Becoming a Lab Rat:
Lessons learned & resources for participating in a clinical trial

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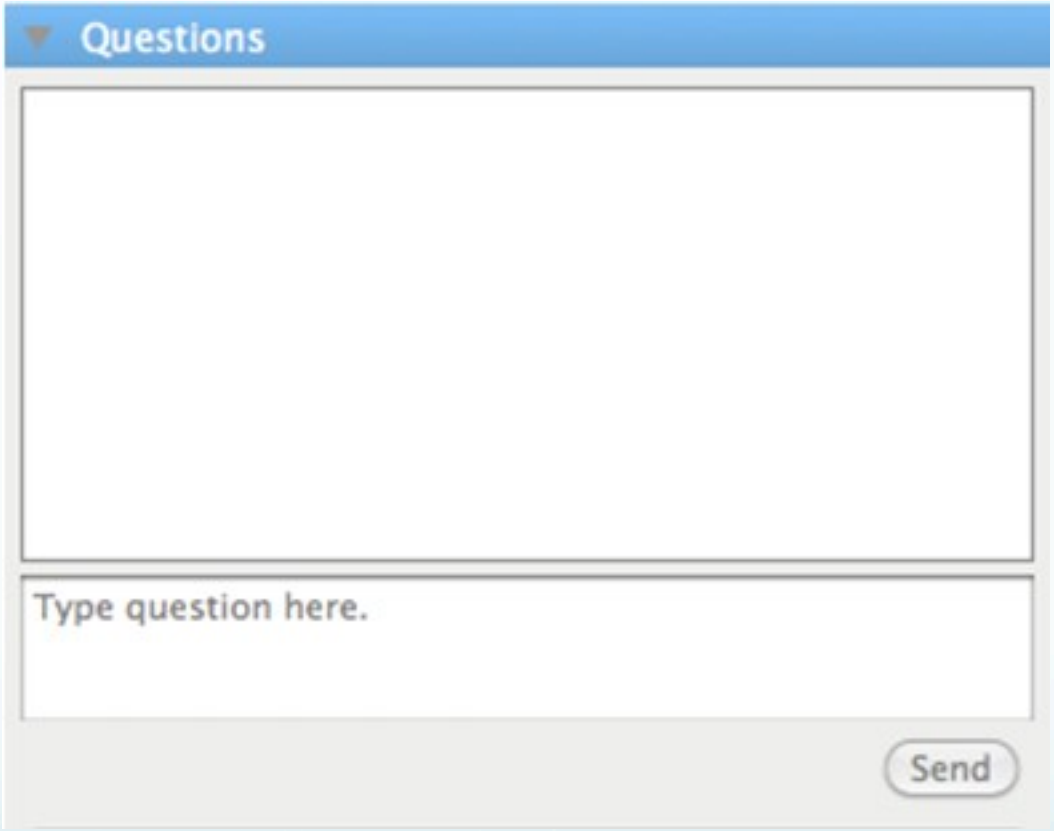
Have a Question?



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www.MiamiProject.miami.edu/

The Miami Project is dedicated to finding more effective treatments and, ultimately, a cure for paralysis resulting from spinal cord injury.

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www.NeurotechNetwork.org

Helping people regain life thru neurotechnology

Focusing on education of and advocacy to access neurotechnology devices, therapies and treatments for people living with impairments, their care-givers and medical professionals.

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Disclaimer page

The information presented in this session is not meant to replace the advice from a medical professional. You should consult a health care professional familiar with your specific case, concerns and condition.

In this presentation we may discuss experimental, investigational, non-FDA approved drugs, devices or biologics

Neurotech Network and its representatives do not endorse, rate, sell, distribute, prescribe, administer or recommend any products, procedures or services. We highly suggest for you to take information to a trained medical professional familiar with your case to discuss options that are best for you.

Disclosure: Dr. Anderson-Erisman: consultant for ASUBIO Pharmaceuticals and BioAxone BioSciences.

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Agenda

- Basics about Clinical Trials
- Overview of spinal cord injuries
- The pipeline of clinical trials for SCI
- What is happening now
- Lessons learned from participating in a clinical trial

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What is a Clinical Trial?

Clinical Research

- Research with human subjects that is:

(1) Patient-oriented research, which includes:

(a) mechanisms of human disease,

(b) therapeutic interventions,

(c) clinical trials, or

(d) development of new technologies.

(2) Epidemiologic and behavioral studies.

(3) Outcomes research and health services research.

Clinical Trials

- A **prospective** biomedical or behavioral research study of human subjects that is **designed to answer specific questions about biomedical or behavioral interventions** (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices).
- Clinical trials are used to determine whether **new** biomedical or behavioral interventions are **safe, efficacious, and effective**.
- Long-term goal is to provide **evidence leading to a scientific basis for consideration of a change in health policy or standard of care**. The definition includes pharmacologic, non-pharmacologic, and behavioral interventions given for disease prevention, prophylaxis, diagnosis, or therapy.

