Clinical Translation of Absorbable Biopolymers and Hydrogels for Acute Spinal Cord Injury

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Clinical Outlooks for Regenerative Medicine

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Robert S. Langer, Sc.D.

- David H. Koch Institute Professor at MIT
- 1,100 articles; 760 patents issued and pending
- 2006 US National Medal of Science
- 2008 Millenium Prize

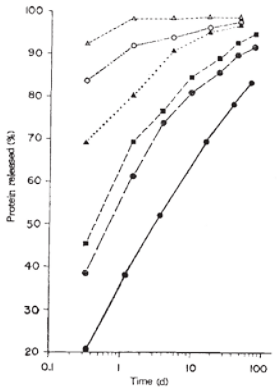
Polymers for the sustained release of proteins and other macromolecules

Table 1 Host response to corneal polymer gel implants

Polymer	No. of tests	Inflammation* None	Mild	Significant
Polyacrylamide, 20%	10	20%	30%	50%
Polyvinylpyrrolidone, 20%	4	0	0	100%
Polyvinylalcohol (unwashed, 1%, 5%, 10%)	20	15%	70%	15%
Polyvinylalcohol (washed, 10%)	6	67%	33%	0
Hydron-S (with and without water in the polymer casting solution)	15	100%	0	0
Ethylene–vinyl acetate copolymer (unwashed)	20	40%	60%	0
Ethylene–vinyl acetate copolymer (washed)	20	100%	0	0

*The criteria were oedema, white cells and neovascularisation as observed through a stereomicroscope. A response was judged to be mild if any one of the three characteristics was detected, and significant if their presence was enough to cause corneal opacity.

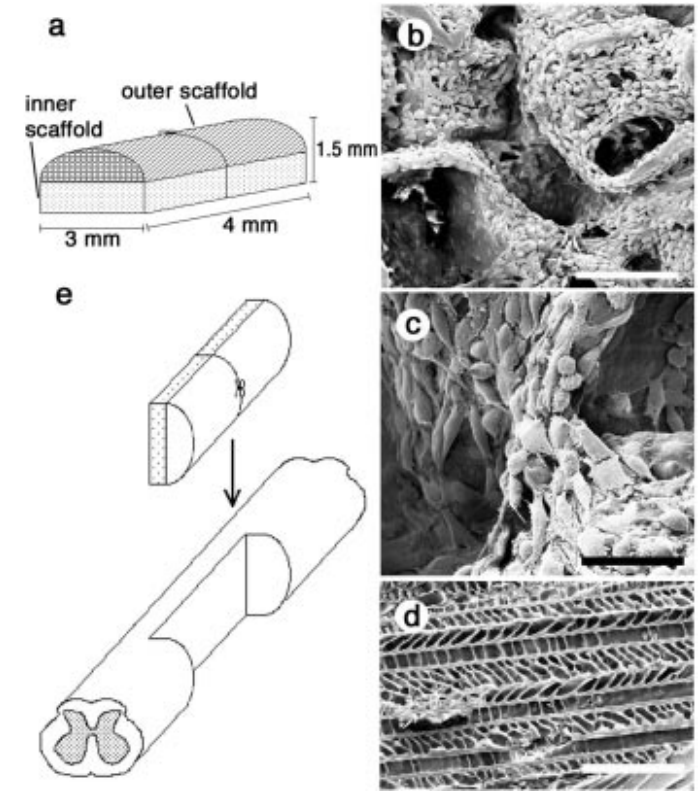
Fig. 1 Release of soybean trypsin inhibitor from polyvinylalcohol. The percentage of polymer in the casting solution was varied. Protein concentration in all casting solutions was 12 mg ml^{-1}. Release characteristics were studied by incubating polymer pellets in small test tubes with lactated Ringer solution at 37 °C. Periodically, pellets were removed to new tubes containing fresh Ringer solution. Protein release from the pellets was assayed by the Lowry method*. Polyvinylalcohol; △, 1.2%; ○, 4.8%; ▲, 6%; ■, 10%; circle and cross, 20%; ●, 10% sandwich.

