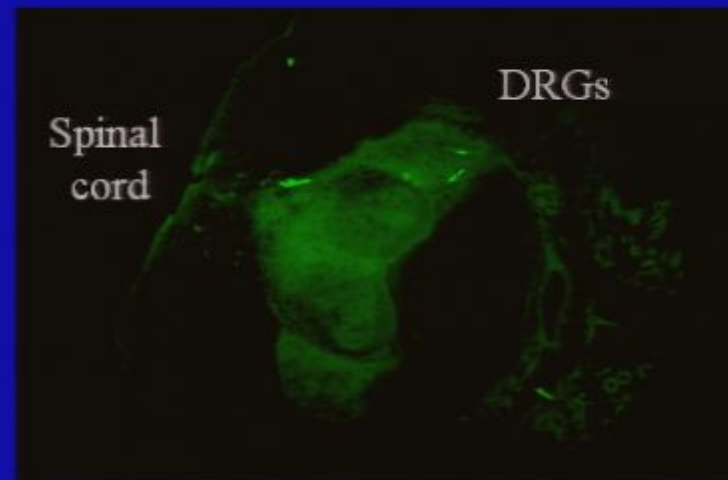
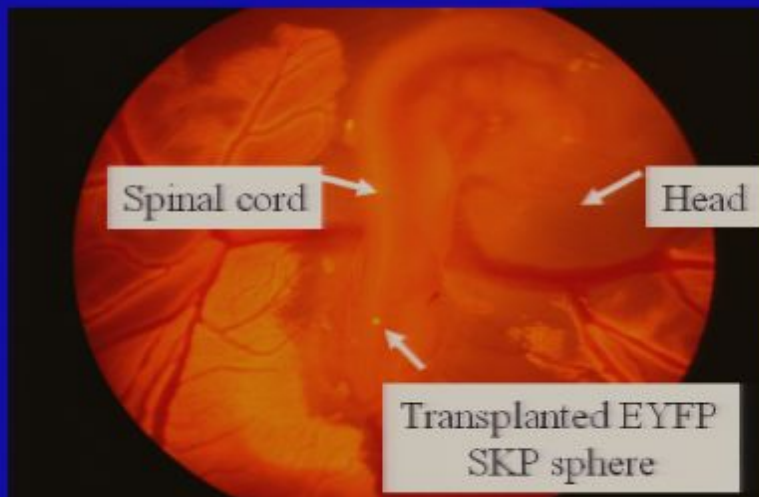


Human SKPs



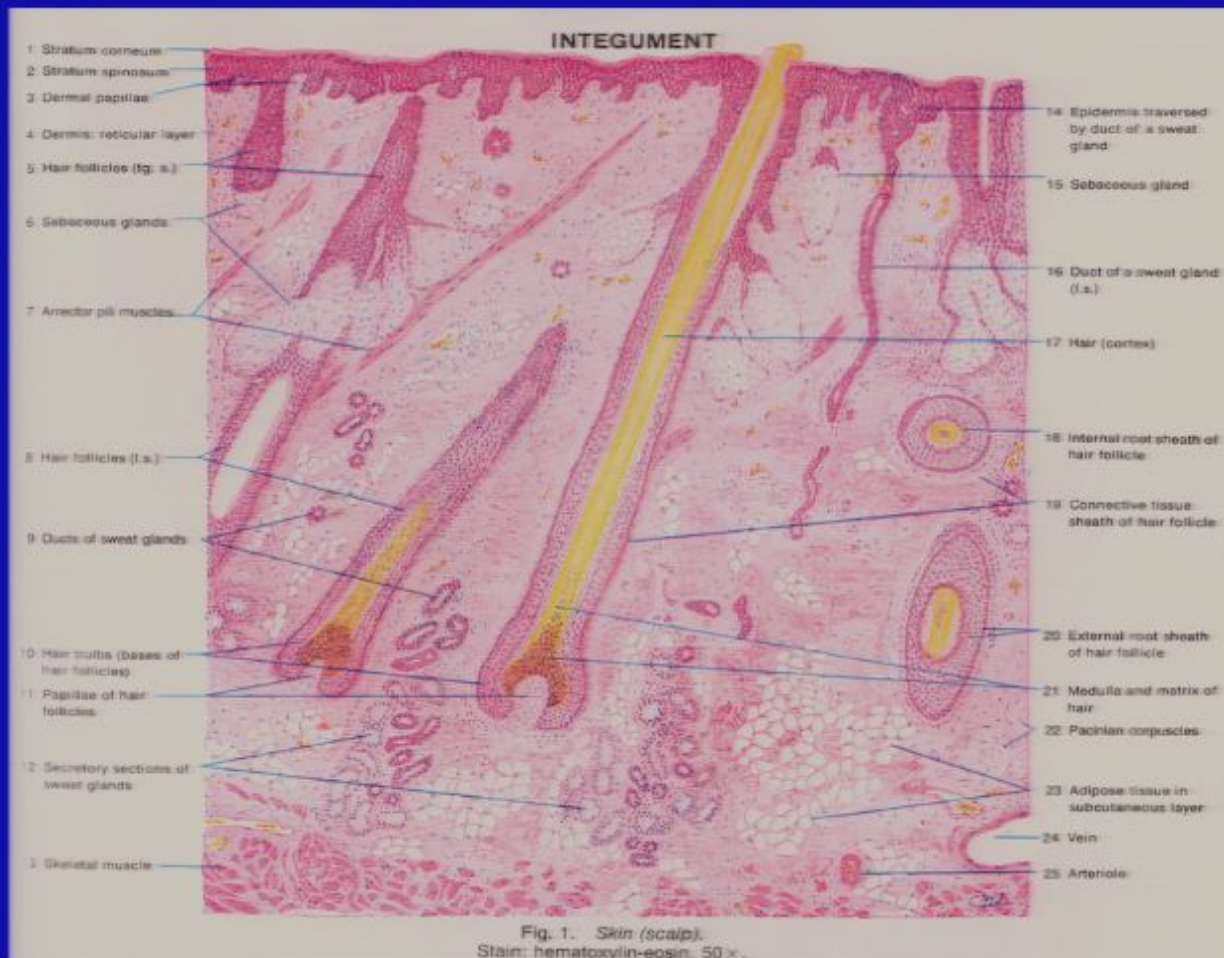
Ian McKenzie, Jean Toma

SKPs transplantation into the developing chick neural crest

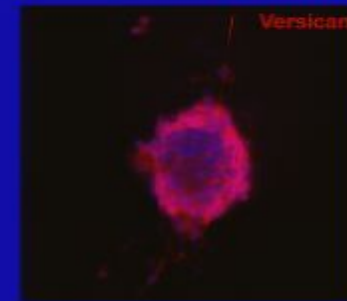
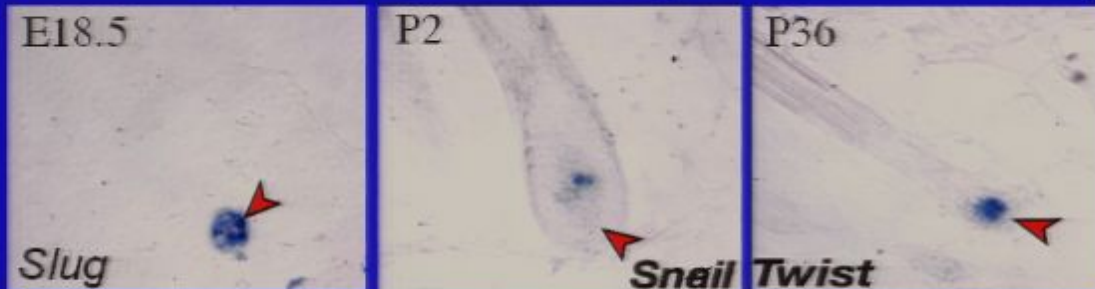


Adrienne
Junek
Vic Rafuse

One niche for SKPs is follicle dermal papillae



SKP markers are expressed in follicle dermal papillae and vice versa throughout development



Karl Fernandes
 Ian McKenzie
 Pleasantine Mills

Whisker follicle papillae contain SKP-like cells

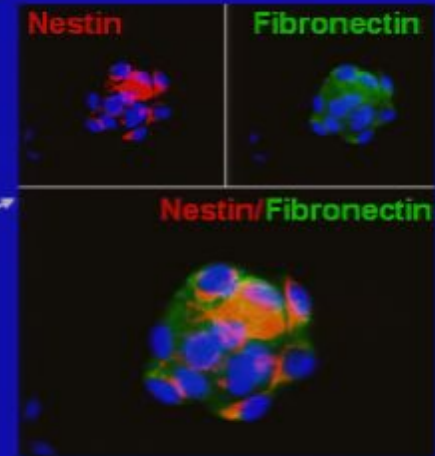


Microdissection of Whisker Dermal Papillae

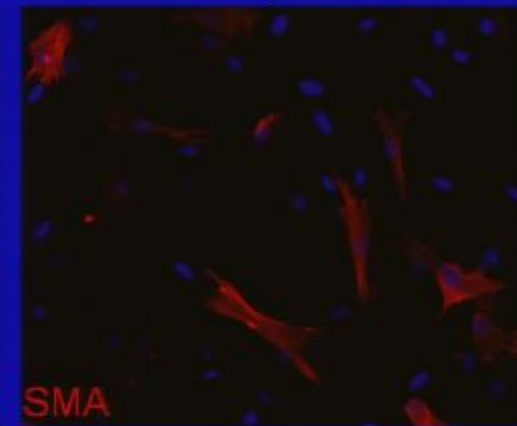
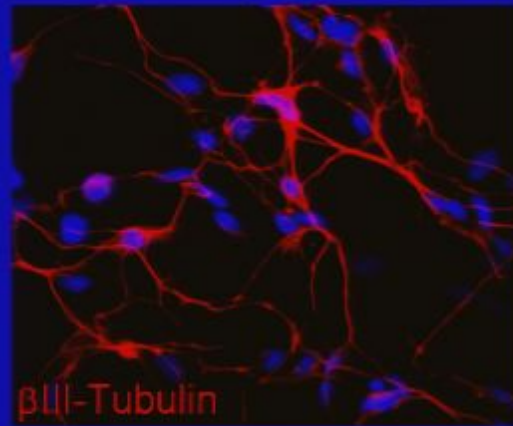
Dissociate & Culture