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How is it different from treatment?

Clinical Study	Usual Health Care
Specific goal	Care or monitor of condition
Strict Protocol	Flexible for treatment

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Basics: Clinical Study Participant Protocol Information

1) Reason for conducting the study
2) Who may participate in the study (eligibility criteria)
3) Number of Participants needed
4) Schedule of tests, procedures, or drugs and dosages
5) Length of the study
6) What information will be gathered about the participants

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Basics: Clinical Study Participant Eligibility Criteria

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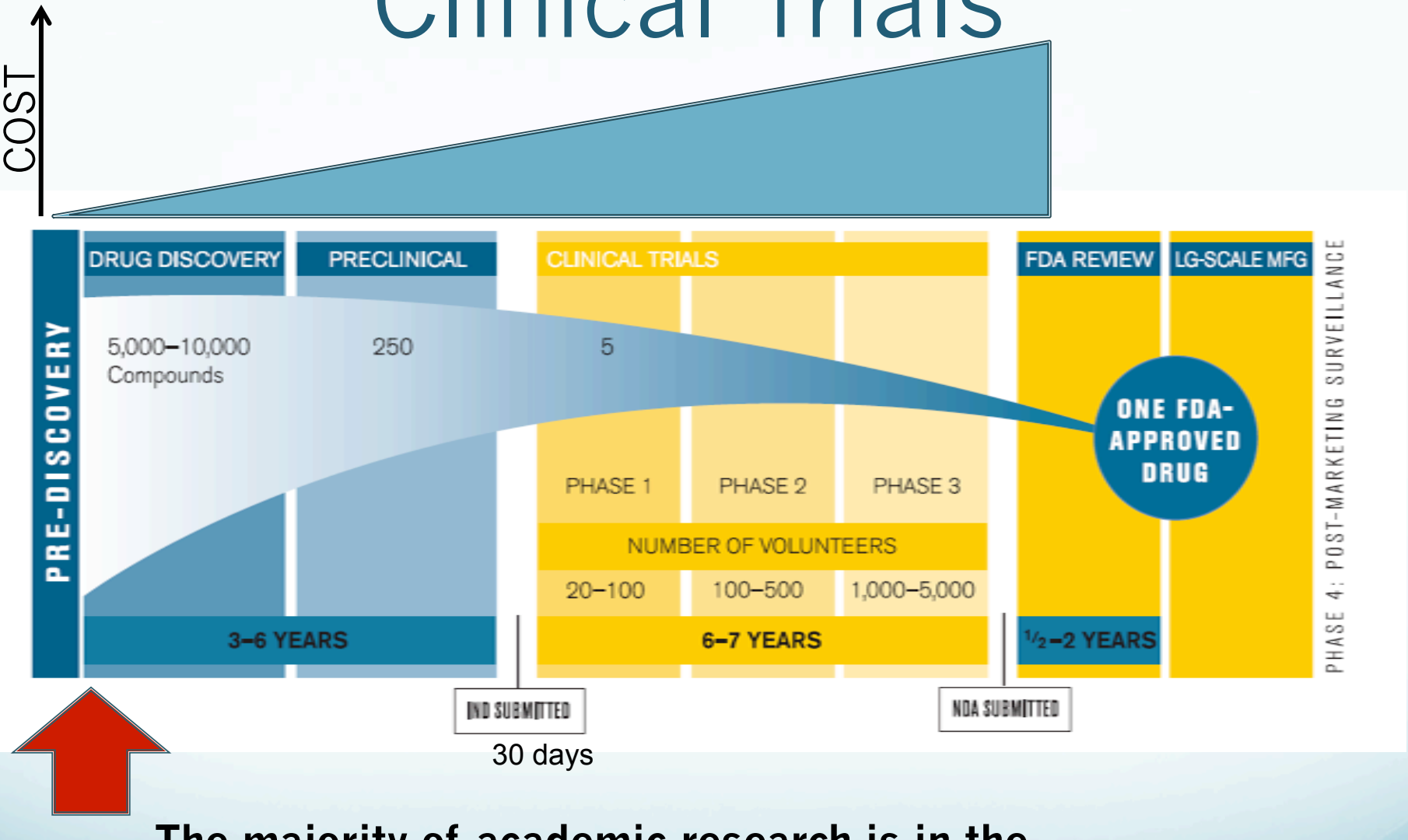
Clinical Trials



The majority of academic research is in the "Pre-Discovery" and "Discovery" phases.

