

Title: Molly Shoichet: Engineering Change in Medicine

Date: Dec 07, 2016 07:00 PM

URL: <http://pirsa.org/16120004>

Abstract: <p>Imagine going beyond treating the symptoms of disease and instead stopping it and reversing it. This is the promise of regenerative medicine.

In her Perimeter Institute public lecture, Prof. Molly Shoichet will tell three compelling stories that are relevant to cancer, blindness and stroke. In each story, the underlying innovation in chemistry, engineering, and biology will be highlighted with the opportunities that lay ahead.

To make it personal, Shoichet's lab has figured out how to grow cells in an environment that mimics that of the native environment. Now she has the opportunity to grow a patient's cancer cells in the lab and figure out which drugs will be most effective for that individual.

In blindness, the cells at the back of the eye often die. We can slow the progression of disease but we cannot stop it because there is no way to replace those cells. With a newly engineered biomaterial, Shoichet's lab can now transplant cells to the back of the eye and achieve some functional repair.

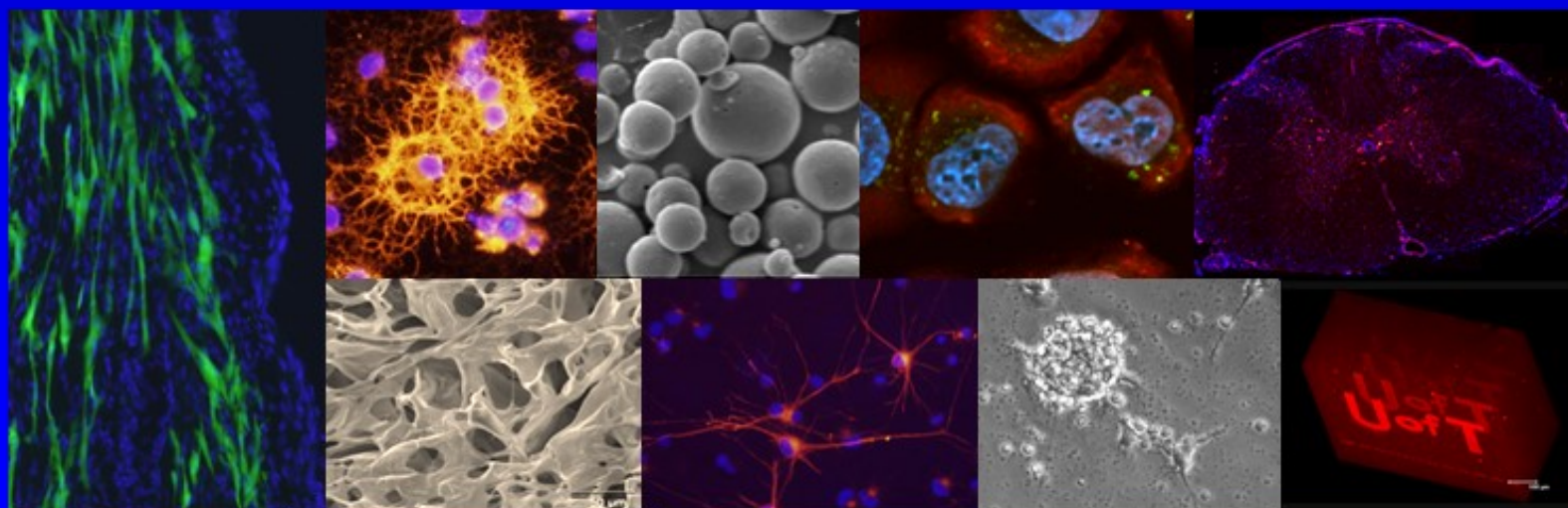
The holy grail of regenerative medicine is stimulation of the stem cells resident in us. The challenge is to figure out how to stimulate those cells to promote repair. Using a drug-infused band-aid applied directly on the brain, Shoichet's team achieved tissue repair.

These three stories underline the opportunity of collaborative, multi-disciplinary research. It is exciting to think what we will discover as this research continues to unfold.</p>



Engineering Change in Medicine

Molly S. Shoichet, PhD, FRSC, O Ont
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Canada Research Chair, Tissue Engineering
*Chemical Engineering & Applied Chemistry,
Chemistry, Biomaterials & Biomedical Engineering
Donnelly Centre, McEwen Centre*



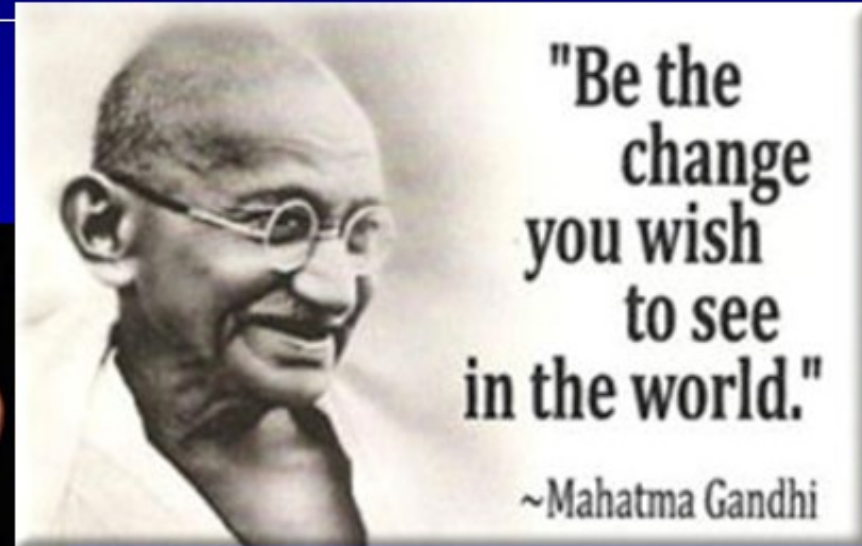
Isn't it time for a change?

LandEscape, Richard Shoichet

**"Your
voice can
change the
world."**



BARACK
OBAMA
2009-PRESENT



**"Be the
change
you wish
to see
in the world."**

~Mahatma Gandhi





Research2Reality

today's research, tomorrow's reality

co-founders:

Molly Shoichet & Mike MacMillan



Social media campaign

- Website: research2reality.com

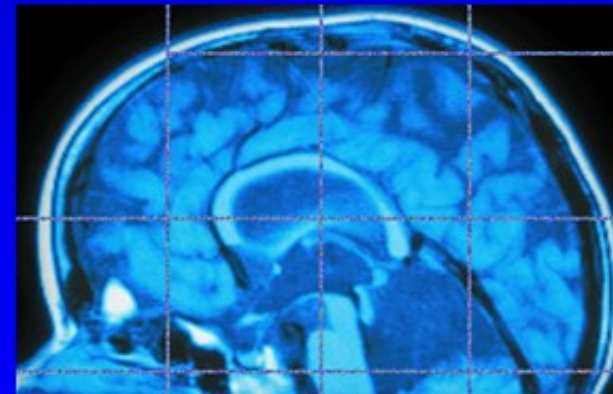


Partners

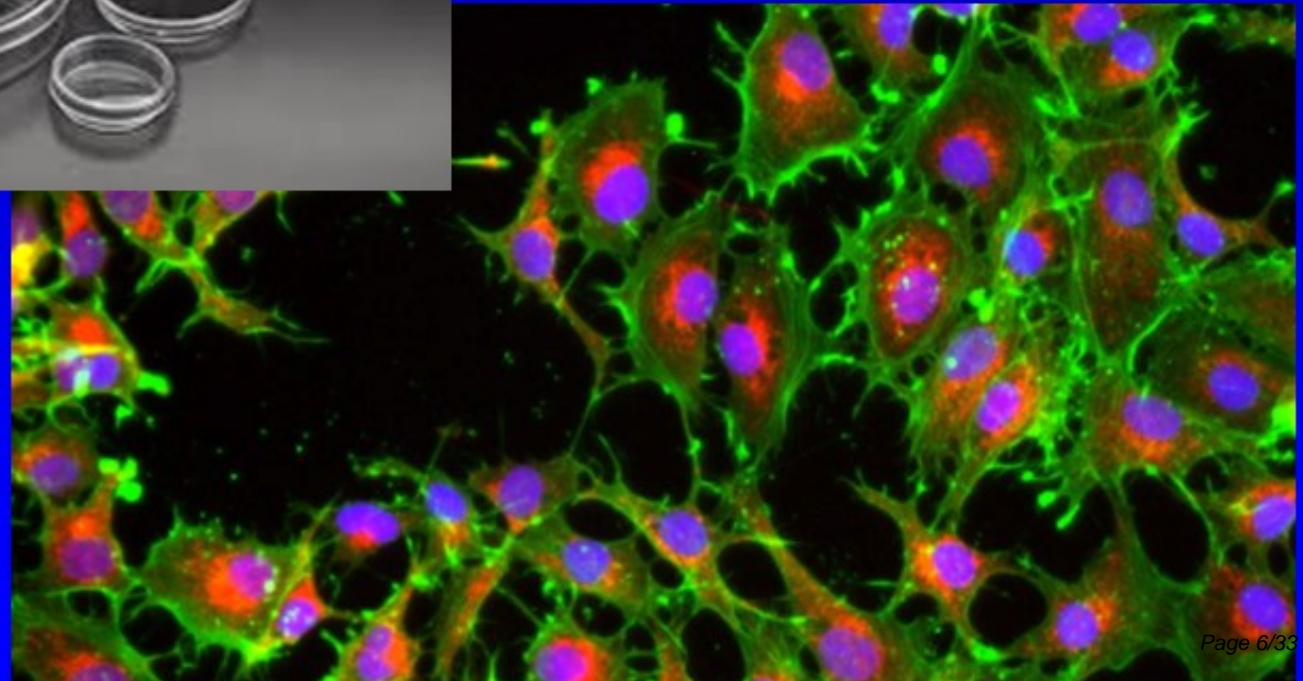
- Top Universities across Canada, CIFAR
- Ontario Government
- Discovery & Discovery Science

Change in Medicine

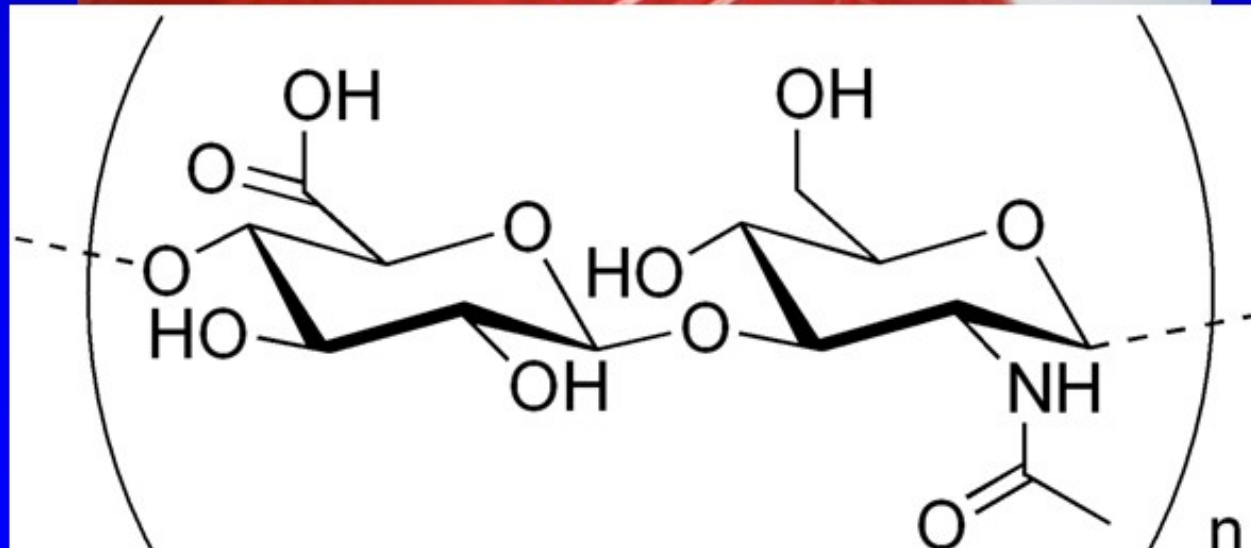
- Personalized Medicine
- Regenerative Medicine