Cytospin

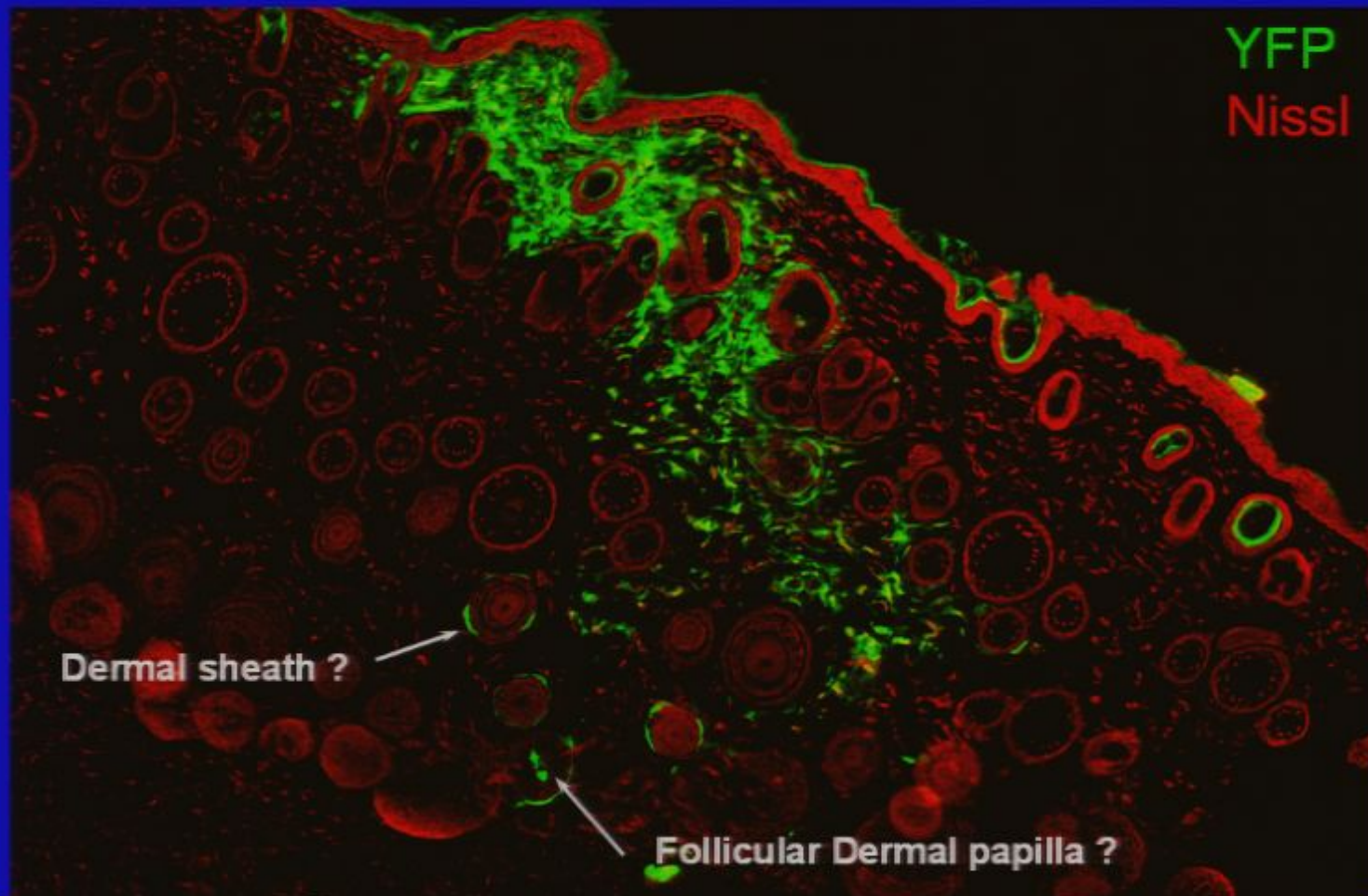


Differentiate

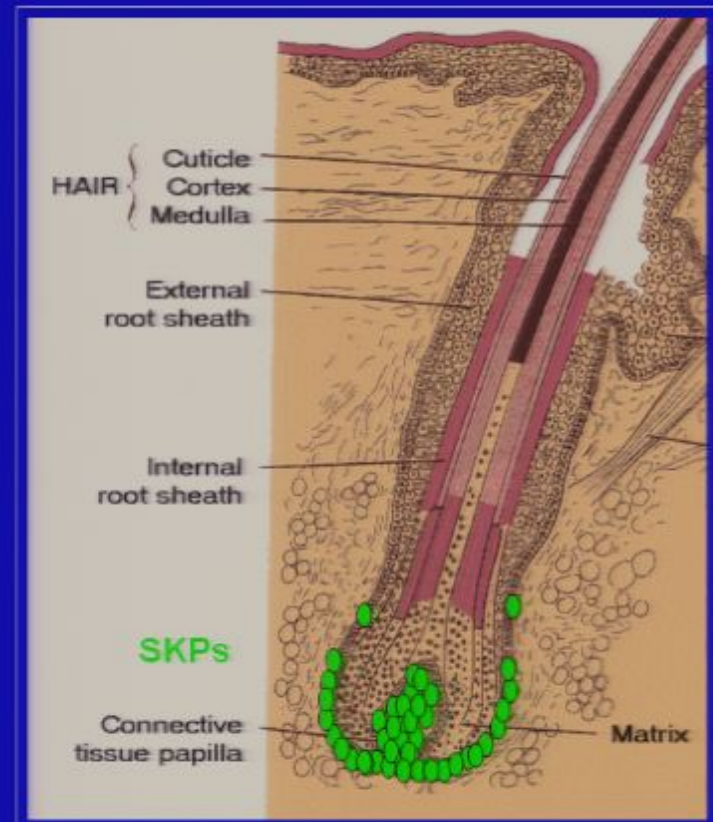
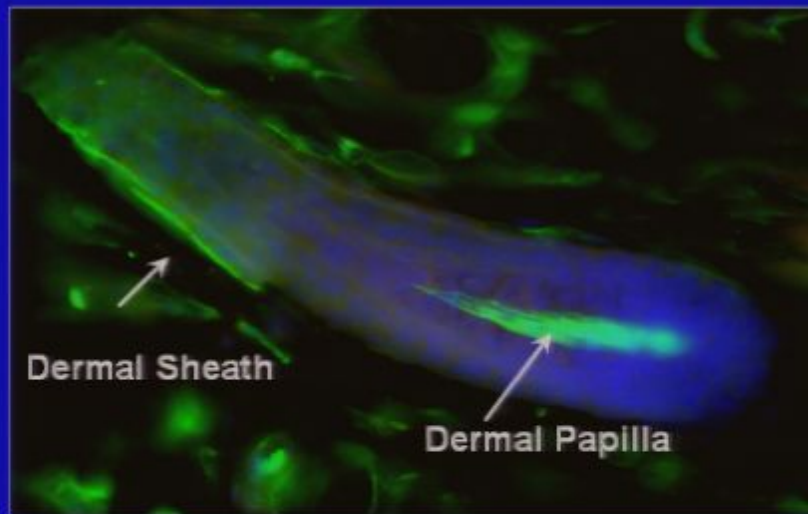