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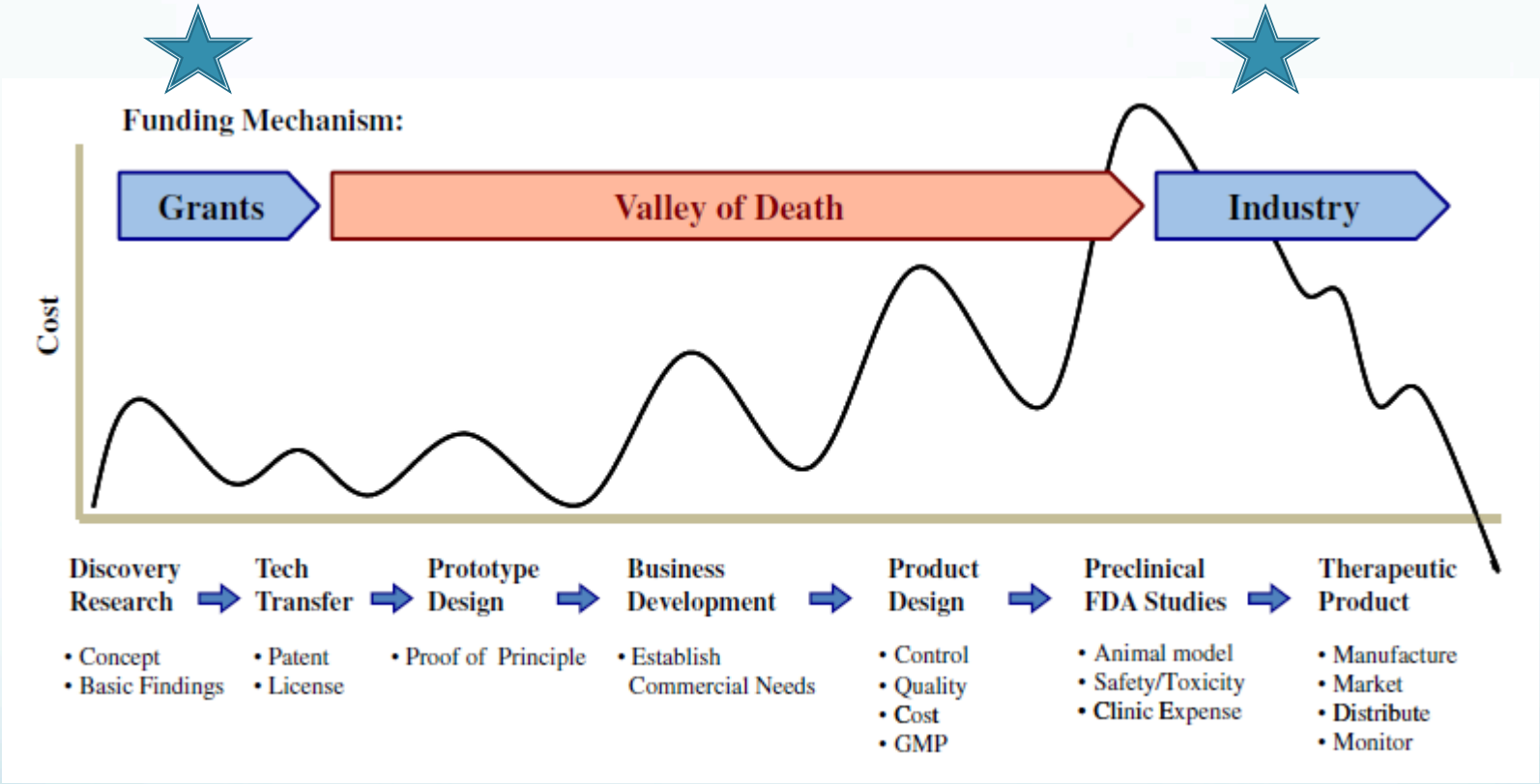
Funding



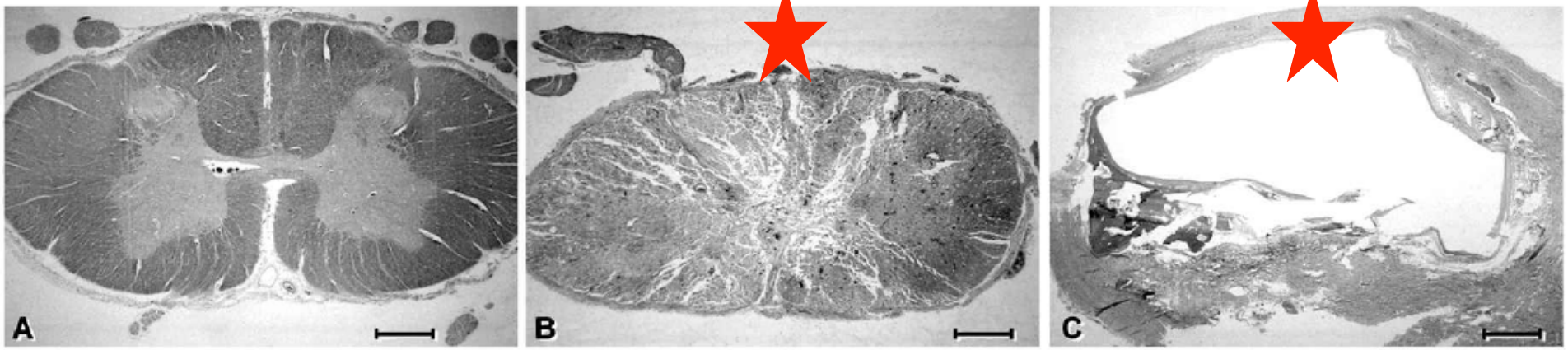
Aboody et al , 2011. *Neuron*. 70:597–613.