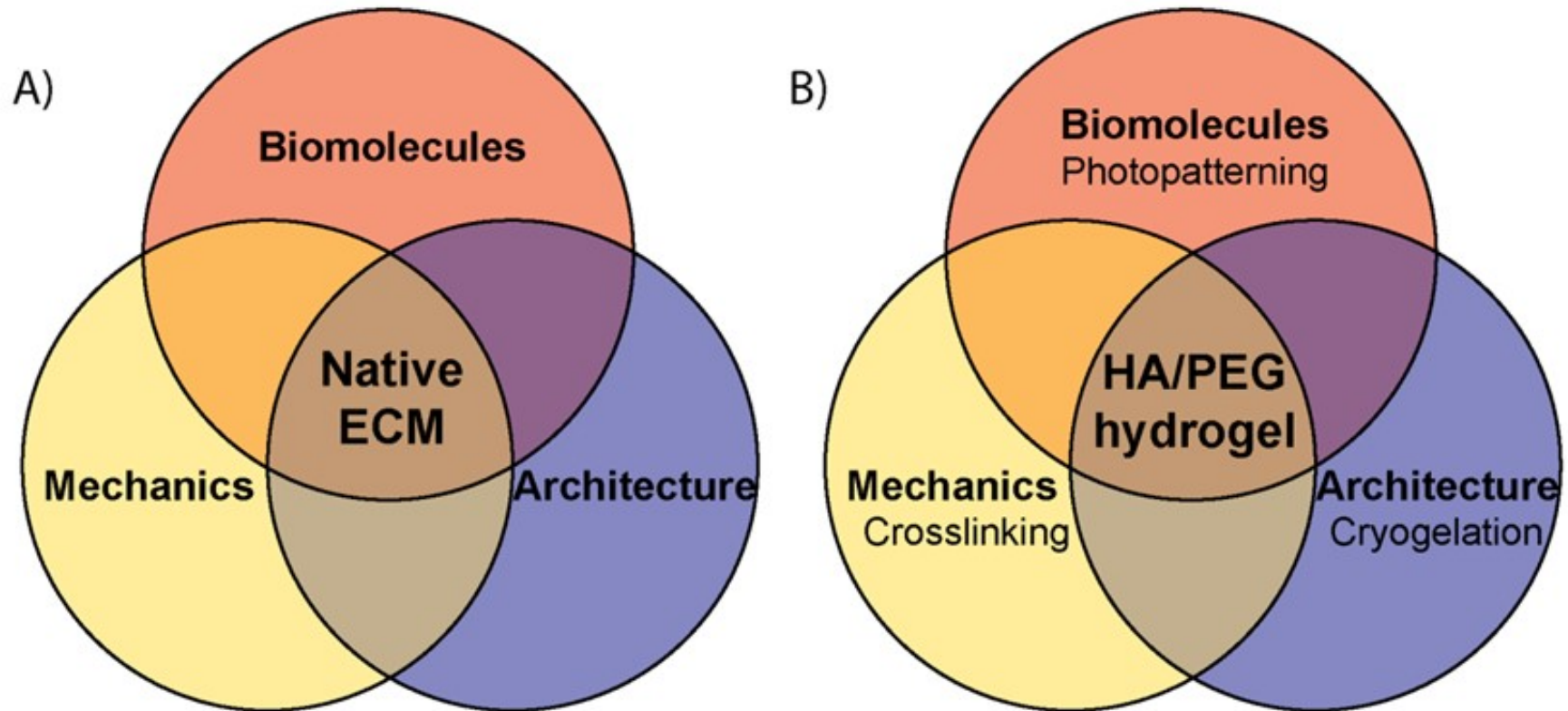
Conventional 2-D Cell Culture



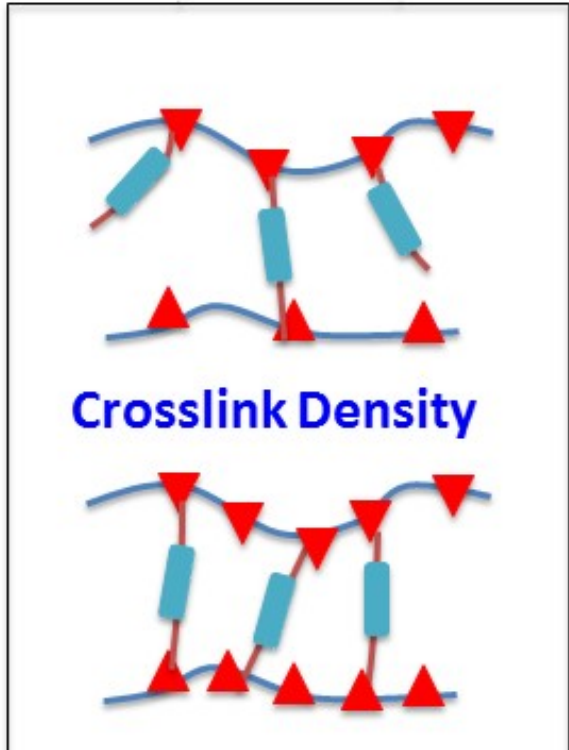
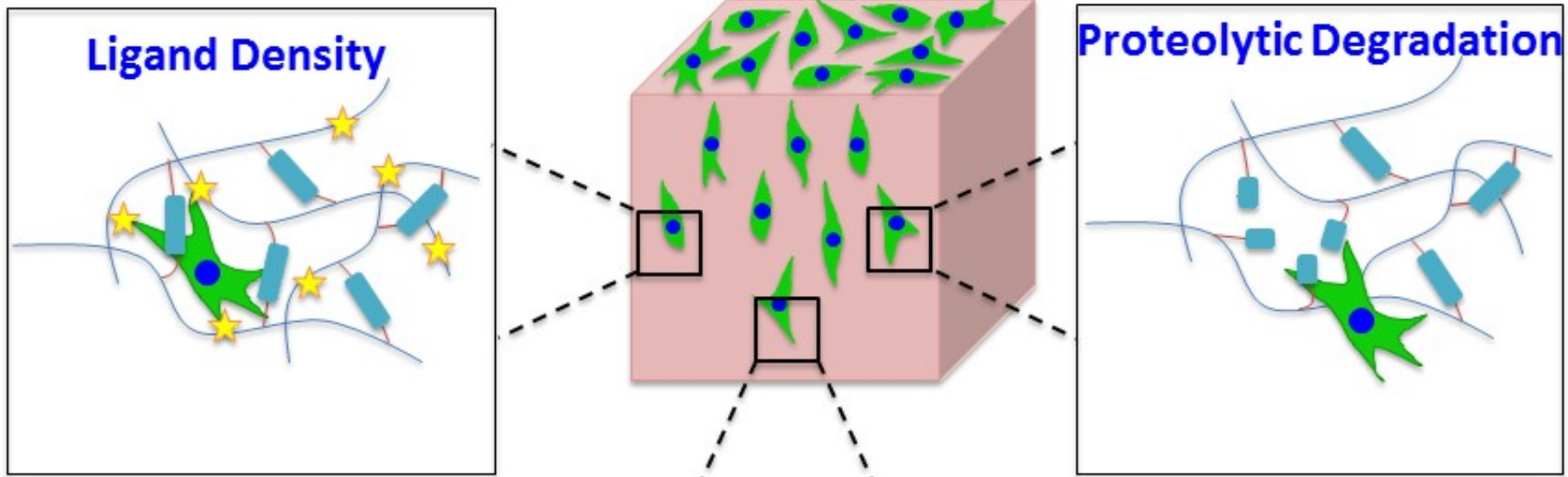
Hydrogels: water-swollen materials




Biomimetic Hydrogels

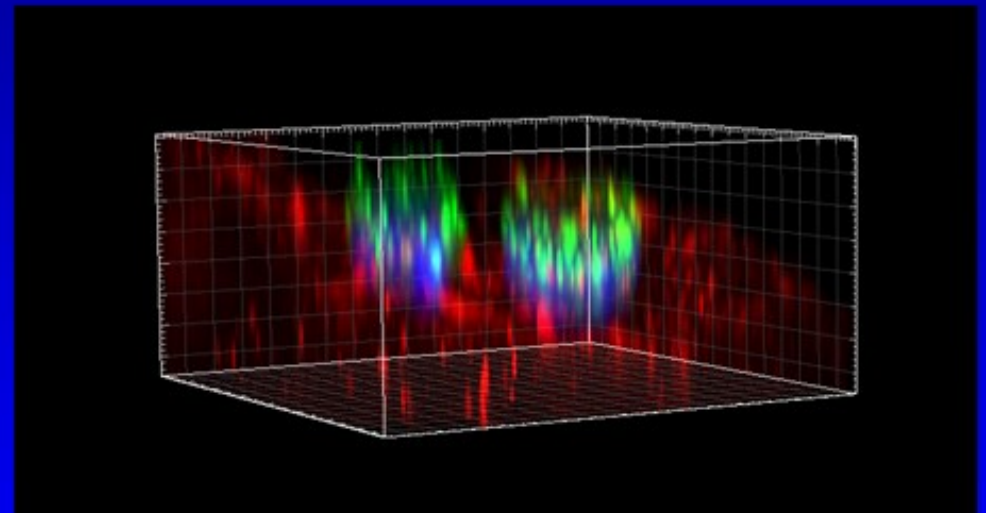
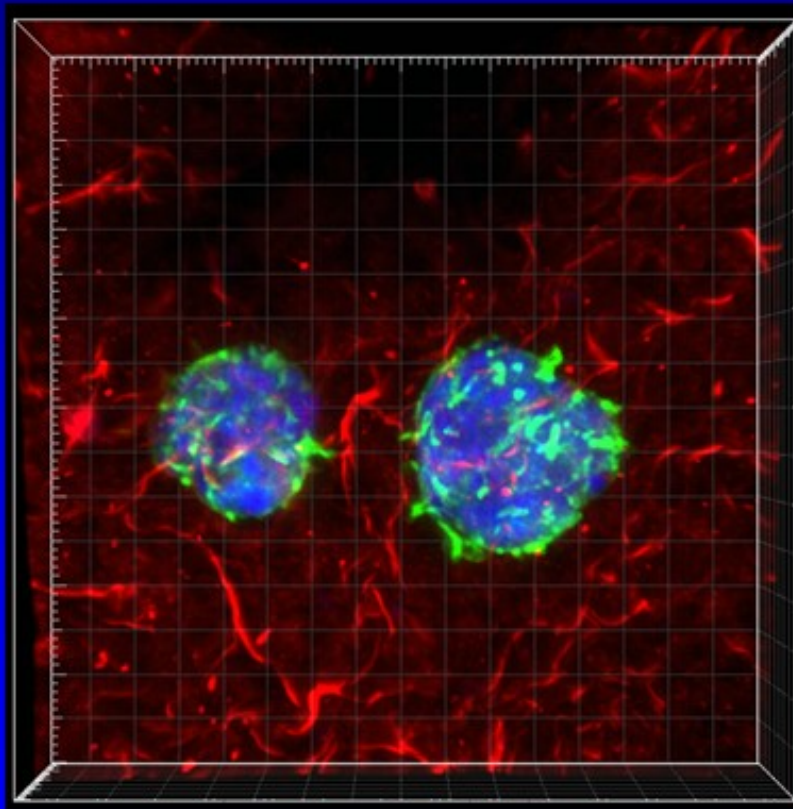