Transplanted SKPs integrate into the wounded dermis

Jeff Biernaskie



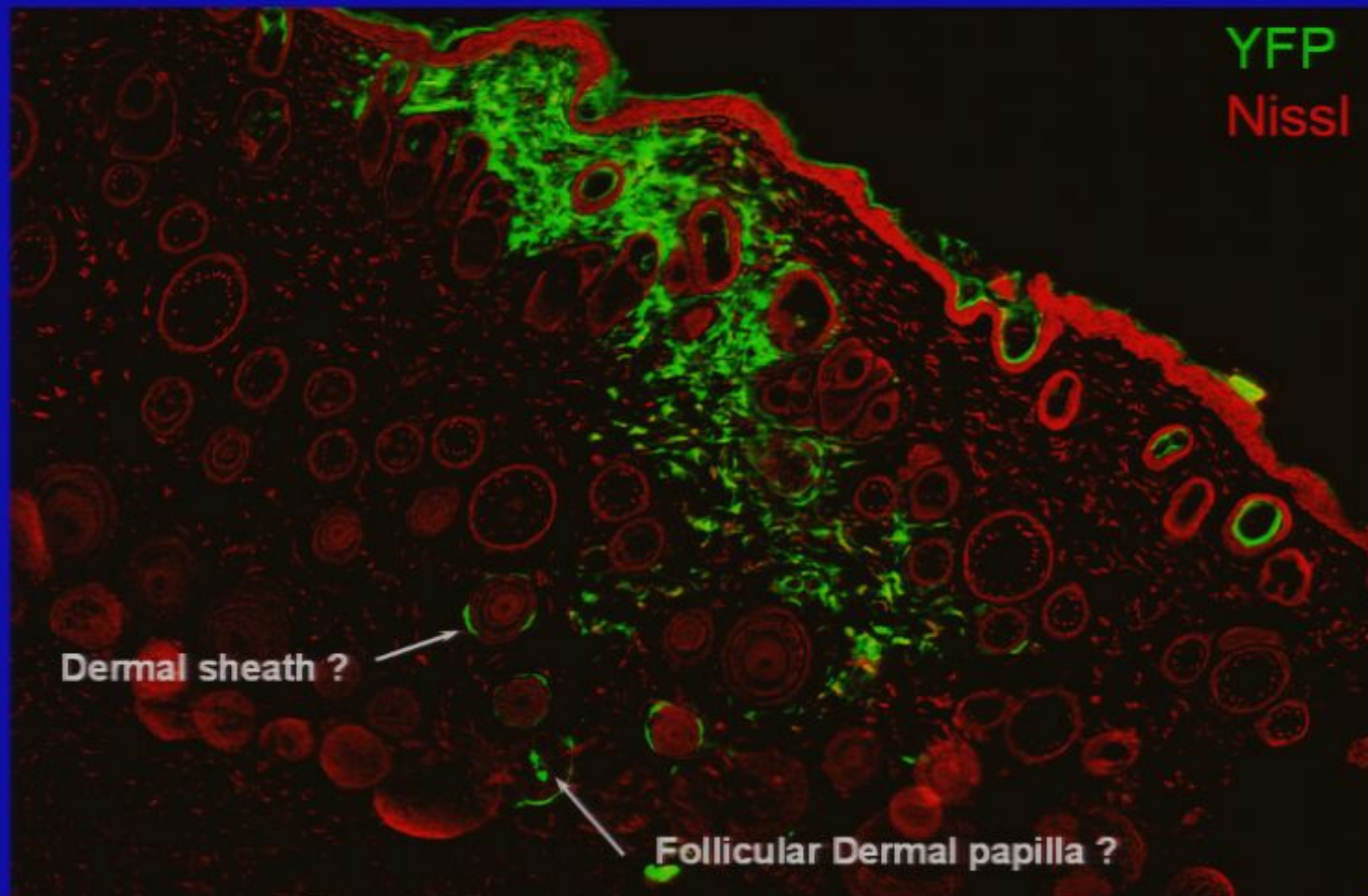
Transplanted SKPs integrate into the follicle dermal papilla and sheath



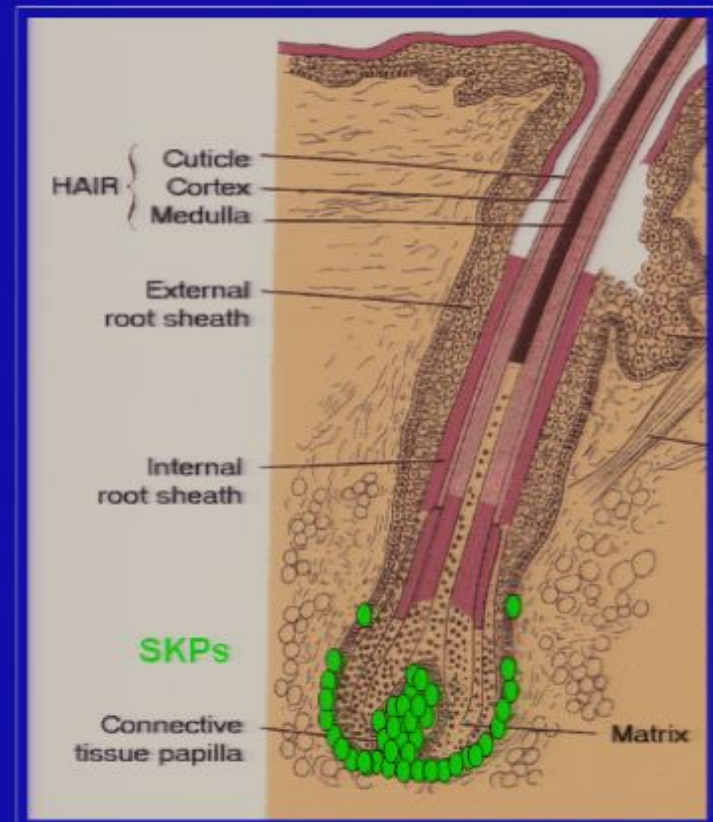
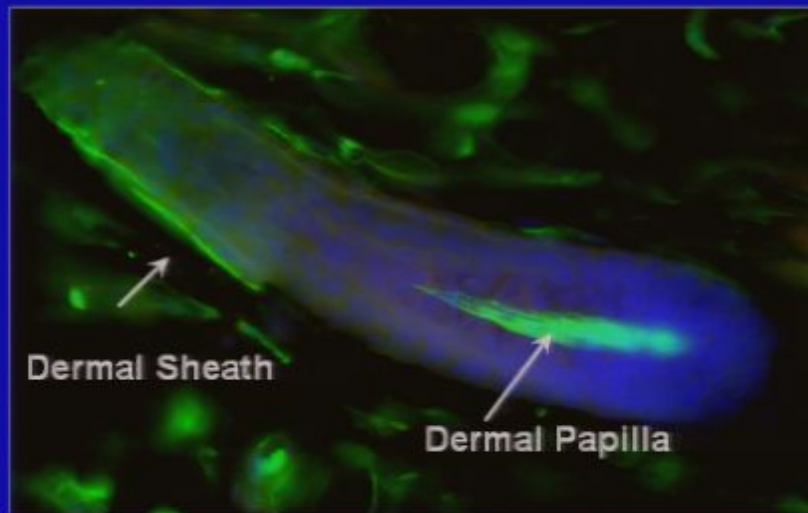
Jeff Biernaskie

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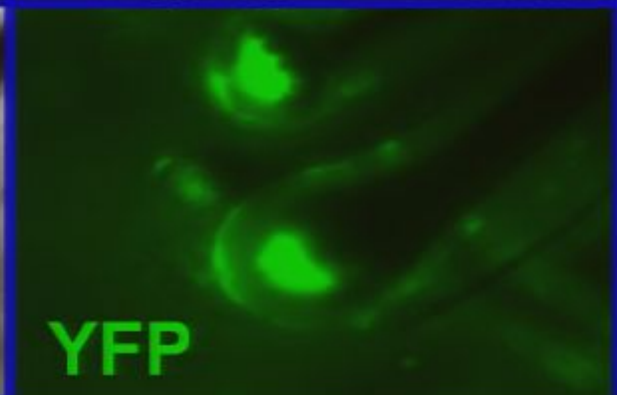
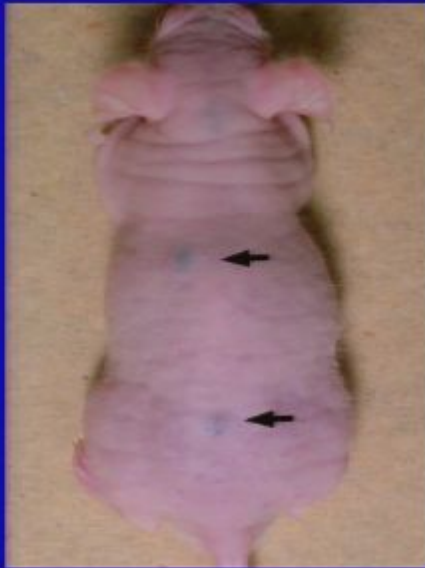