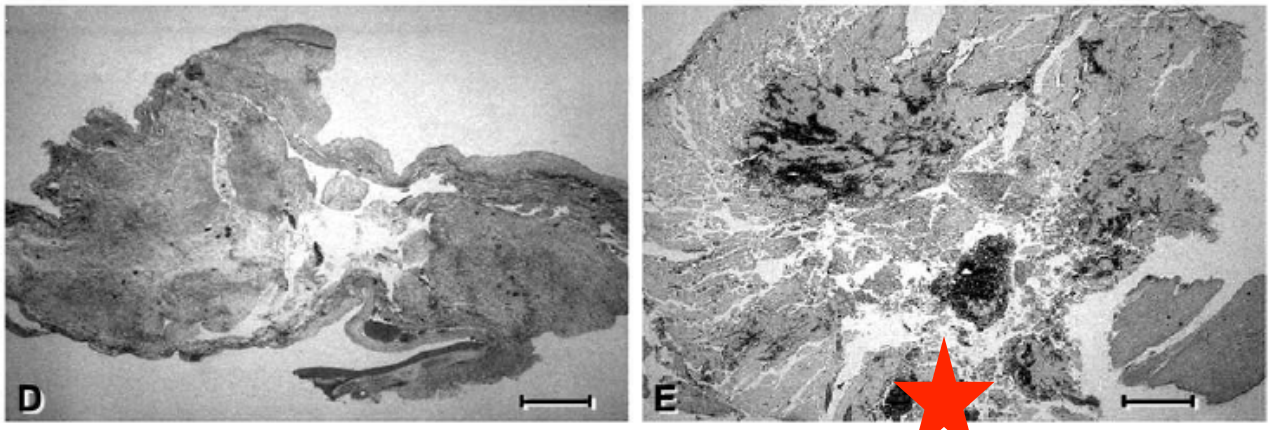
What is Spinal Cord Injury (SCI)?

Normal

Solid cord damage

Contusion w/ cyst





Laceration

Massive Compression

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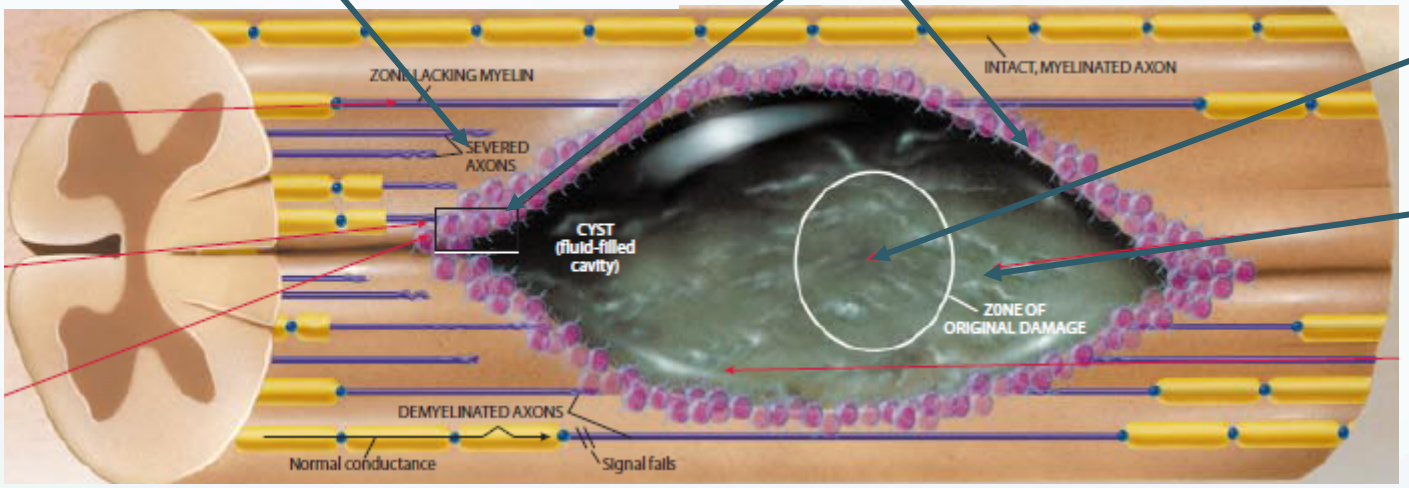
Norenberg et al., 2004. *J. Neurotrauma*. 21:429-440

What happens inside the spinal cord?