Hydrogel Microenvironment

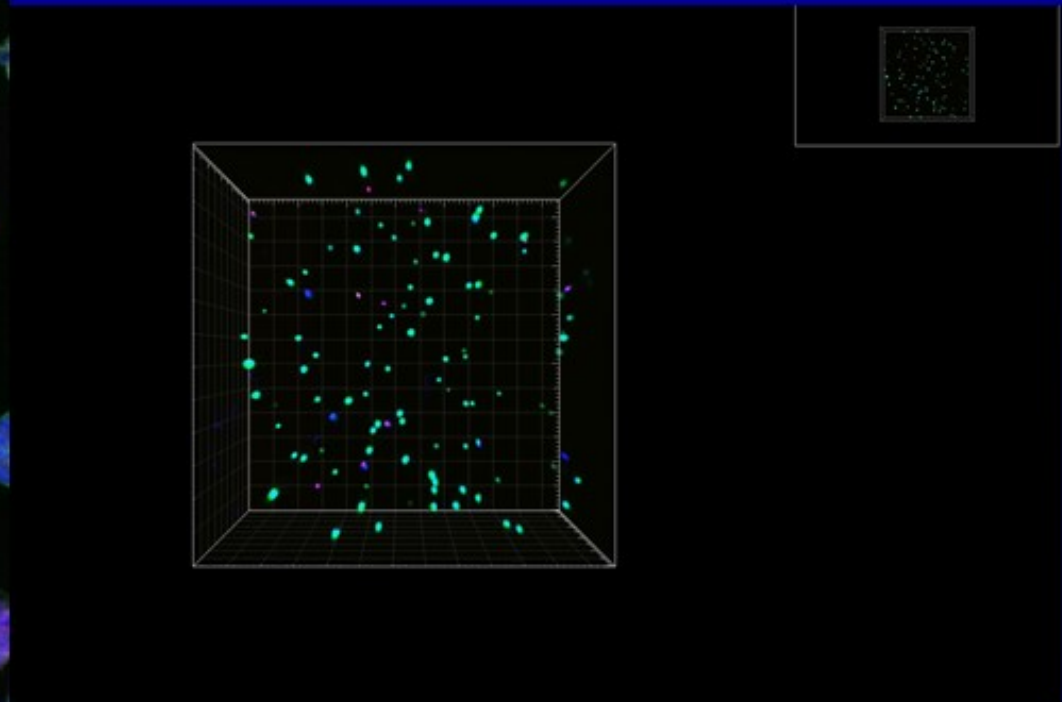
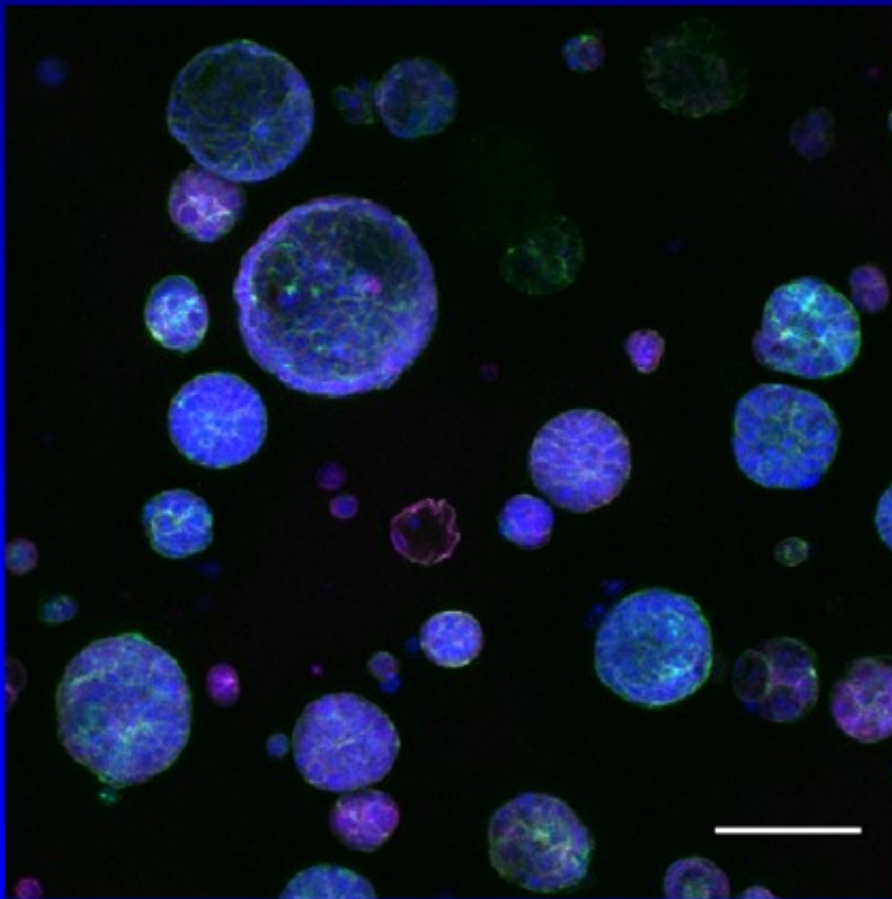


-  Hyaluronic Acid
-  MMP Cleavable Crosslink
-  Furan Functionality
-  Pendant GRGDS
-  Breast Cancer Cell