Transplanted SKPs integrate into the follicle dermal papilla and sheath

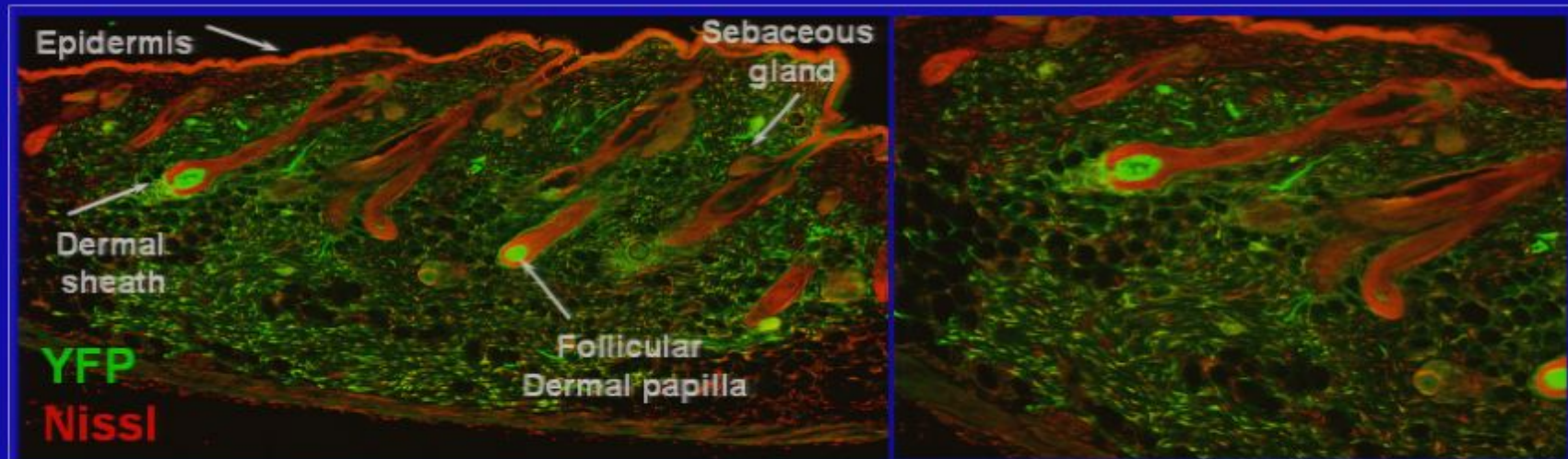


Jeff Biernaskie

SKPs generate a dermal papilla and "tell" epidermal cells to make hair follicles



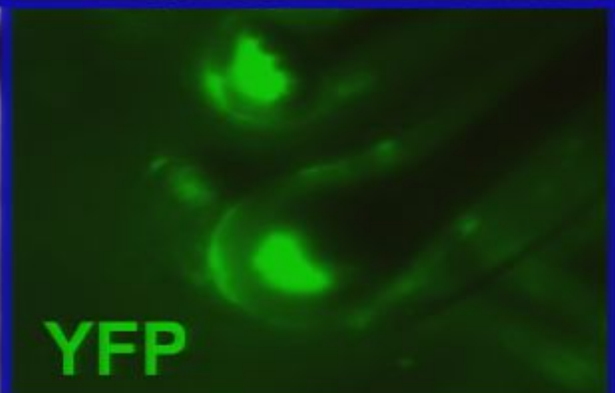
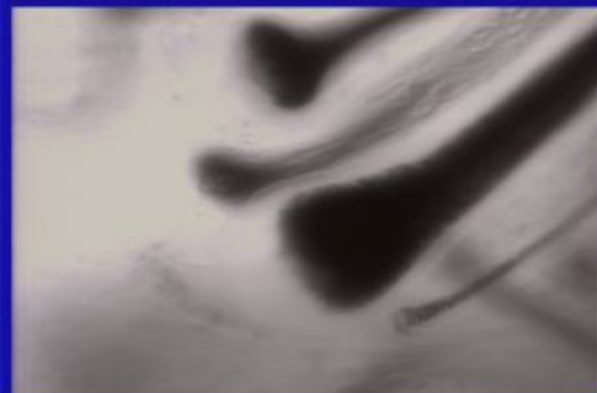
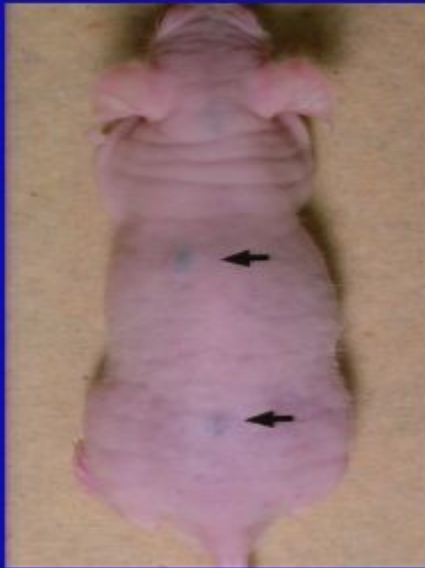
Rat SKPs "tell" mouse epidermal cells to make rat hair



Adult Rat SKPs
1 month post-graft



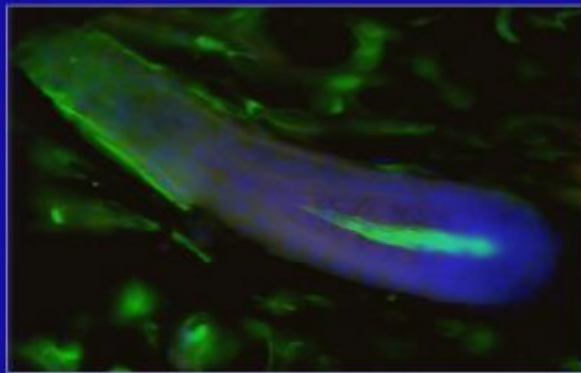
SKPs generate a dermal papilla and "tell" epidermal cells to make hair follicles



SKPs: What, where and why?

What? An embryonic neural crest precursor that persists into adulthood in the dermis and other neural crest targets

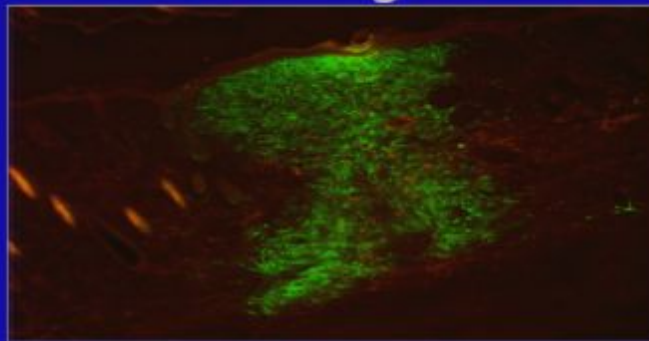
Where?



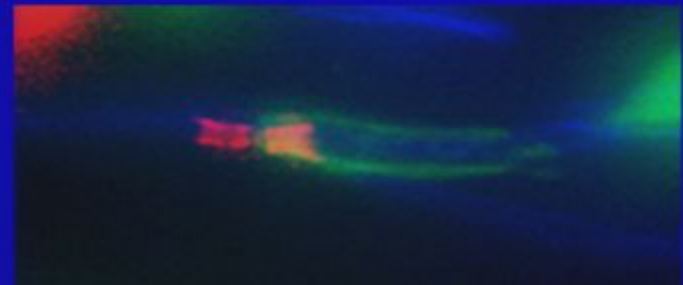
In a hair follicle "niche"

Why?

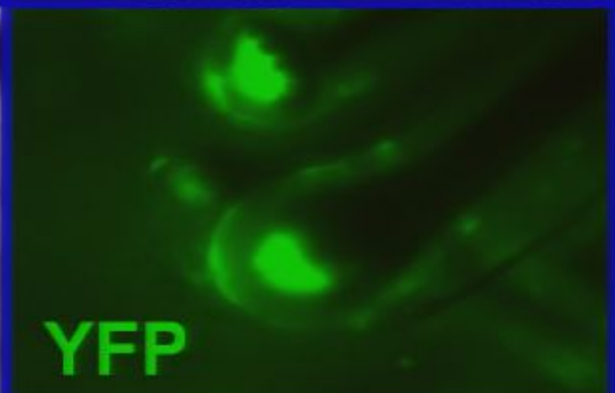
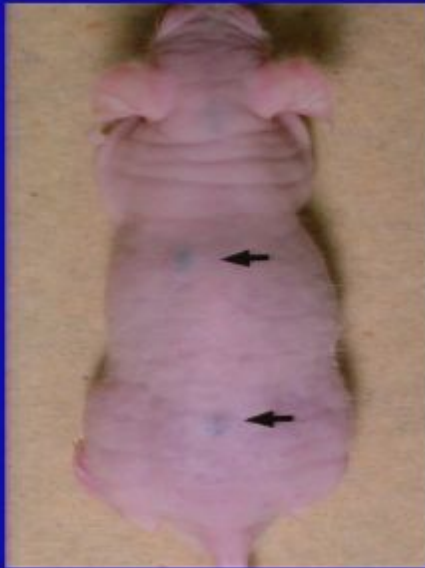
Wound-healing