McDonald , 1999. *Sci. Amer.* 281:64-73

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Past Studies

- Methylprednisolone (NASCIS I, II, and III) - Upjohn
  - Mandated by NIH, never FDA approved
- Sygen (GM-1) – FIDIA
  - Phase III, 760 people; primary outcome was too high of a bar = 2 AIS levels
- Gacyclidine (GK-11) – Beaufour-Ipsen
  - Phase II, discontinued, not much information
- Cethrin (BA-210) - Alseres Pharmaceutical
  - Phase I/IIa; intraoperative epidural delivery
  - Successful motor improvement in cervical injuries
  - Dropped by company

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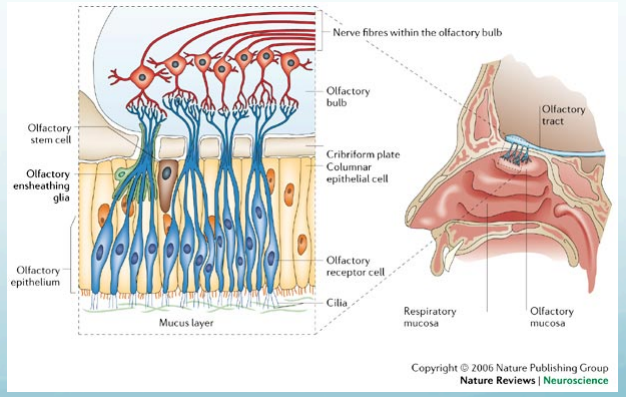
Past Studies

- Activated macrophage – Procord/Proneuron
  - Phase I – 16 people (AIS A, C5-T11); no adverse events; Phase II - Randomized into treatment or non-surgical control group;
  - Enrollment stopped for financial reasons after 2/3 of subjects enrolled; however, recent review of data reveals that the experimental group had less natural recovery than control group
- Olfactory ensheathing cells - Australia
  - Phase I - 6 people, AIS A, T4-T10; injections of autologous, purified OECs into spinal cord within 18-32 months post-injury
  - Established safety



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Past Studies

- Upper Extremity Neural Prosthesis/Freehand
  - Studies completed and brought to market
  - Taken off the market in 2001
  - Maintenance & research available thru Cleveland FES Center
- Bladder Control Systems
  - Studies completed, various systems brought to market
  - Example: InterStim (Medtronic), Finetech-Brindley/VoCare (Finetech Medical), Urgent*PC (Uroplasty)
- Respiratory Neural Prosthesis
  - Studies completed and brought to market
  - Mark IV (Avery Labs), AtroStim (Atrotech), NeuRx DPS (Synapse Biomedical)
- Drop Foot Stimulation
  - Studies completed, various systems available
  - L300 (Bioness), WalkAide (Innovative Neurotronics), STIMuStep (Finetech Medical), Odstock DFS (Odstock Medical)
- Oscillating Field Stimulator (OFS)
  - Studies completed, FDA required more info. for HDE, study halted
  - Andara/Cyberkinetics technology acquired by NeuroMetrix

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Current Studies

- Riluzole (NACTN)
  - Already FDA-approved for Lou Gehrig's disease (ALS)
  - Within 12 hrs post-injury, continue for 14 days; Oral
  - Phase I safety study (n=36); multi-center; COMPLETE; Phase II/III efficacy (n=351); multi-center
- Minocycline (University of Calgary)
  - Already FDA approved for acne
  - Within 12 hrs post-injury, continue for 7 days; IV
  - Phase I/II safety & preliminary efficacy (n=52); single center; COMPLETE; Phase III efficacy (n=248); single-center?
- Therapeutic hypothermia (University of Miami)
  - Intravascular catheter, lower temperature to 33°C
  - Phase I safety & preliminary efficacy, ongoing; Phase II multi-center trial in development

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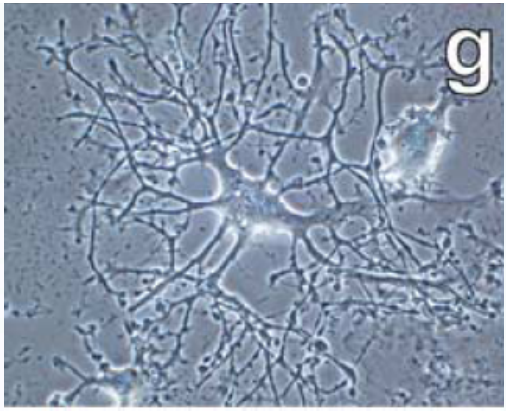
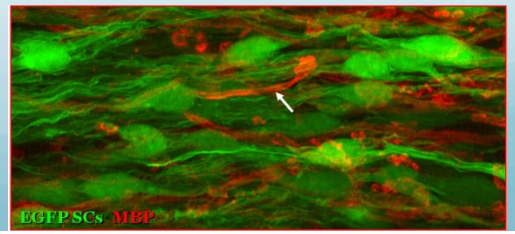
Current Studies