Breast Cancer Cells in 3D

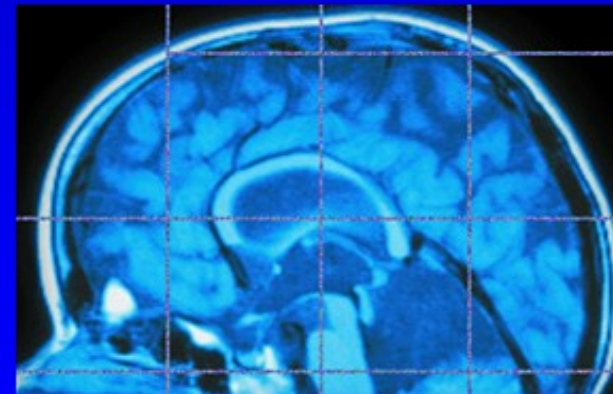


Breast Cancer Cells in 3D

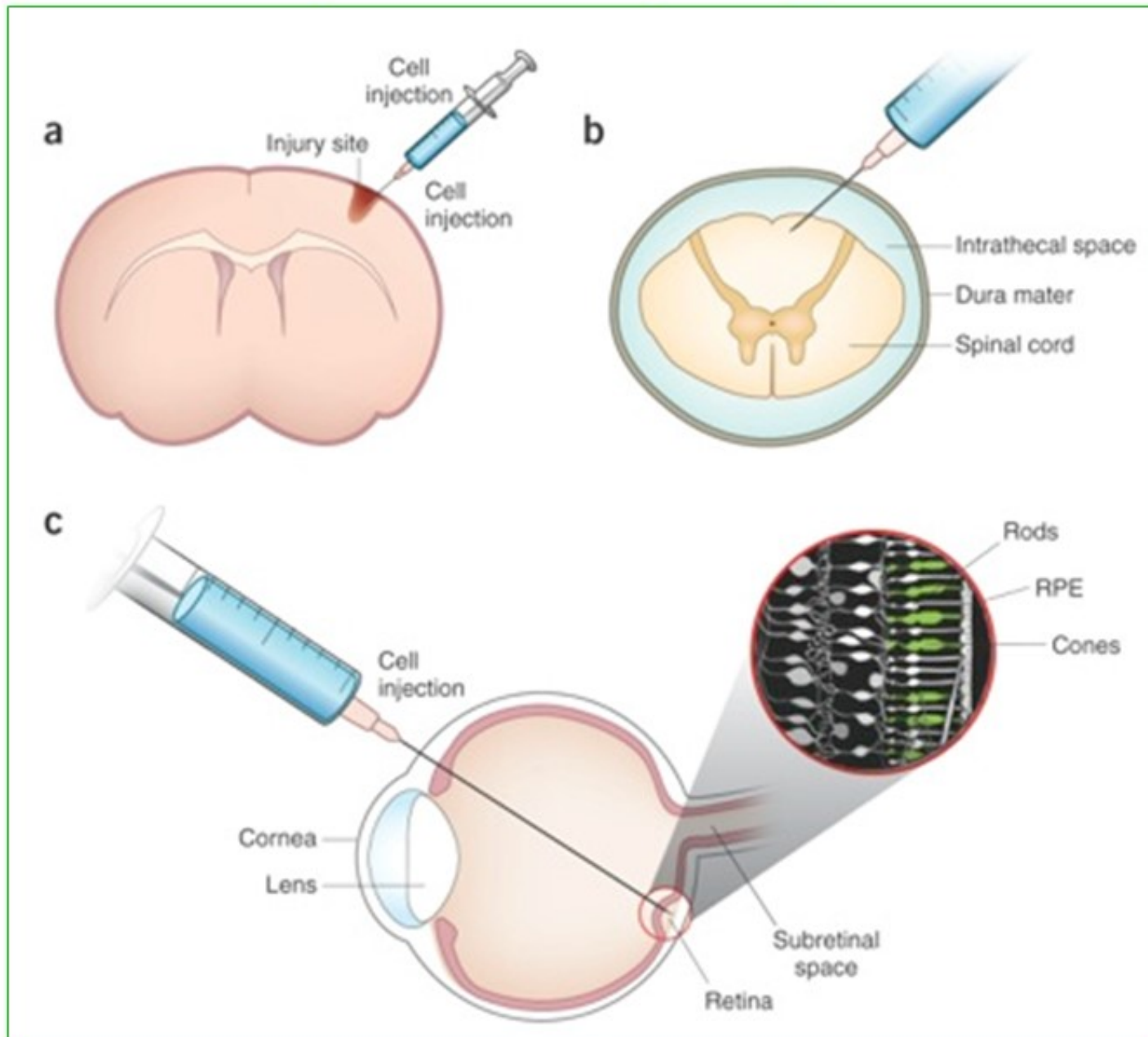


Change in Medicine

- Personalized Medicine
- Regenerative Medicine

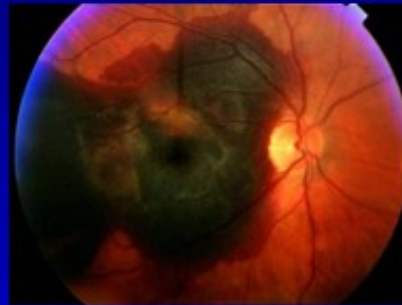


Injectable hydrogels

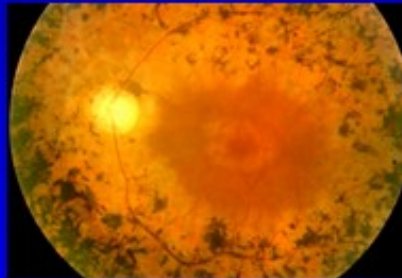


Leading causes of vision loss: retina degeneration

Age-related macular degeneration



Retinitis Pigmentosa

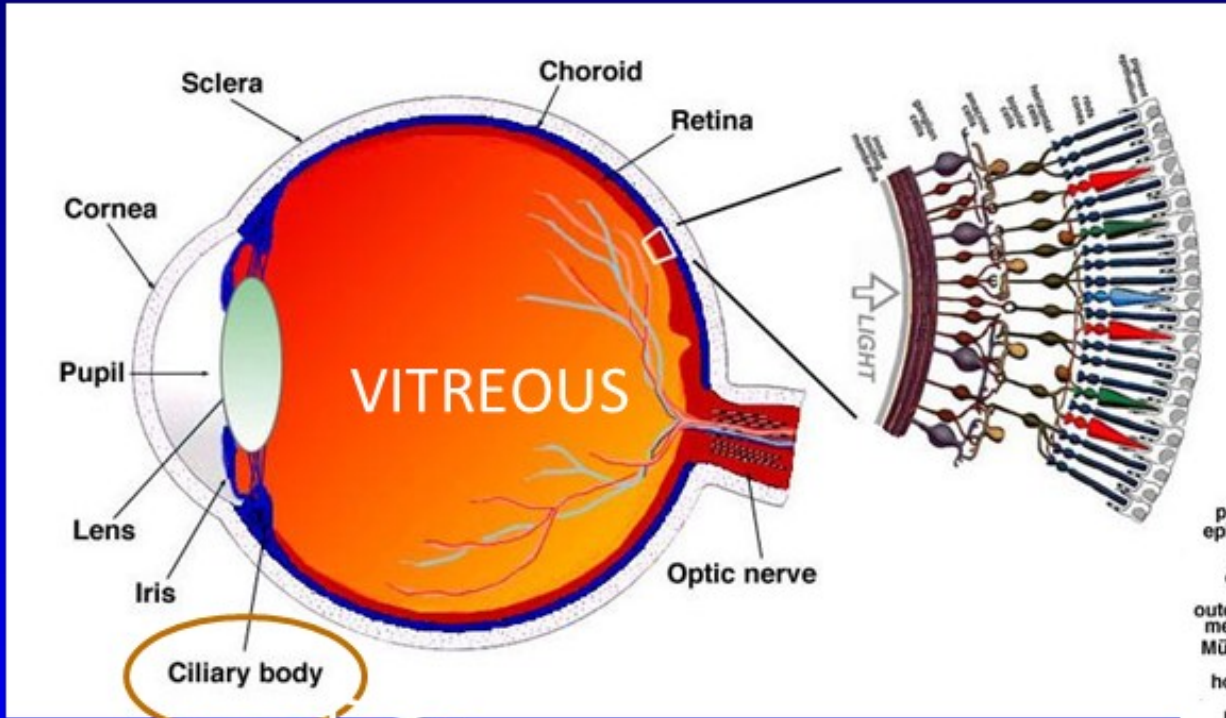


Diabetic Retinopathy

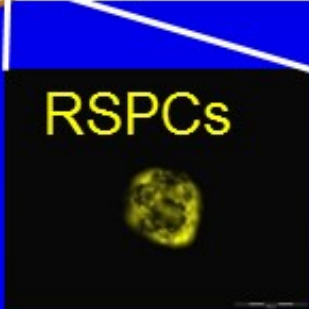
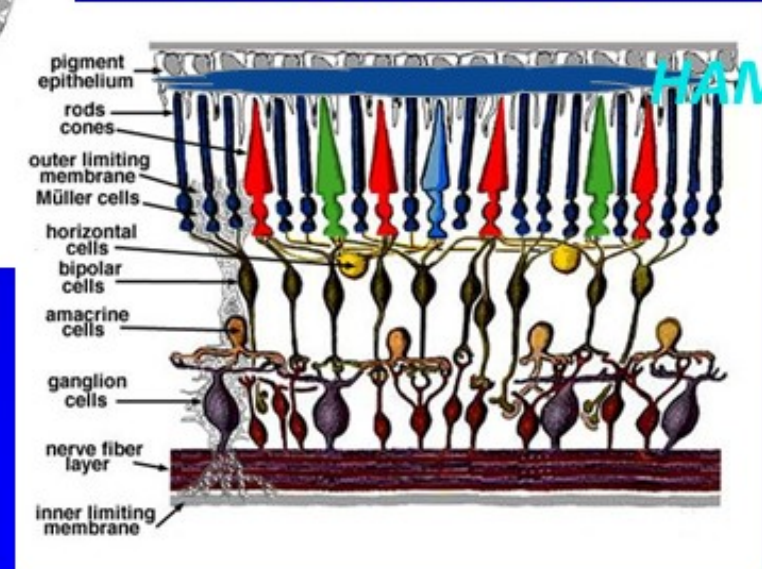


No definitive regenerative treatment
Pharmacologics only supportive

Vision Repair: Cell Transplantation in HAMC



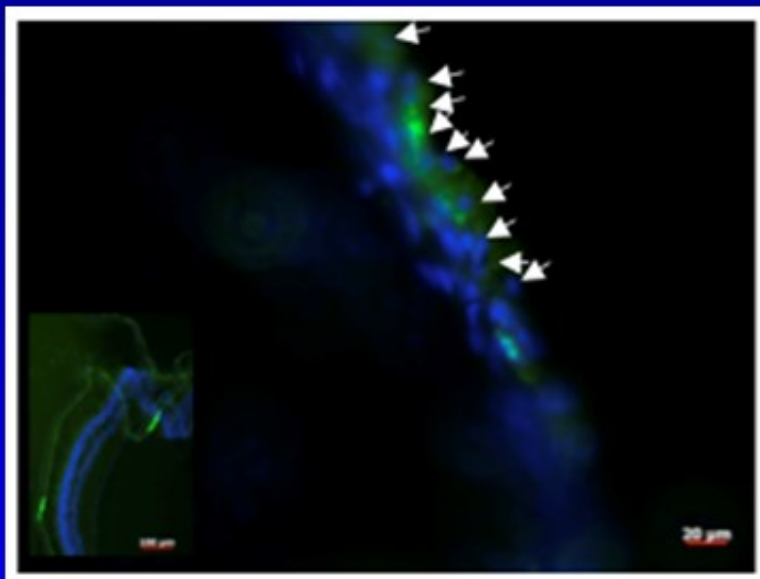
OUTSIDE OF EYE



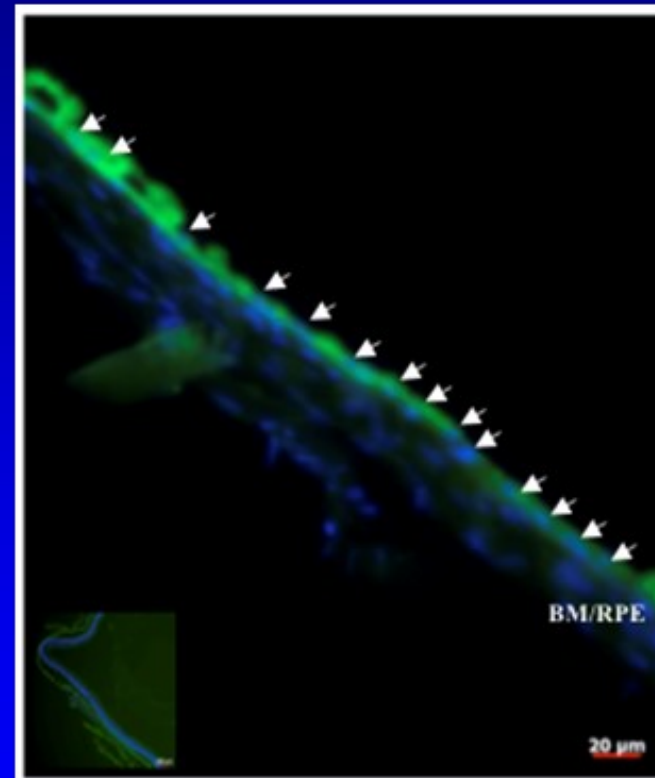
RSPCs

VITREOUS Page 15/33

Injectable biomaterial enhances cell survival and distribution required for regeneration