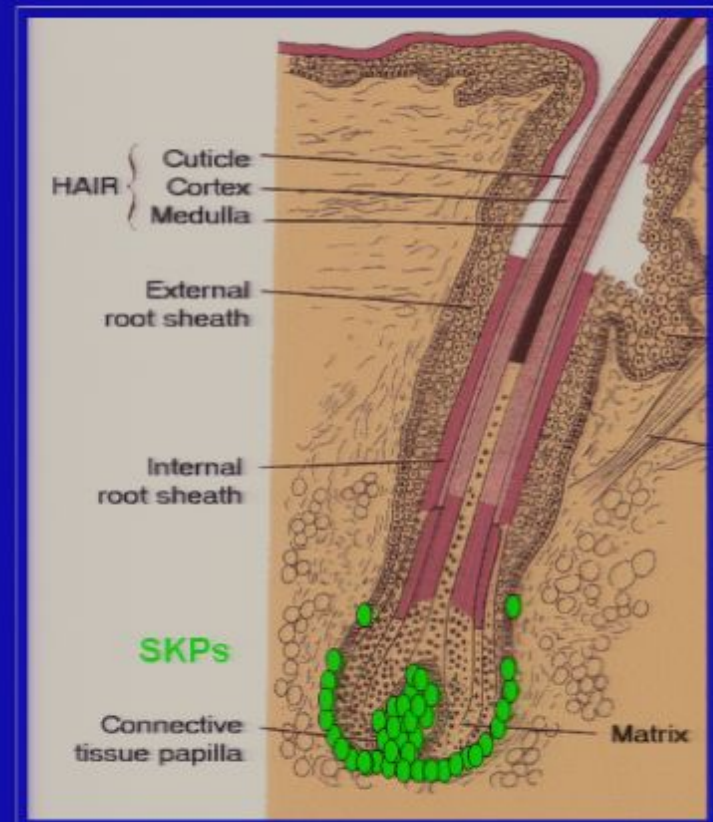
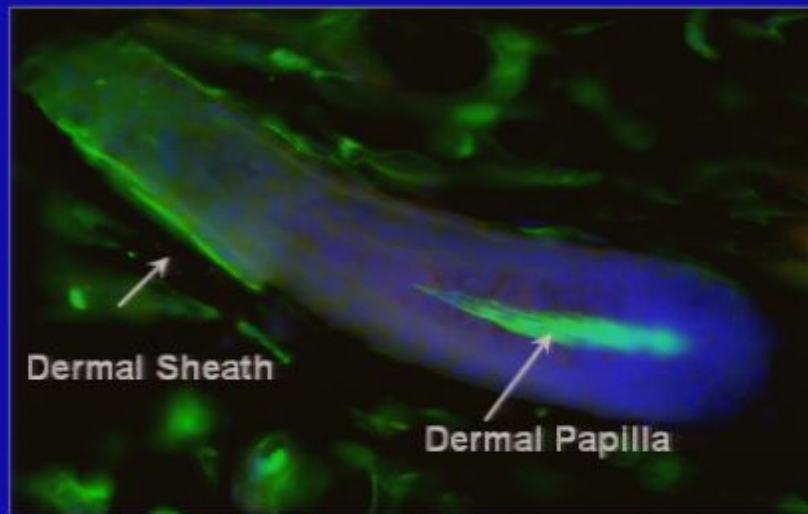
Regulation of morphogenesis in an adult tissue; hair growth and adult cell genesis



SKPs generate a dermal papilla and "tell" epidermal cells to make hair follicles

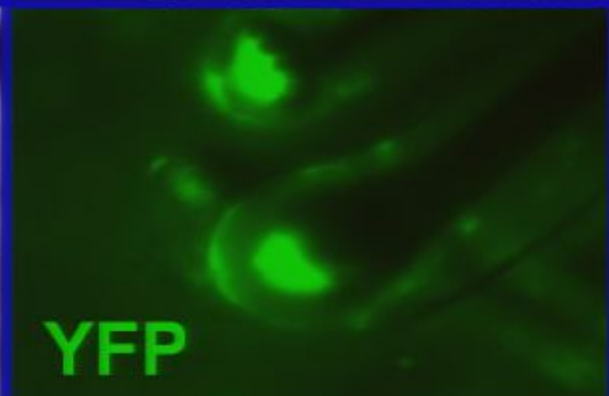
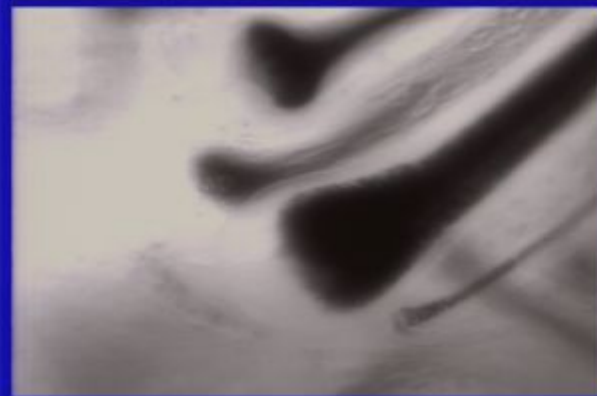
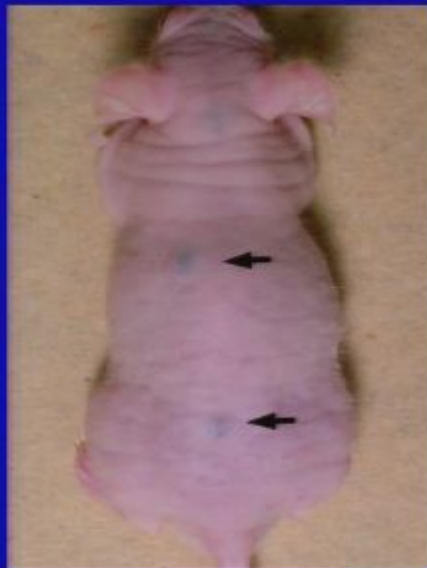