Keirstead et al., 2005 J. Neurosci. 29(19):4694

- Human Embryonic stem cells
  - Geron Corp.; multi-center
  - Phase I safety study of GRNOPC1
  - Complete thoracic SCI; within 14 days of injury
  - Intraspinal injection; single dose
  - Temporary immunosuppression
  - Enrolled 5 people of 10
  - Halted for financial reasons
- Human Schwann cells
  - The Miami Project/University of Miami; single center
  - Phase I safety study of ahSC
  - Complete, thoracic SCI; within 5 days post-injury
  - Intraspinal injection; single dose
  - Autologous (no immunosupression)
  - Enrolled 2 people of 8



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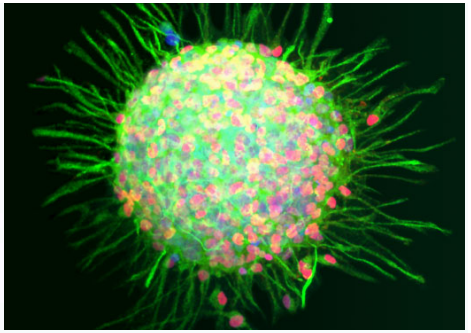
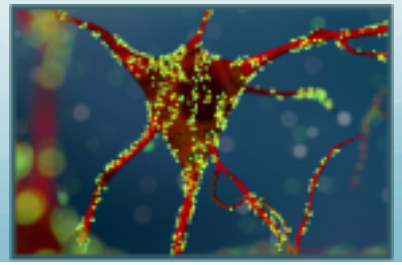
Current Studies



- Human fetal CNS stem cells
  - StemCells, Inc.; single center* (+Canada)
  - Phase I/II safety & preliminary effiacy of HuCNS-SC
  - Complete and incomplete thoracic SCI (3 cohorts; T2-11; AIS A, B, C); within 3 to 12 months post-injury
  - Intraspinal injection
  - Temporary immunosuppression
  - Enrolled 4 of 12 so far (3 complete, 1 incomplete)
- Human fetal spinal cord neural precursors
  - Neuralstem, Inc.; multi-center
  - Phase I safety of NSI-566
  - Complete thoracic SCI (2 dose cohorts; T2-12; AIS A, B, C)
  - Within 1 to 2 years post-injury
  - 6 intraspinal injections
  - Temporary immunosuppression



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Current Studies

- Transcranial Direct Current Stimulation (tDCS)
  - Chronic Pain, neuroplasticity upper extremity
- Repetitive Transcranial Magnetic Stimulation (rTMS)
  - Hand Motor Function, Chronic Pain, Spasticity
- Compex Motor Stimulation, non-invasive surface FES
  - Upper Limb Function
- FES Cycling & FES Rowing
  - Upper & Lower extremity
- Treadmill Training & Exoskeleton
  - Gait training
- Brain Computer Interface
  - Environmental control, upper extremity
- Implanted Neural Prosthesis
  - Cough, Hand Grasp/Arm & Shoulder, Trunk/Posture Control, Standing, Walking
- Network Neural Prosthesis
  - Combined: Upper Extremity, Bladder, Cough, Trunk
- Epidural Stimulation
  - Standing

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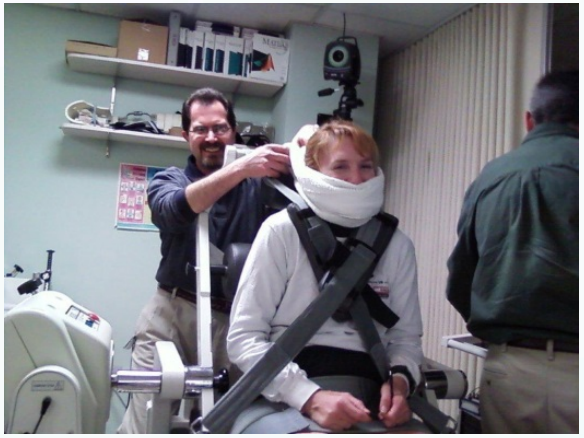
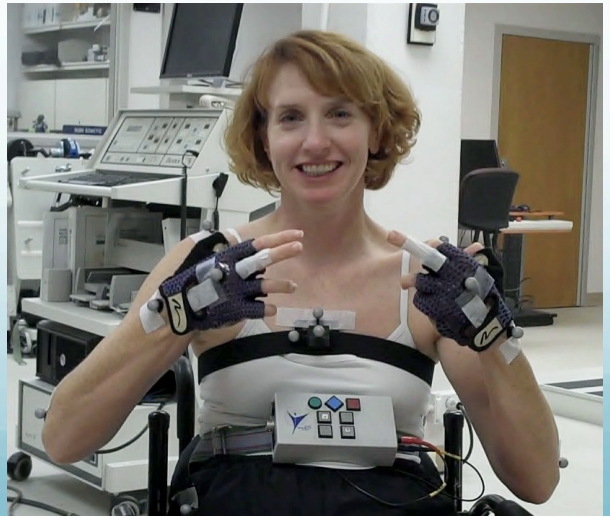
Lessons Learned