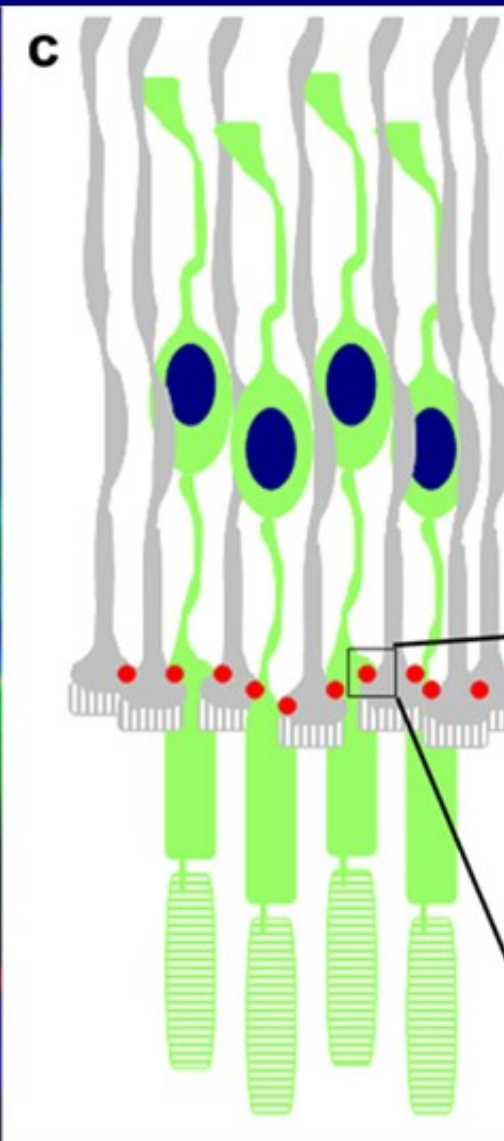
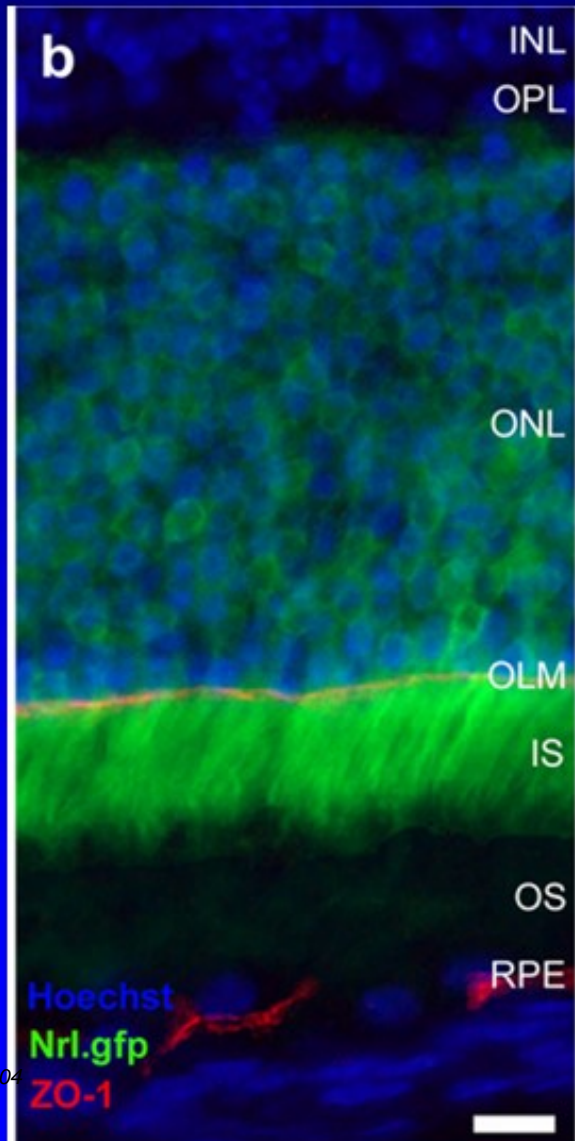


Saline Injection of Cells

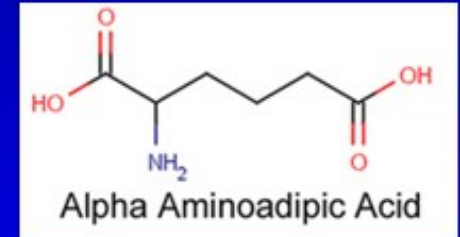


Biomaterial Injection of Cells

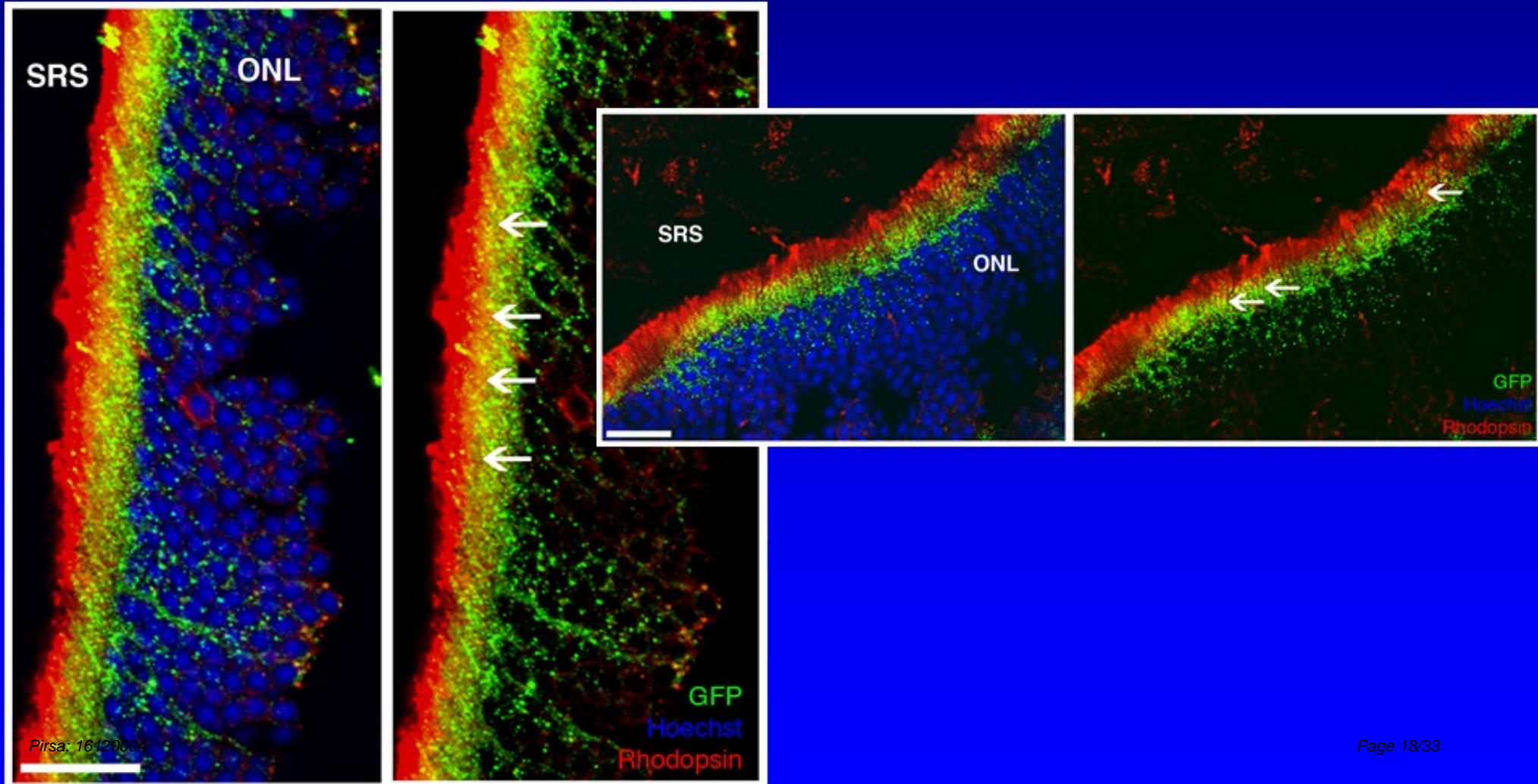
Addressing integration directly



AAA

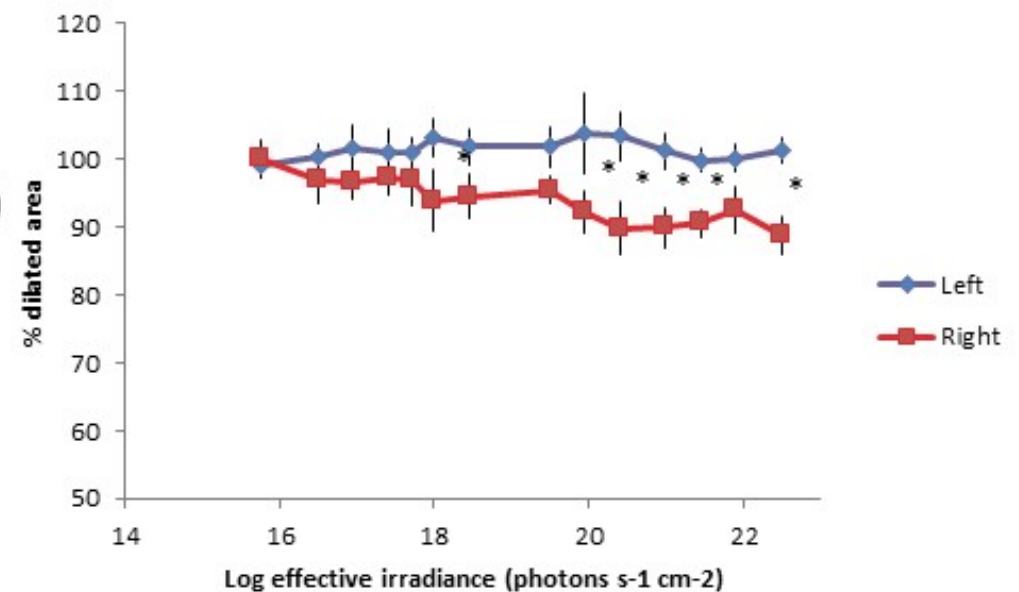
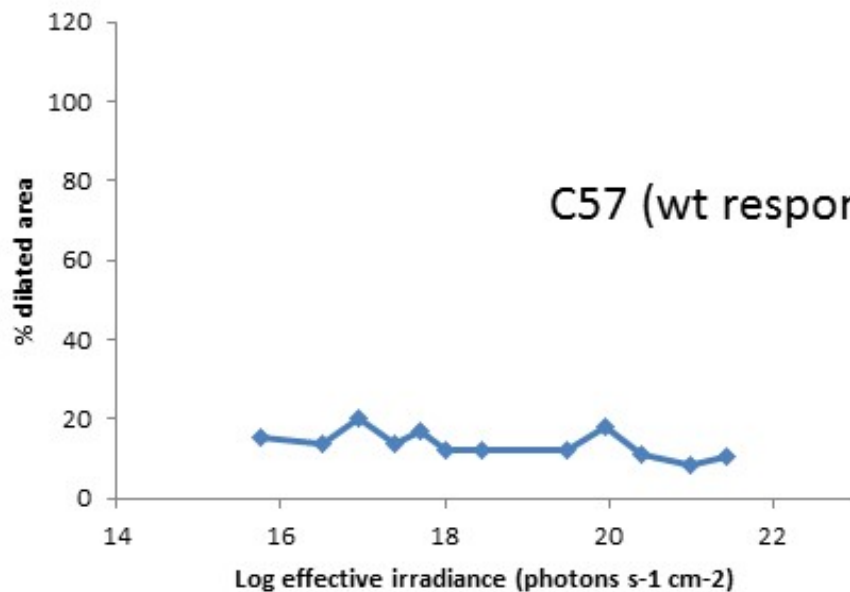


Retinal Stem Cell-derived Rods Integrate into Adult Retina



TKO mice show functional recovery of pupillary light response after injection of RSC-derived rod photoreceptors

Subretinal injection into adult TKO animals ($Gnat1^{-/-}; CngA3^{-/-}; Opn4^{-/-}$)



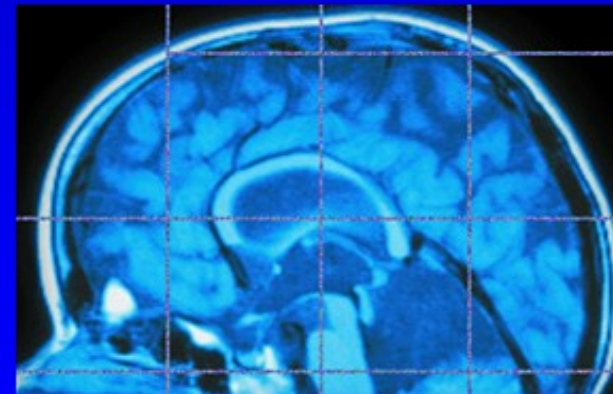
Left eye = vehicle injection (HAMC+AAA)
Right eye = HAMC+AAA+RSC-derived rods

Is greater cell survival possible with an enhanced delivery vehicle?