Transplanted SKPs integrate into the follicle dermal papilla and sheath



Jeff Biernaskie

SKPs generate a dermal papilla and "tell" epidermal cells to make hair follicles



Rat SKPs "tell" mouse epidermal cells to make rat hair

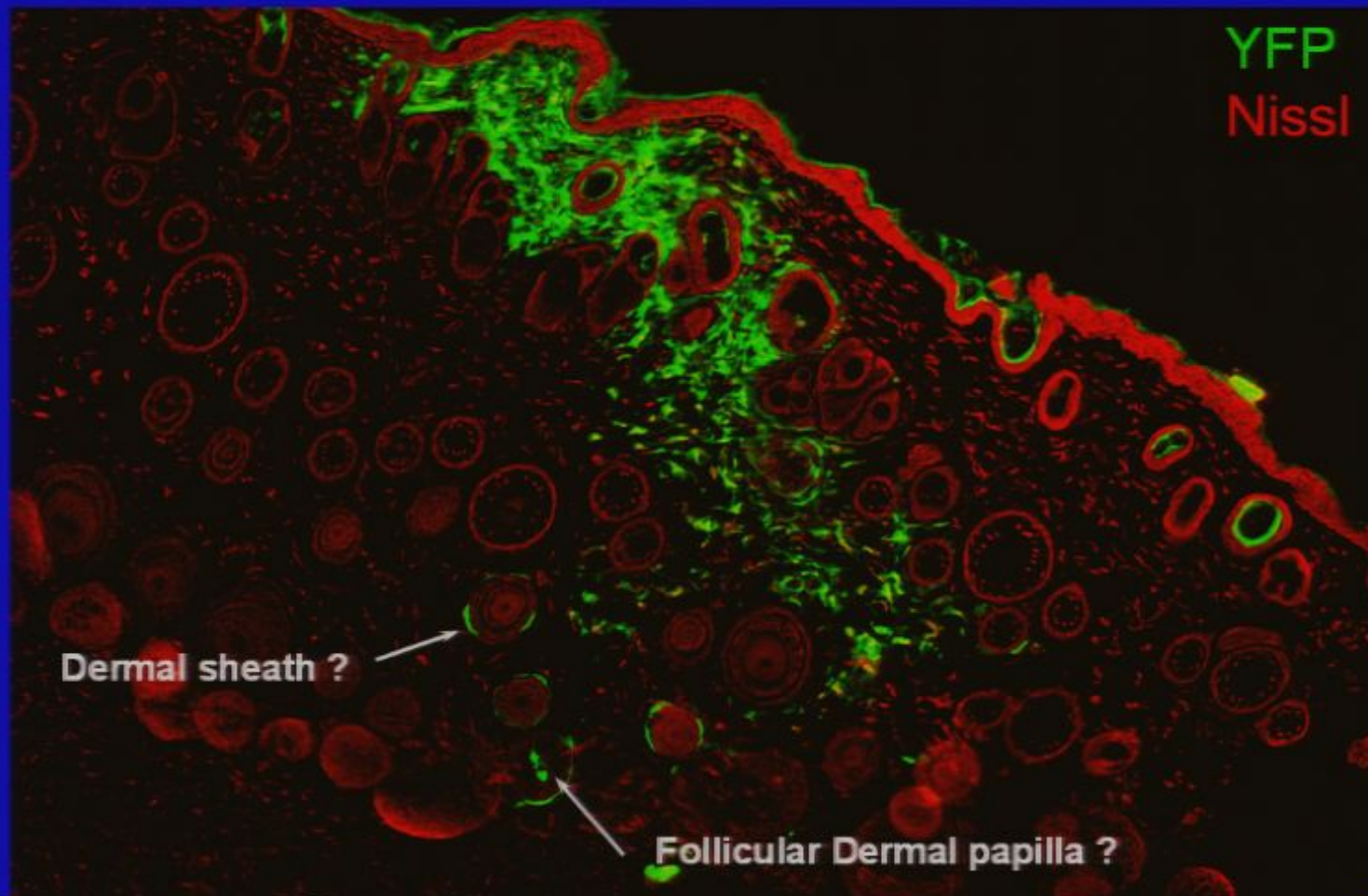


Adult Rat SKPs
1 month post-graft



Transplanted SKPs integrate into the wounded dermis

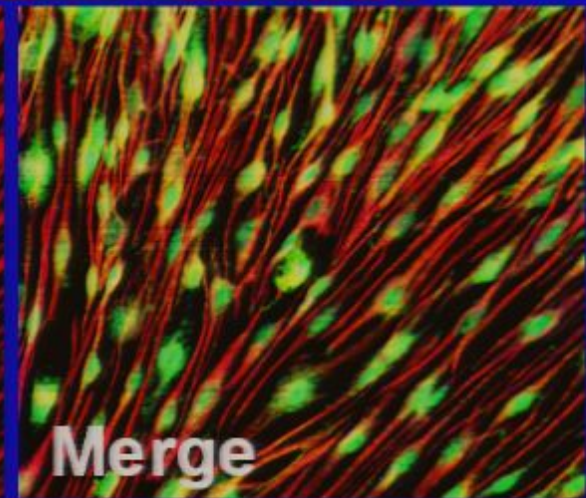
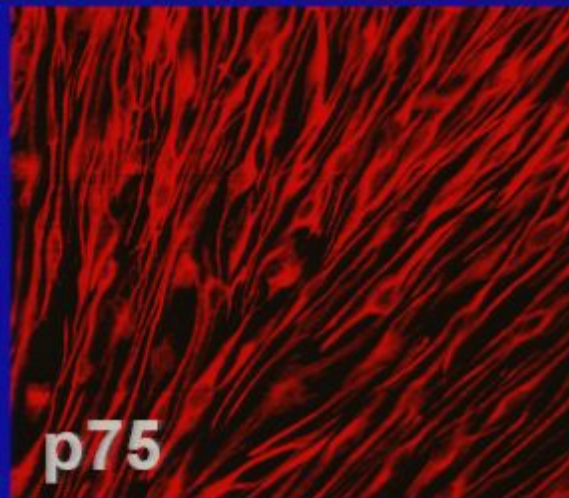
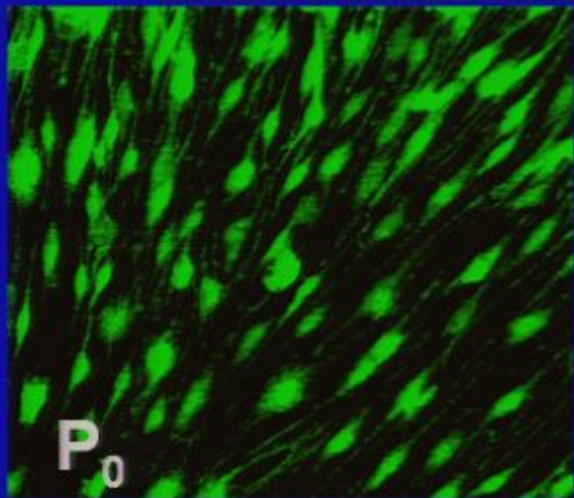
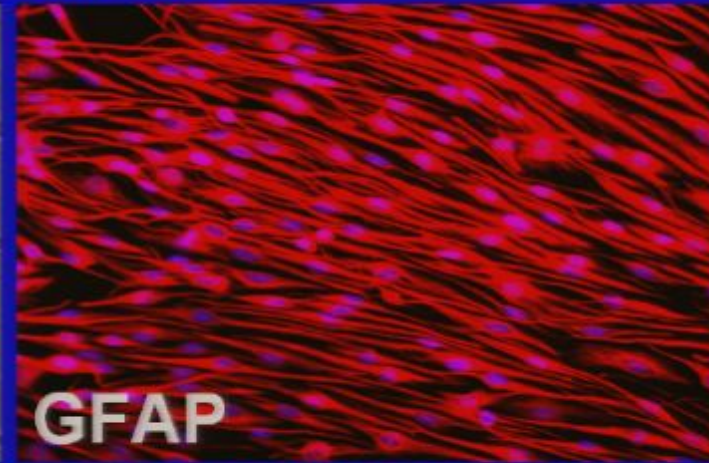
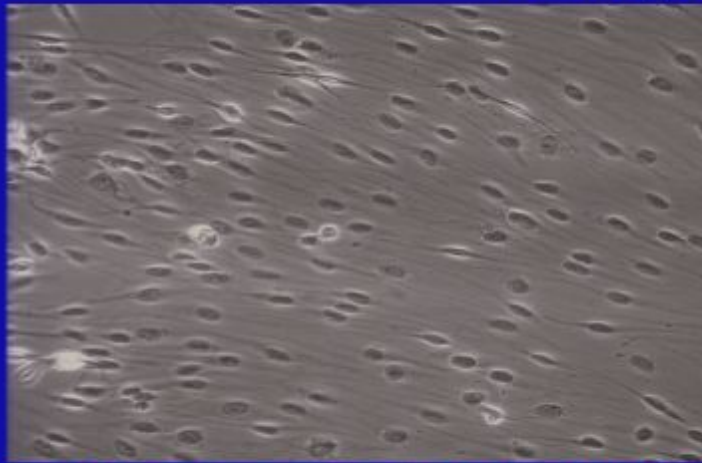
Jeff Biernaskie



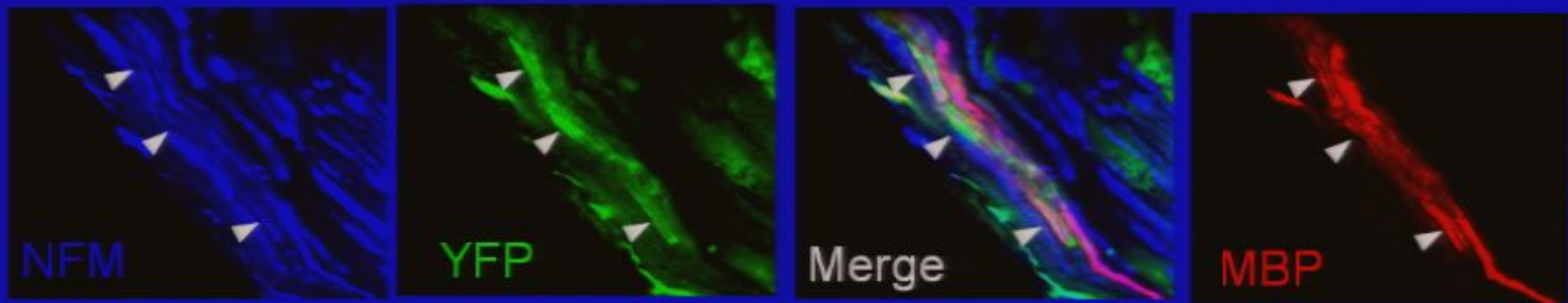
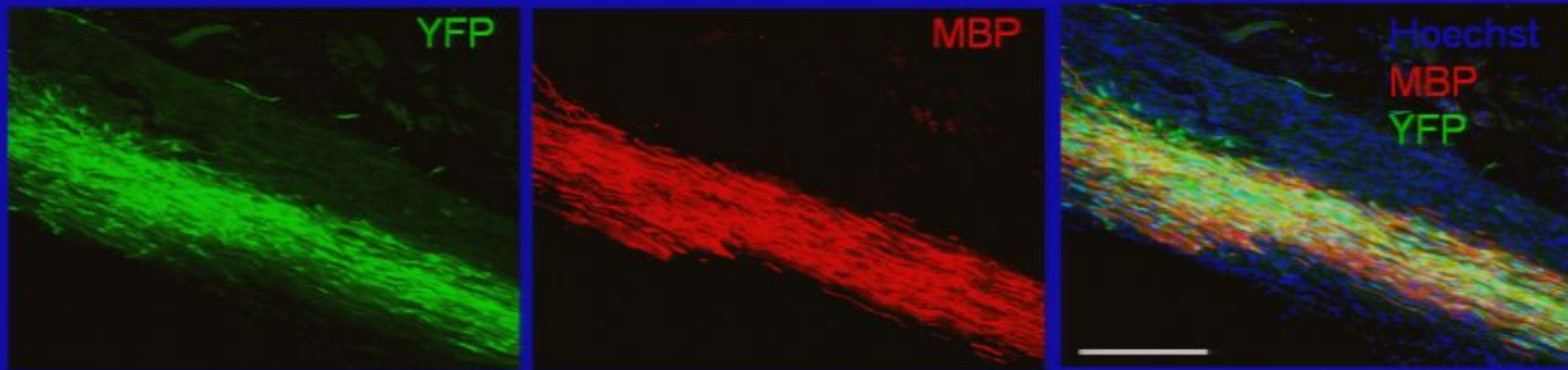
·SKPS: WHAT, WHERE AND WHY?

·CAN SKPS BE USED THERAPEUTICALLY?