It takes a team, become part of it

Have Fun



Patience



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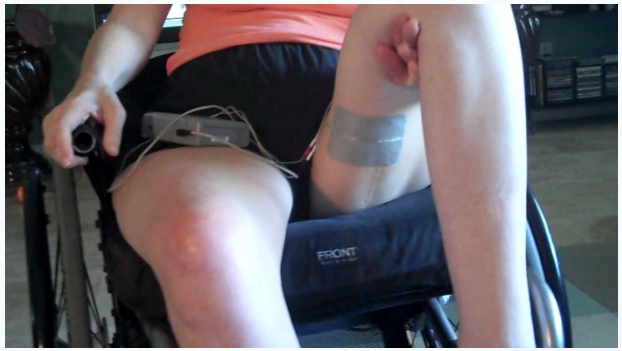
Lessons Learned

- Know your rights & risks
- Informed Consent
- Read the fine print

- Understand your commitments



- Manage your expectations

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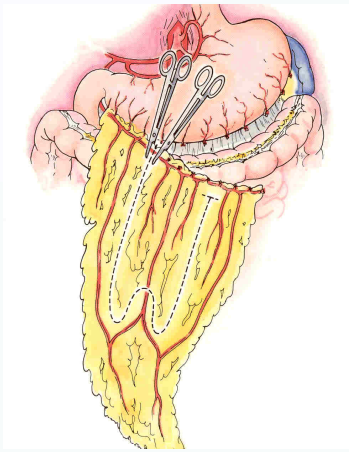
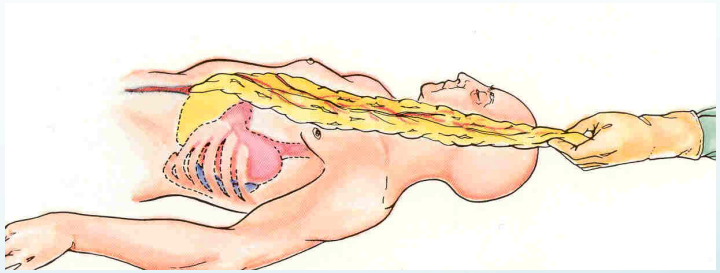
Lessons Learned

- The omentum is a highly vascular, fatty tissue approximately 14-inches long and 10-inches wide that hangs like an apron over the intestines and lower abdomen area.
- Blood supply
- Biological Material





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Lessons Learned

- Beware – of "trials" that are unapproved, even in the US – just because a US doctor is doing it does not mean it is legitimate!
- Do your research – get a second or third opinion from a research center or hospital that specializes in current SCI
- Never pay for experimental treatments
- Expect follow up

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Risks of unapproved trials

- Increased and long-lasting pain and/or muscle spasticity
- Further loss of function
- Increased disability
- Medical complications or death

  (FDA requires evidence that complications are minimal)

- Loss of health care coverage should complication occur after unapproved treatment
- Exclusion from future SCI clinical trial

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Caution - Stem cell tourism

- A form of medical travel to purchase unproven stem cell-based therapies. These unproven treatments hold significant risk for people.
- There is no evidence yet that stem cells have a reparative effect on chronically damaged spinal cord tissue.
- It is unethical to charge people money for unproven, risk-laden medical interventions.
- Be aware of selling Hope for Money
- No Oversight/Reporting

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Sample Questions to Ask

- Anyone interested in participating in a clinical study should know as much as possible about the study and feel comfortable asking the research team questions about the study, the related procedures, and any expenses.
- What is being studied?
- Why do researchers believe the intervention being tested is effective?
- How do the possible risks, side effects, and benefits of this trial compare with those of my current treatment?
- What are my out of pocket costs?
- How will it be determined which intervention is effective?