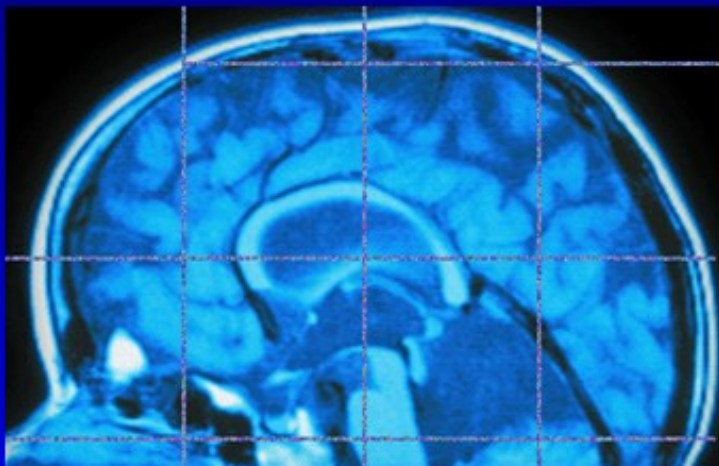


Change in Medicine

- Personalized Medicine
- Regenerative Medicine

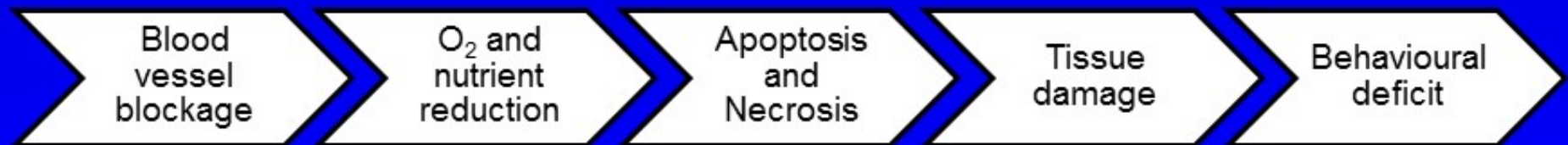


Stroke Problem: Traumatic loss of function and tissue



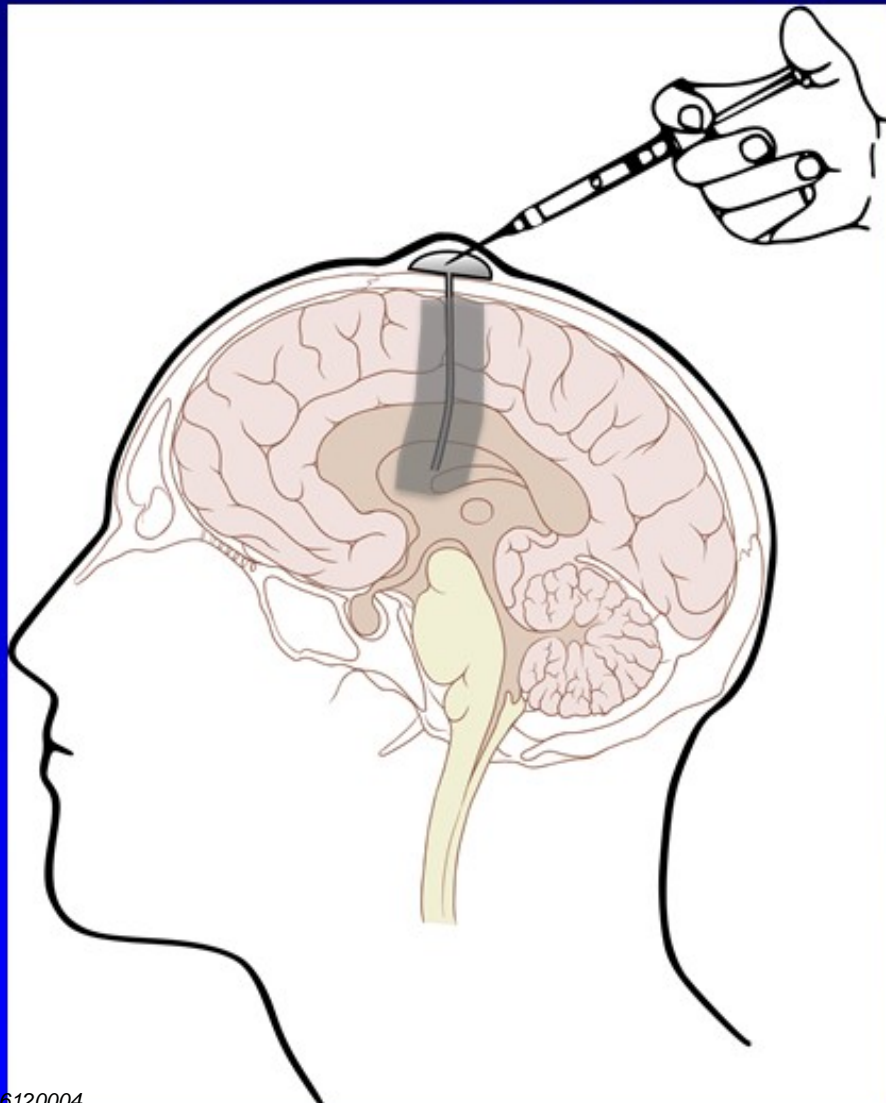
Stroke: rapidly developing loss of brain function(s) due to an interruption in the blood supply to the brain: ischemic or hemorrhagic

- affected area of the brain is unable to function
- inability to move limb(s) on 1 side of body
- inability to understand or formulate speech
- inability to see one side of the visual field.