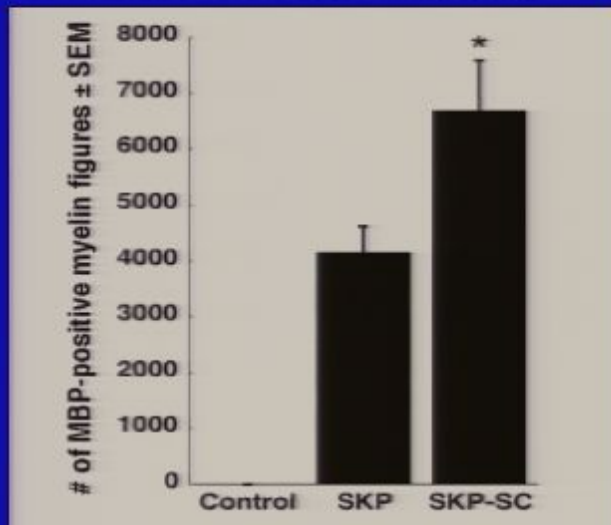
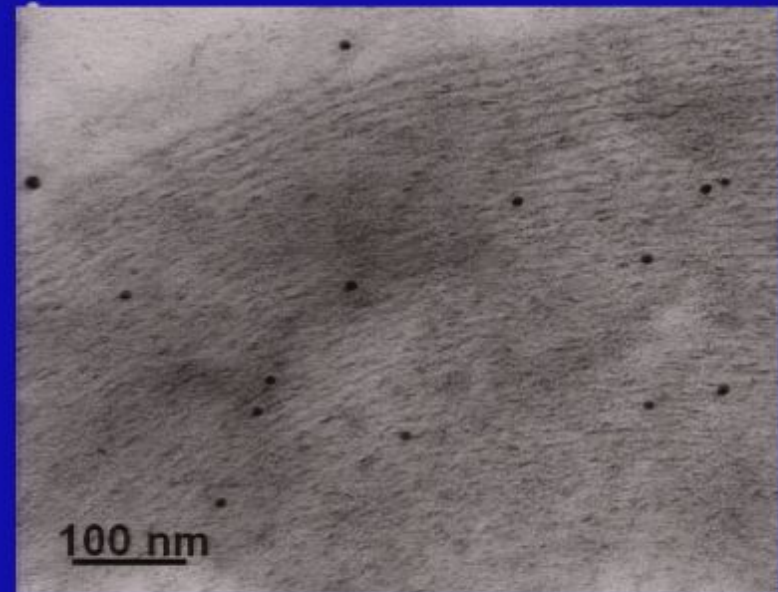
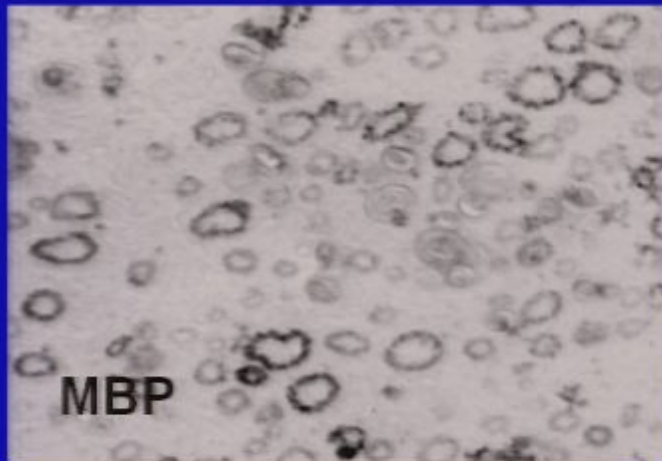
SKPs generate Schwann cells in response to embryonic cues



Transplanted SKP-derived Schwann cells remyelinate the injured nerve



SKP-derived Schwann cells myelinate regenerating axons

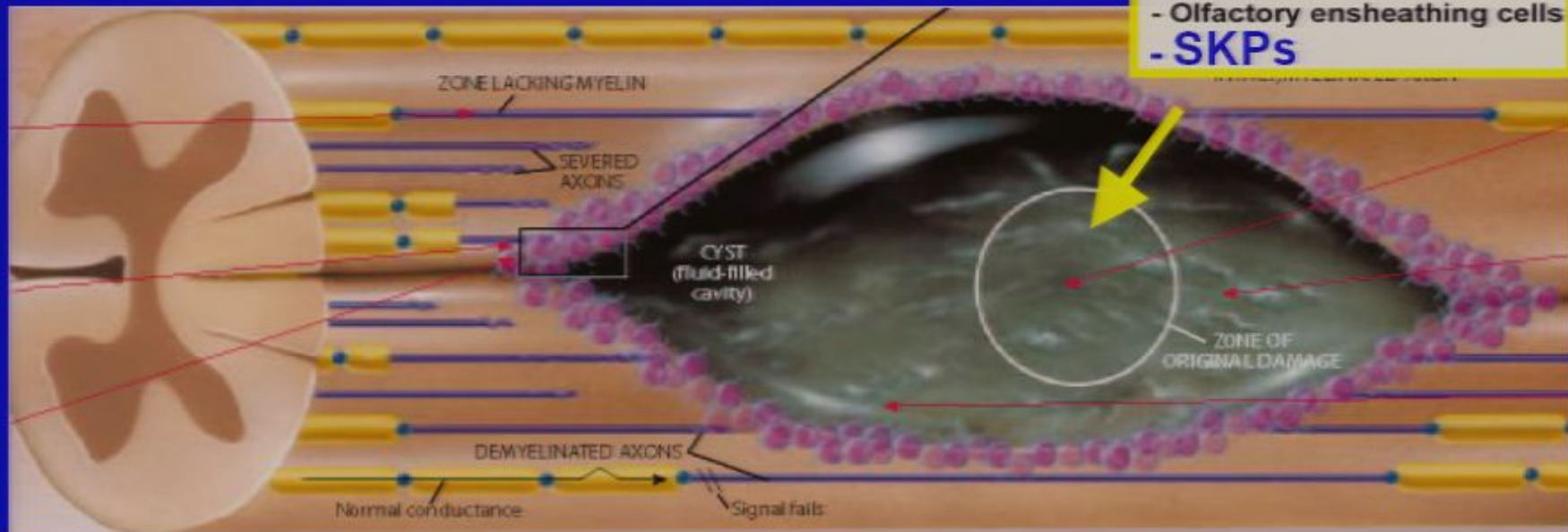


Schwann cells are a candidate for spinal cord injury repair

- 1) Bridge the lesion site, modify the scar to promote axonal regeneration
- 2) Remyelination of both spared and regenerating axons
- 3) Recruit endogenous myelinating glia to injury

Cellular Bridges

- Fetal tissue
- Schwann cells
- Stem cells
- Olfactory ensheathing cells
- **SKPs**



After McDonald, Sci.Am.

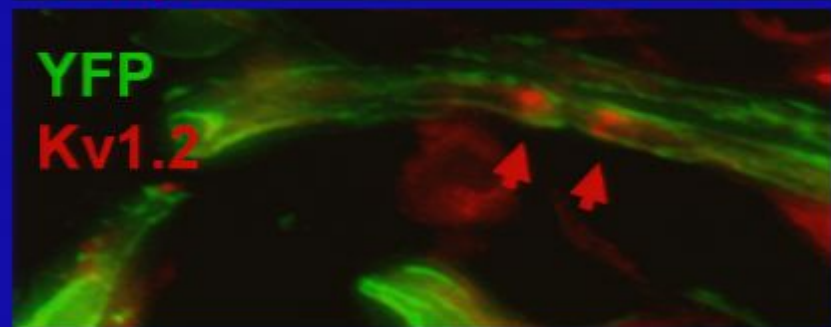
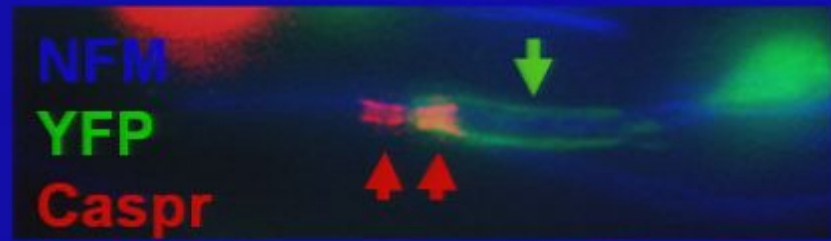
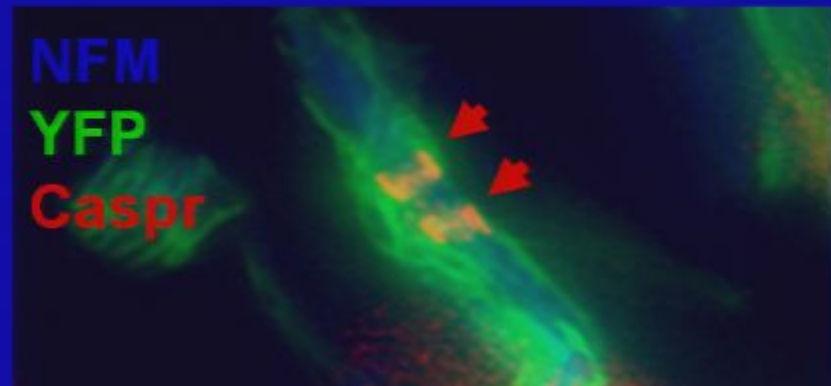
Transplanted SKP-derived Schwann cells myelinate new growing axons in the injured spinal cord