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APPENDIX B: What to ask before taking part in a clinical trial or human study? (your participation checklist)

Note: most of these questions should be answered during the informed consent process

Question	YES	NO	Additional Information
1. Safety			
a. Are there safety risks associated with this experimental treatment?			
b. Could my condition or my health get worse after this experimental treatment?			
c. If so, can you describe the possible risks associated with this experimental treatment?			
2. Possible benefits			
a. Can you describe the possible specific benefits of this experimental treatment?			
b. Can you describe the maximum level of recovery I might see after this treatment?			
c. Can you describe how any potential benefit will be measured?			
3. Clinical trial protocol			
a. Is this study registered as a clinical trial with an appropriate qualified regulatory body?			
b. Can you describe what clinical trial phase this particular human study falls within (Phase 1, 2, or 3) and what is the emphasis of study for this phase of the trial program?			
c. Is there a control group in this study?			
d. Could I be randomly assigned to the control group?			
e. Can you tell me how long I will be assessed for any change in outcome?			
f. Will I be blinded to whether I have received the experimental or control treatment?			
g. Will the investigators and examiners be blind to what treatment I have received?			

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Question	YES	NO	Additional Information
4. Payments and costs			
a. Do I have to pay for this treatment?			
b. As a possible participant, are there other costs I have to pay to be involved in this study?			
c. Will my expenses associated with participating in this study be paid (e.g. travel to center for follow-up assessment)?			
5. Participation in Other Trials			
a. Will my participation in this clinical trial limit my participation in other SCI clinical trials?			
b. If I am assigned to the control group and the experimental treatment is subsequently shown to be an effective therapy for my type of SCI by this clinical trial program, will I be eligible to receive this treatment later?			
6. Preclinical or prior clinical evidence			
a. Can you describe the preclinical or prior clinical evidence that indicates this experimental treatment might be beneficial?			
b. Have these findings been independently confirmed by other researchers?			
c. Are there any dissenting opinions and do these arguments have some validity for not going forward with this treatment?			
7. Independent assessment of the treatment and investigator			
a. Can you provide me several names of scientists and clinicians (not involved with this study) who can provide me independent advice about this treatment and your reputation?			

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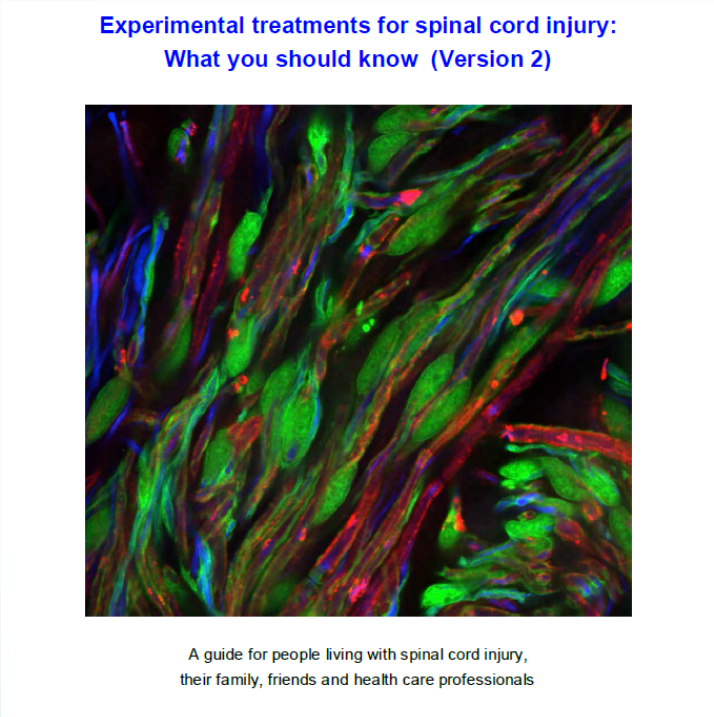
Resources

ClinicalTrials.gov

www.ClinicalTrials.gov

National Library of Medicine &
National Institutes of Health



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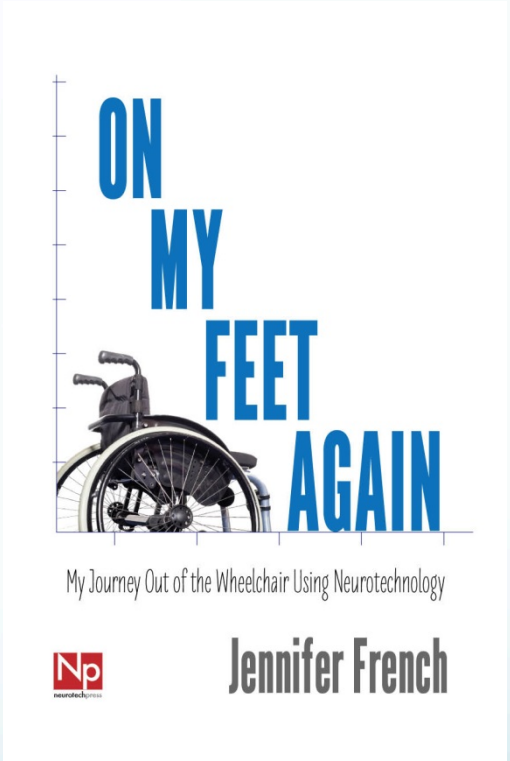

www.OnMyFeetAgain.org

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