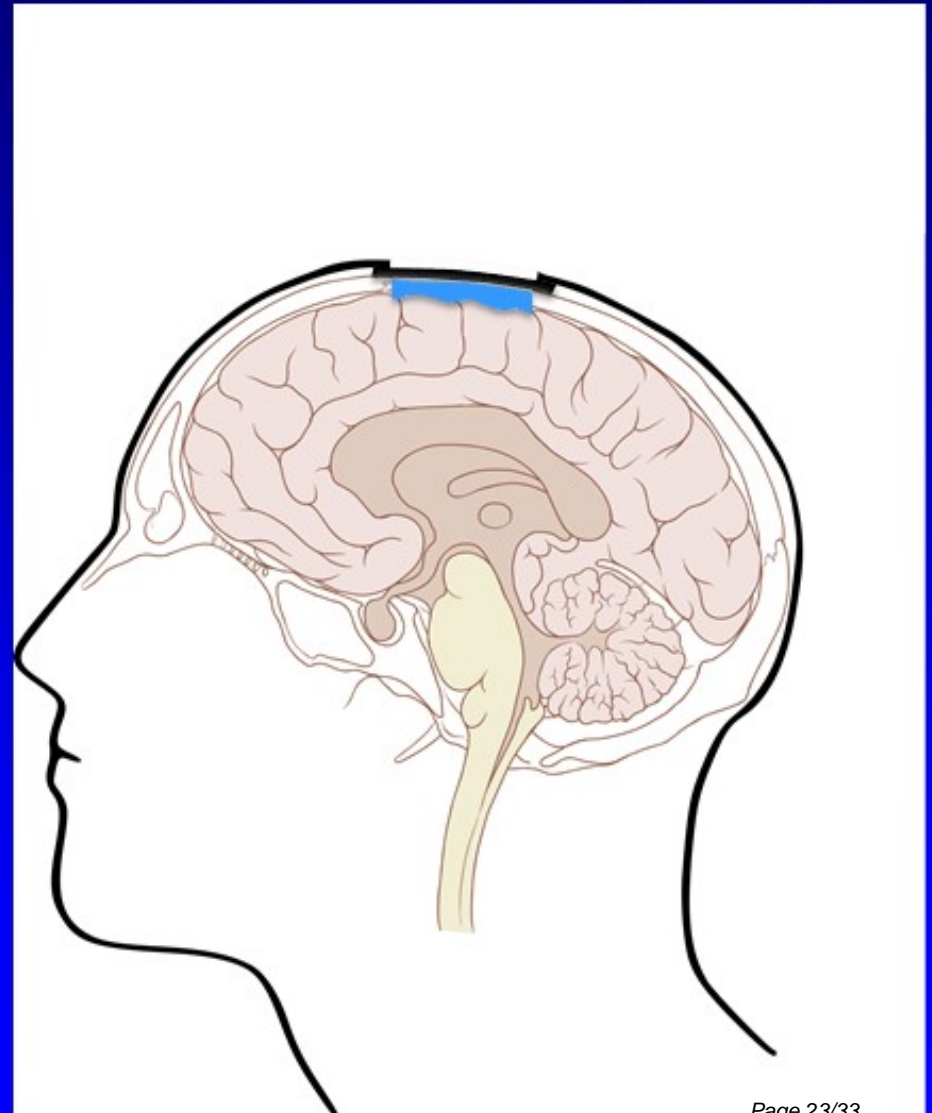


3rd leading cause of death in America

Invasive Catheter/Pump

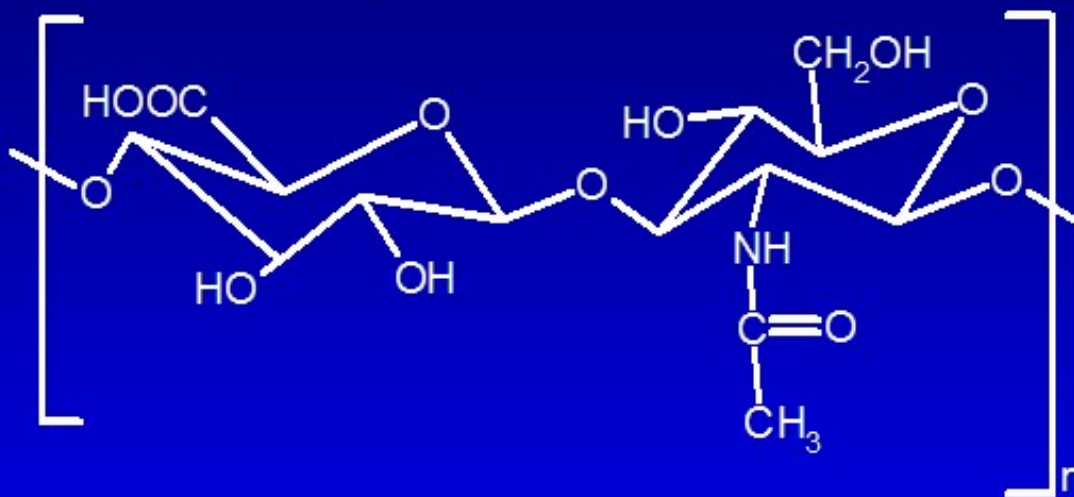


Less Invasive Hydrogel

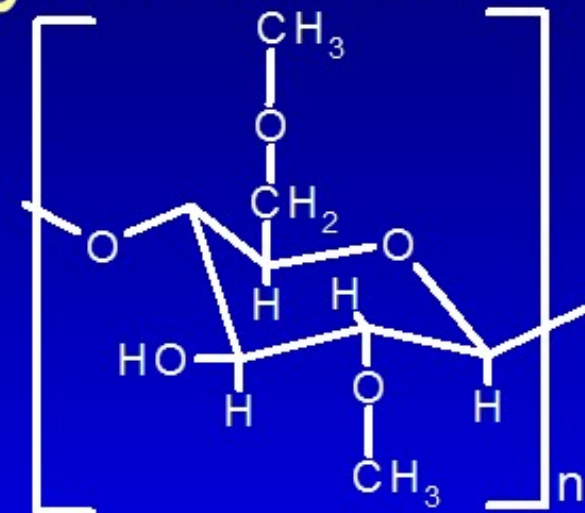


Biomaterials that Promote Healing

Hyaluronan / Methylcellulose



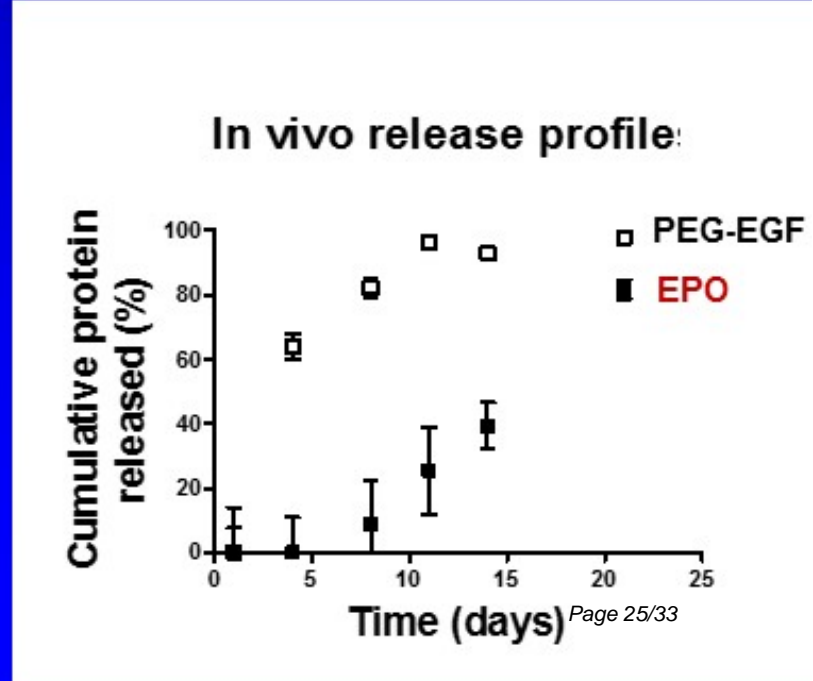
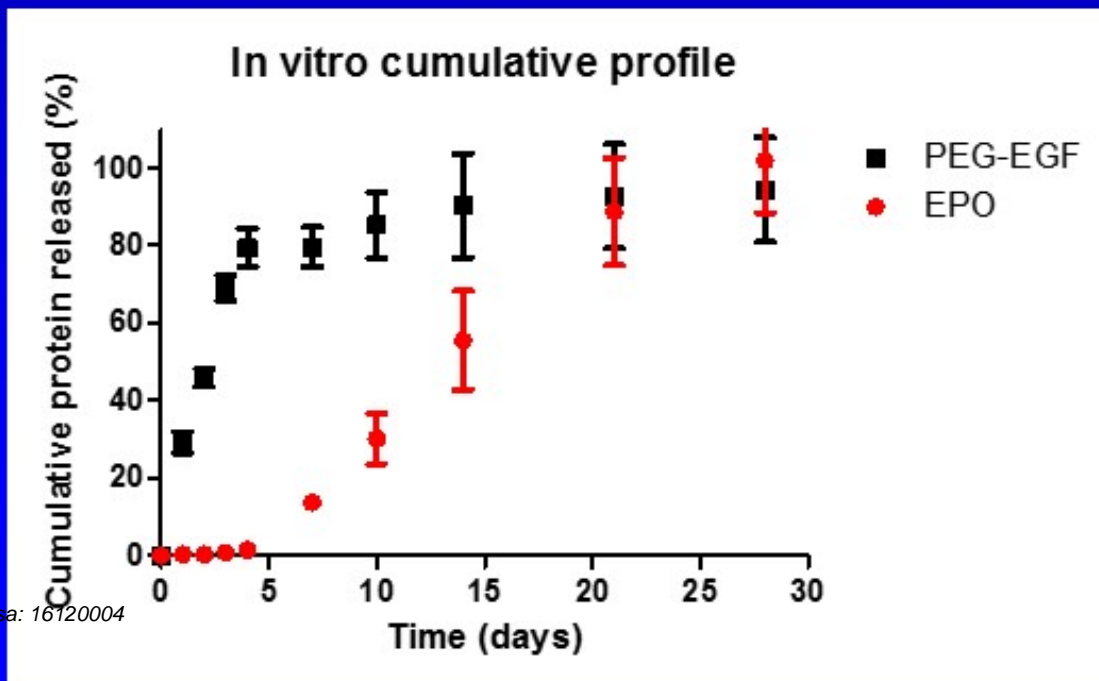
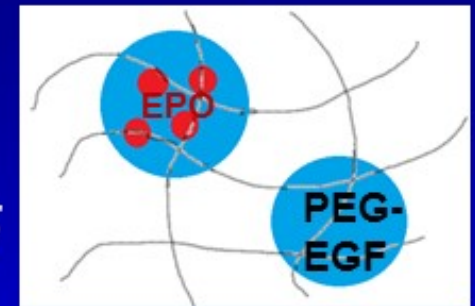
HA
Shear Thinning



MC
Thermal Gelling

Sequential Delivery of PEG-EGF & EPO

- Delivery Profile Goal:
 - Release PEG-EGF for 7 days followed by EPO for 7 days
- Composite delivery system:
 - HAMC
 - Nanoparticles encapsulate PEG-EGF
 - Biphasic particles encapsulate EPO

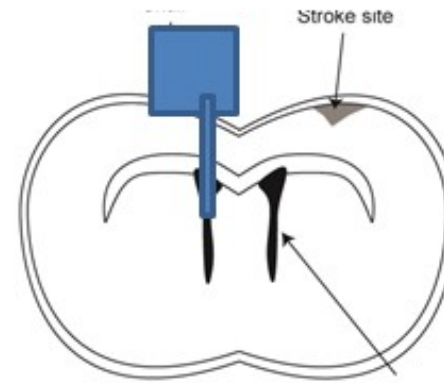


Hydrogel delivery vs. Catheter/pump

Composite DDS



Pump infusion



Day 0

Day 4

Day 11

Day 18

Day 32

PEG-EGF

EPO

Stroke

Implant pumps **or** composite DDS

Switch pumps

Remove pumps

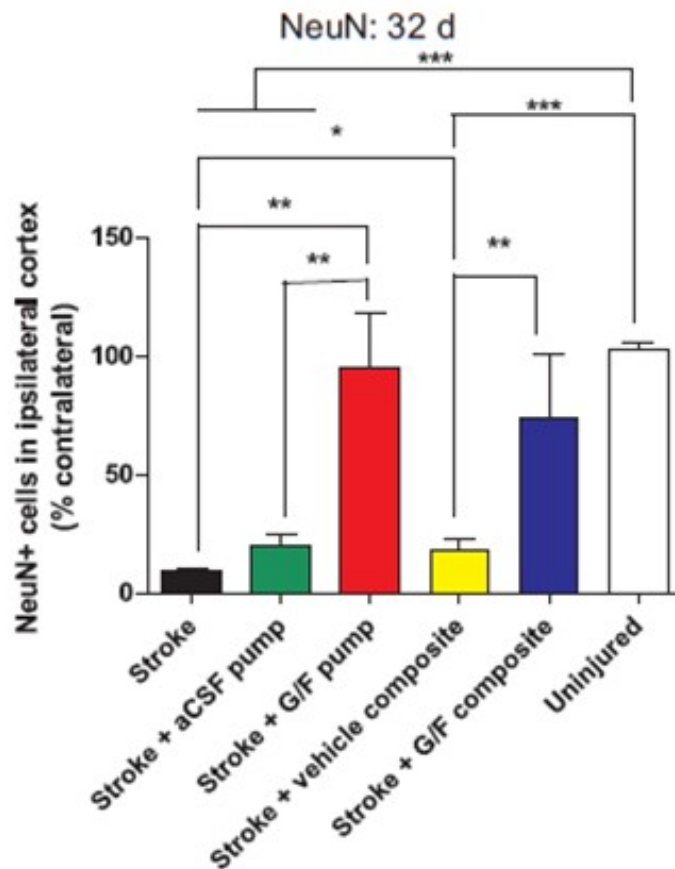
Sacrifice

Cannula Implant

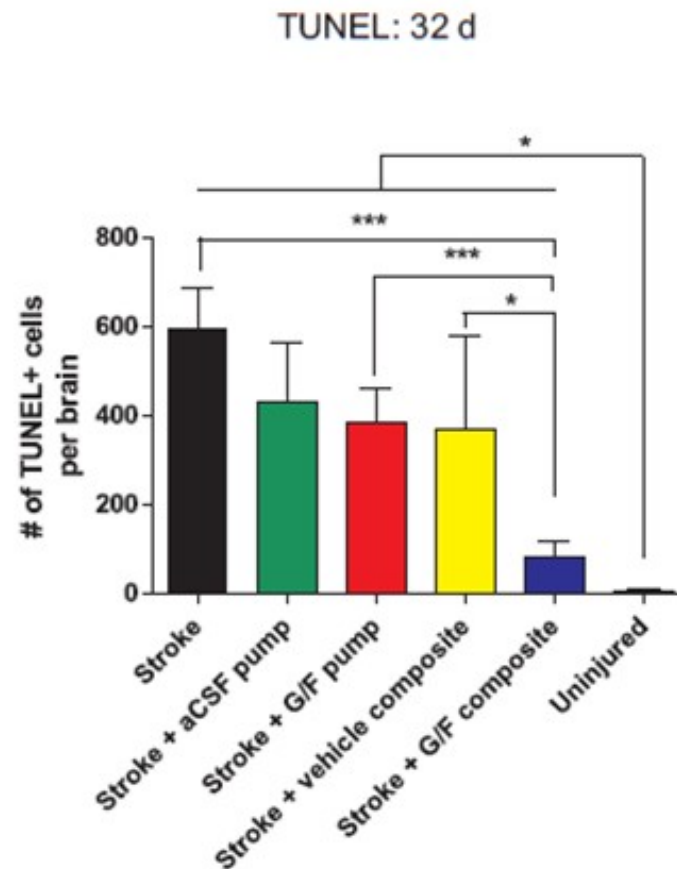
Brain Repair with Growth Factor Delivery

Hydrogel delivery vs. Catheter/pump

Same Nerve Tissue

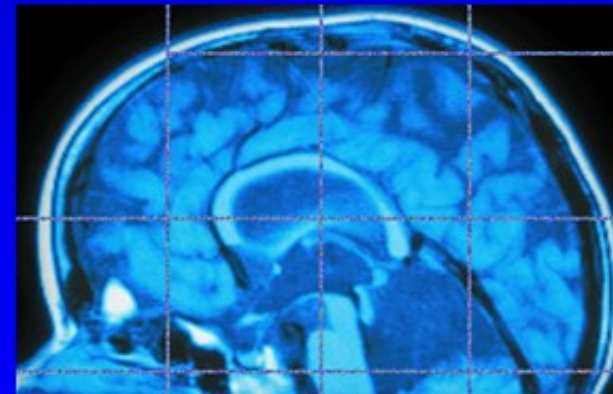


Reduced Cell Death



Change in Medicine

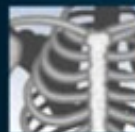
- Personalized Medicine
- Regenerative Medicine



Restore, maintain and improve tissue function

THE NEW ERA OF REGENERATIVE MEDICINE

Dozens of biotech companies and university labs are developing ways to replace or regenerate failed body parts. Here are a few of the projects:



BONE

Bone-growth factors or stem cells are inserted into a porous material cut to a specific shape, creating new jaws or limbs. A product that creates shinbones is in clinical trials.