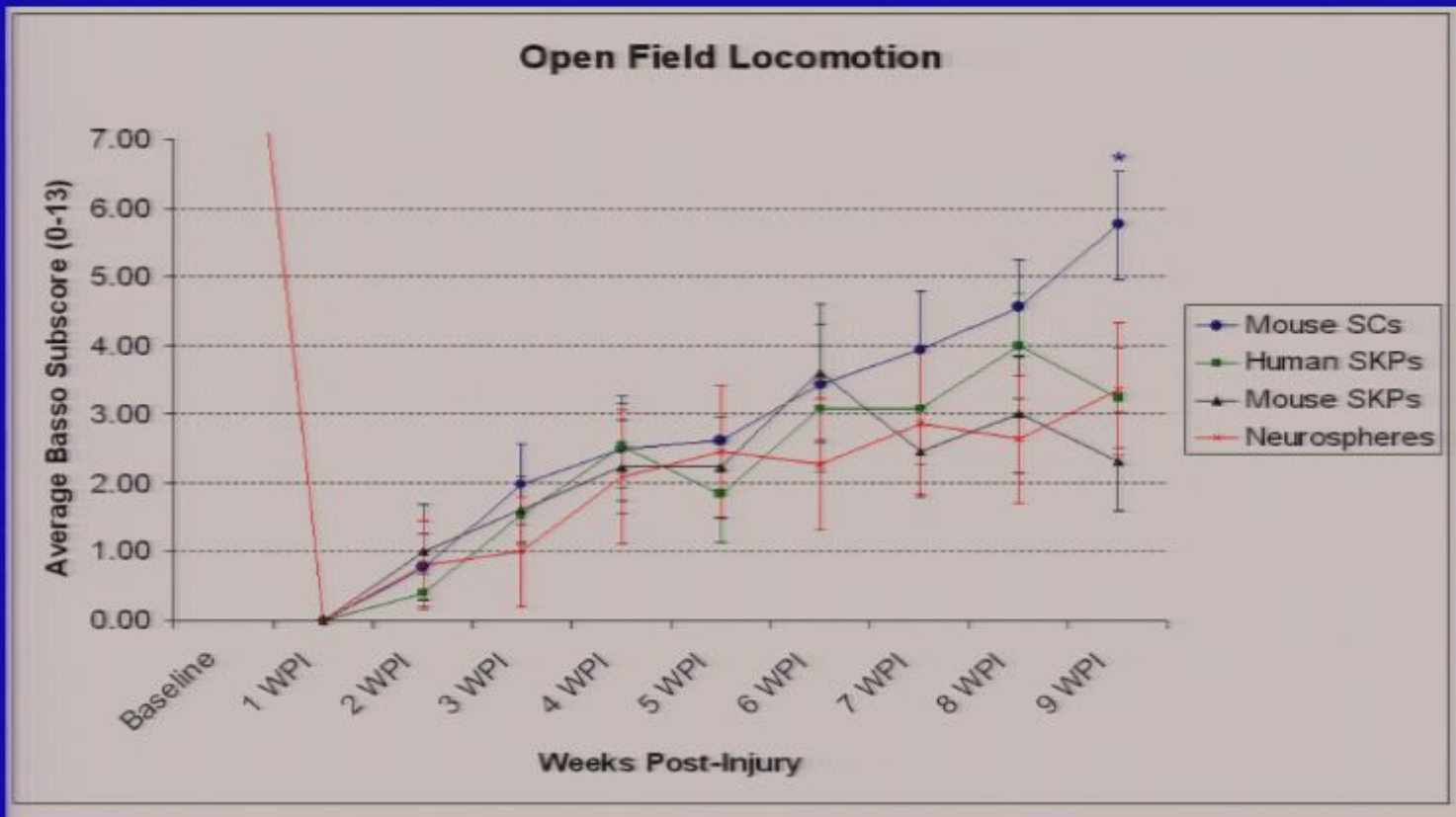
SKP-SCs



Control



SKP-derived Schwann cells enhance functional recovery



STEM CELLS AND BASIC BIOLOGY

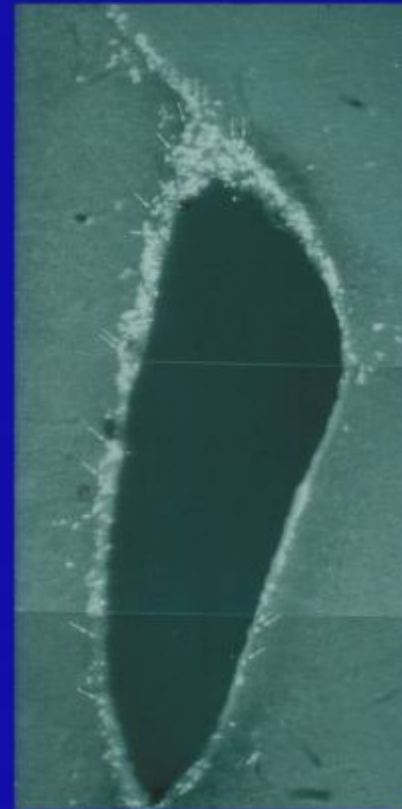
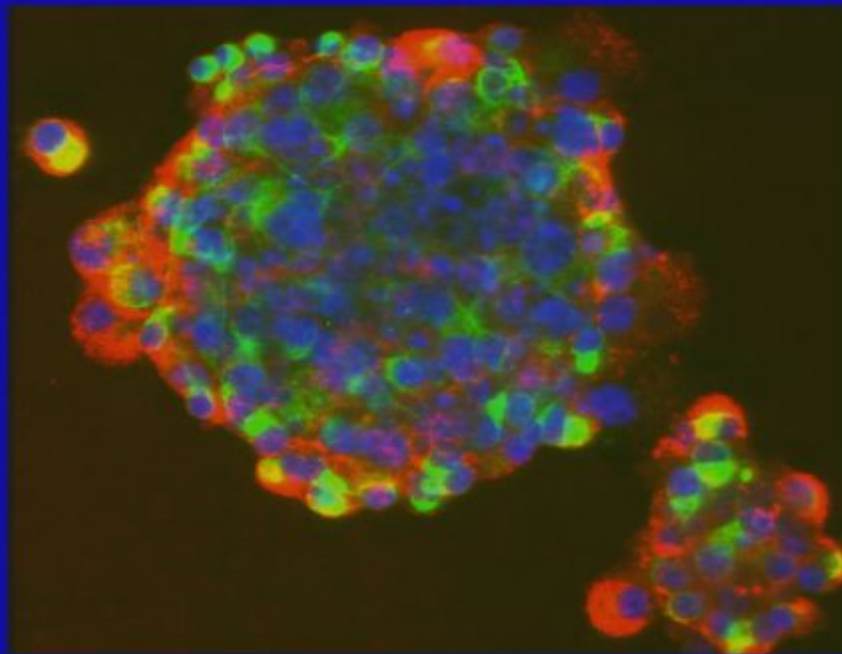
- Do all adult tissues contain an adult stem cell? What are the biological roles of such cells? Are they a remnant from animals that can regenerate?
- How "plastic" are adult stem cells?
- Is there an "adult" ES cell?

The Future of Stem Cell Therapy

Transplantation

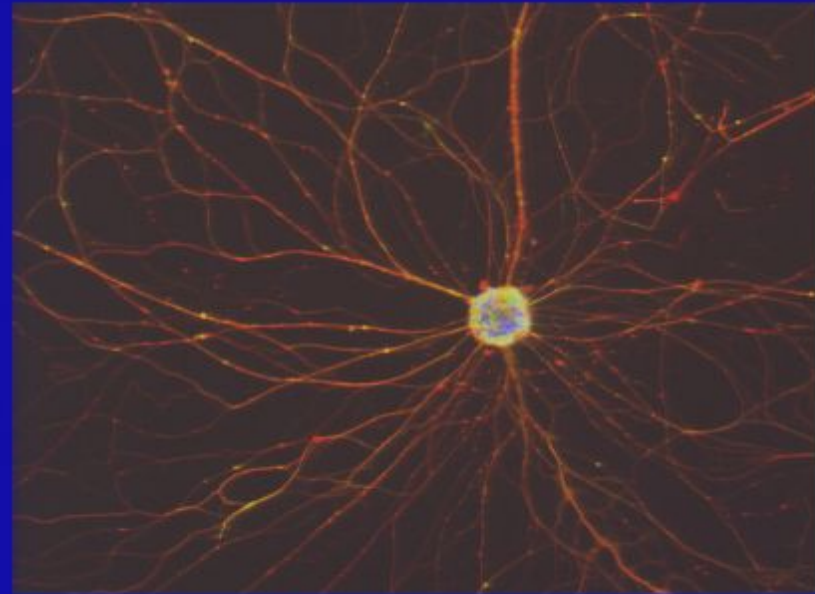
or

Recruitment



Cell therapy is not the only clinical use for stem cells

- Discovery research with, for example, genetically-compromised patient populations
- Screening for novel, potentially individualized therapeutics
- Cancer stem cells



THE SKPS TEAM

Collaborators

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Adrienne Junek

C.C. Hui, U. of T.

Pleasantine Mills

Darius Bagli, U. of T.

Rajiv Midha, U. of C.

Wolfram Tetzlaff, U.B.C.

Joe Sparling

Ben Alman, U. of T.

The Lab

Jean Toma

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