COMPANIES: Creative BioMolecules, Orquest, Sulzer Orthopedics Biologics, Genetics Institute, Osiris Therapeutics, Regeneron.



SKIN

Organogenesis' Apligraf, a human-skin equivalent, is the first engineered body part to win FDA approval, initially for leg ulcers. Other skins are in the works for foot ulcers and burns.

COMPANIES: Organogenesis, Advanced Tissue Sciences, Integra LifeSciences, LifeCell, Ortec International.



PANCREAS

Insulin-manufacturing cells are harvested from pigs, encapsulated in membranes, and injected into the abdomen. The method has been tested in animals and could be in human trials in two years.

COMPANIES: BioHybrid Technologies, Neocrin, Circe Biomedical



HEART VALVES, ARTERIES, AND VEINS

A 10-year initiative to build a heart has just started. Genetically engineered proteins have been successfully used to regrow blood vessels.

COMPANIES: Organogenesis, Advanced Tissue Sciences, Genetech, LifeCell, Regeneration.



SALIVA GLANDS

Proteins called aquaporins that allow cells to secrete water are used to recreate saliva glands damaged by disease or radiation. Glands are also being engineered to secrete healing drugs. The technique has proven successful in mice.

COMPANIES: None yet.



URINARY TRACT

Cartilage cells are taken from the patient, packed into a tiny matrix, and injected into the weakened ureter, where they bulk up the tissue walls to prevent urinary backup and incontinence. The method is in late-phase clinical trials.

COMPANIES: ReProgenesis, Integra LifeSciences.



BLADDER

Doctors at Children's Hospital in Boston have grown bladders from skin cells and implanted them in sheep.

They are about to try the same process on a patient.

COMPANIES: ReProgenesis.



CARTILAGE

A product is already on the market that regrows knee cartilage. A chest has been grown for a boy and a human ear on a mouse.

COMPANIES: Genzyme Tissue, Biomatrix, Integra LifeSciences, Advanced Tissue Sciences, ReGen Biologics, Osiris Therapeutics



TEETH

Enamel matrix proteins are used to fill cavities. It works in dogs; human trials are a few years away.

COMPANIES: Biora, Atrix Laboratories, Creative BioMolecules.



BREAST

In preclinical studies, several companies have been able to create a cosmetic nipple by inserting a ball of cartilage. Researchers are now trying to grow a whole cosmetic breast.

COMPANIES: ReProgenesis, Integra LifeSciences.



LIVER

A spongy membrane is built up and then seeded with liver cells. Organs the size of a dime have been grown, but a full-size liver could take 10 years due to its complexity.

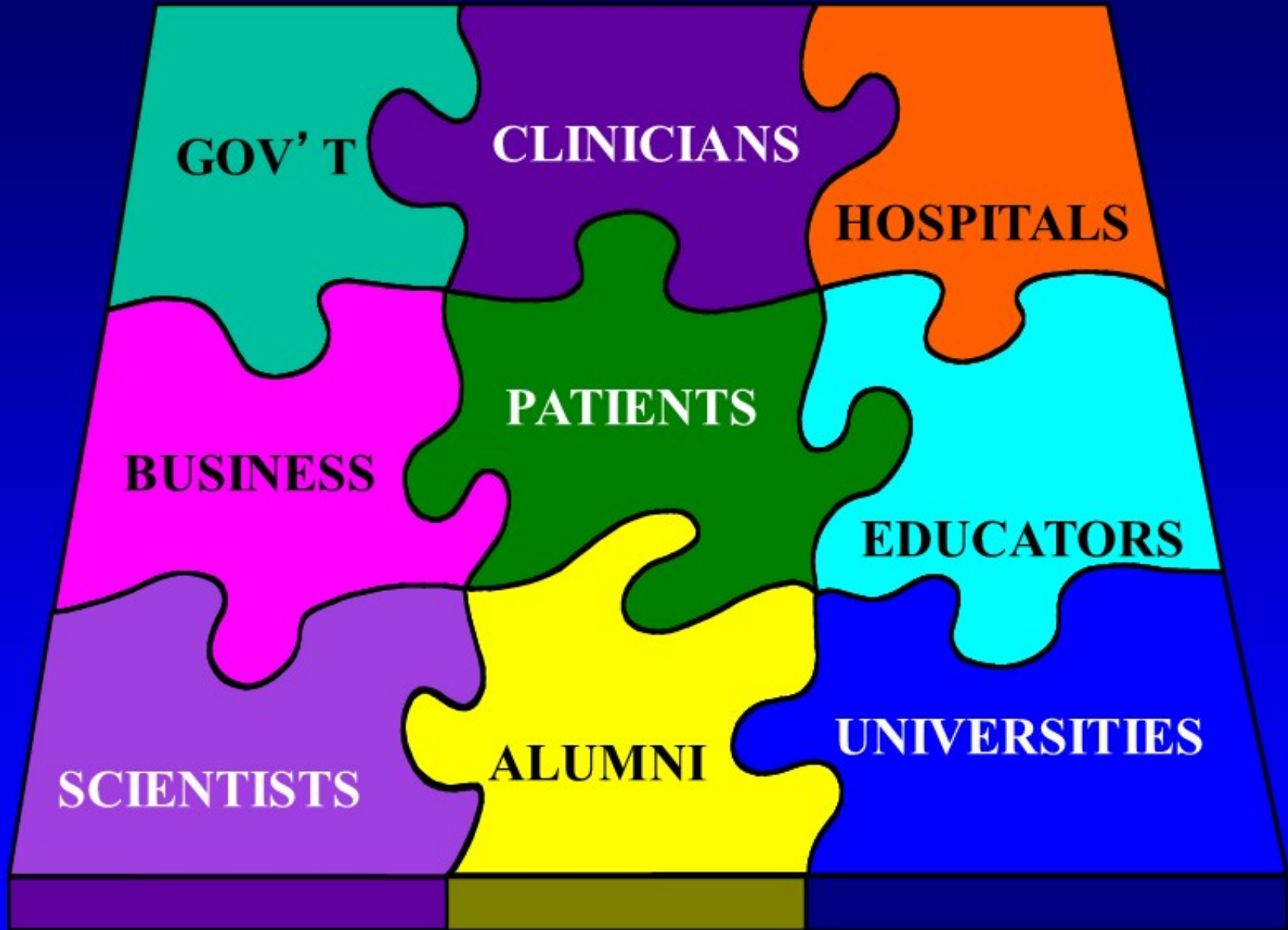
COMPANIES: Advanced Tissue Sciences, Human Organ Sciences, Organogenesis.



SPINAL CORD NERVES

Scientists are investigating nerve-growth factors, injecting them at the site of damage to encourage regeneration or seeding them along biodegradable filaments and implanting them. Rats have been made to walk again.

COMPANIES: Acorda, Regeneron, CytoTherapeutics, Guilford Pharmaceuticals.



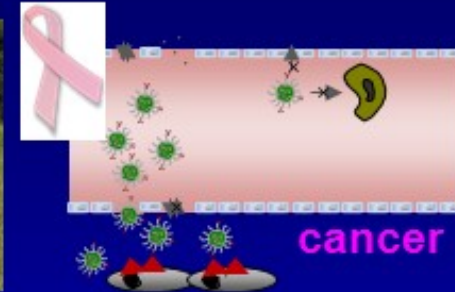
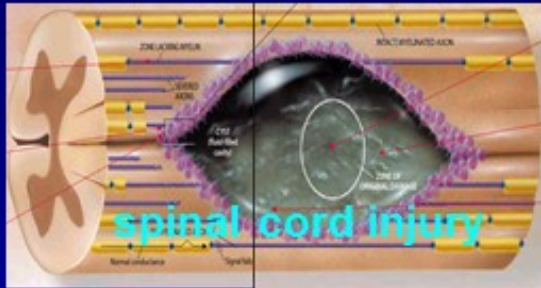


Former Graduate Students and Post-doctoral Fellows

Ryan Wylie
Howard Kim
Catherine Kang
Michael Conrad
Meng Shi
Laura Yu
Jeff Karp
Ying Luo
Maria Jimenez-Haman
Xudong Cao
Yen Tong
R Dan Lousenberg
Chantal Holy
Dianna Chan
Chelsea Nimmo
Jason Stanwick
Yuanfei Wang
Brian Ballios

Doug Baumann
Tasneem Zahir
Yakov Lapitsky
Nic Leipzig
Jordan Wosnick
Thomas Freier
Bilal Baradie
Paul Dalton
Stephane Levesque
Molly Gregas
Henry Peng
Yumin Yuan
Karyn Ho
Jiao Lu
Yukie Aizawa
Devang Odedra
Shawn Owen
Katarina Vulic

Nafees Rahman
Anne Hsieh
Vanessa Scanga
Patricia Musoke-Zawedde
Dimpy Gupta
Alex Goraltchouk
Tina Ting-Ting Yu
Alexandra Piotrowicz
Kathryn Moore
Cristina Enescu
Yusuke Katayama
Margaret MacSween
Terri Kapur
Derek Shaw
Samar Saneinejad
Sabeshan Kanagalingam
Daniel McLean
Jamie Parker
Leah Kesselman

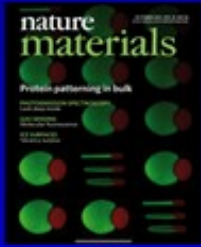


Charles Tator (UHN)
Michael Fehlings (UHN)
Greg Borschel (HSC)

Cindi Morshead (UT)
Dale Corbett (UofO)

Derek van der Kooy (UT)
Andras Nagy (MSH)
Valerie Wallace (UHN)

Dev Sidhu (UT)
Jason Moffat (UT)
Masad Damha (McGill)
Brian Shoichet (UCSF)
Tad Koch (UColorado)
Armand Keating (PMH)
Kevin Petrecca (McGill)
Rima Al-awar (OICR)



Tissue Mimetics

Karen Maxwell (UT)
Peter Dirks (HSC)
Penney Gilbert (UT)
Eugenia Kumacheva (UT)
Bill Stanford (UOttawa)



Alzheimer's Disease
Peter Hyslop (UT)
Paul Fraser (UT)
Charlie Glabe (UCIrvine)