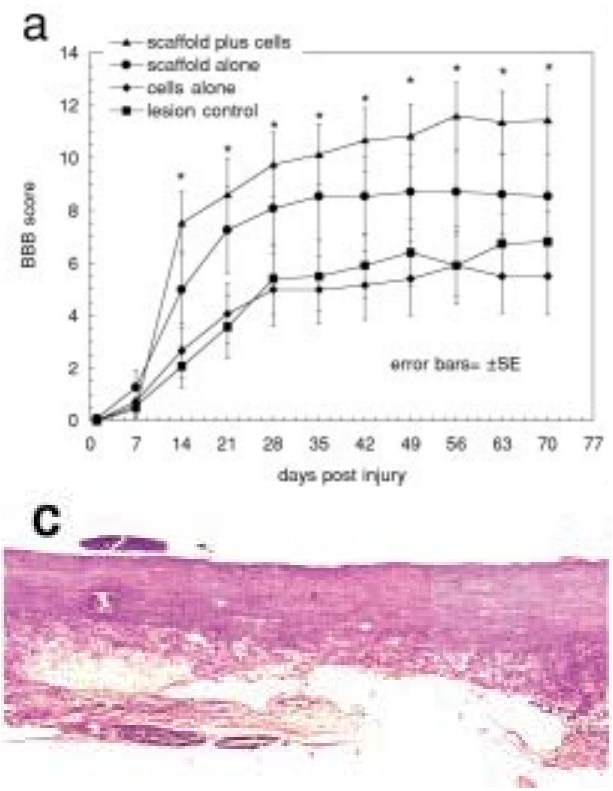


Polymer Scaffold Proof of Concept in SCI

Functional recovery following traumatic spinal cord injury mediated by a unique polymer scaffold seeded with neural stem cells

Yang D. Teng*†, Erin B. Lavik†‡, Xianlu Qu*, Kook I. Park*, Jitka Ourednik*, David Zurakowski§, Robert Langer¶IJ**, and Evan Y. Snyder*IJ** PNAS March 5, 2002

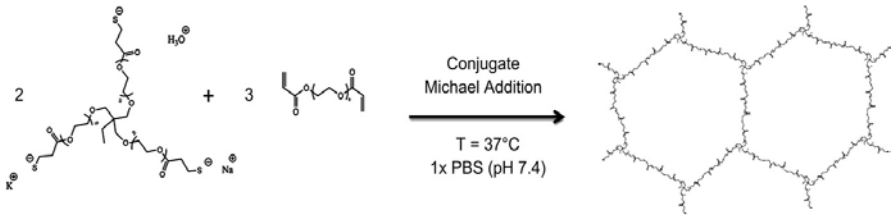




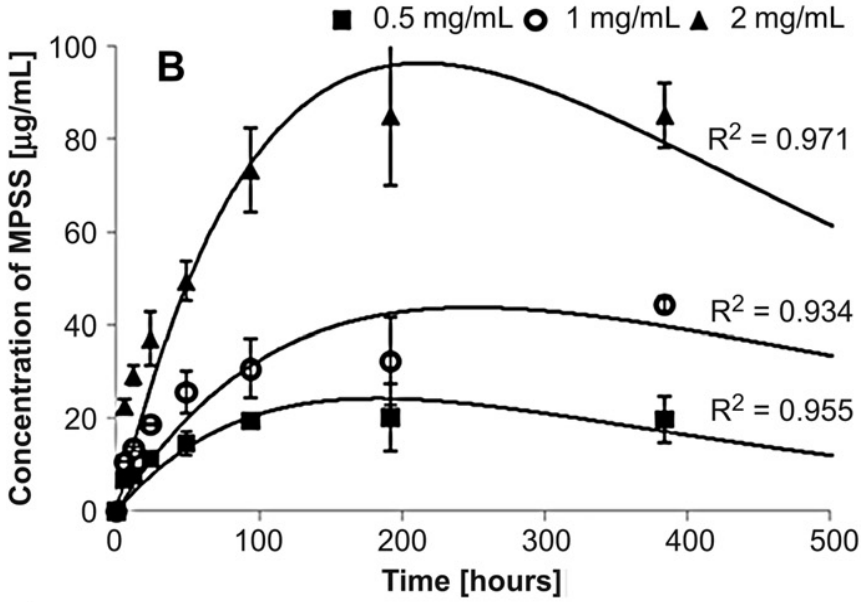
Rationale for Polymer Scaffolds in Acute SCI

- PLGA is widely used clinically; PLL is not neurotoxic – excellent biocompatibility
- Numerous publications from multiple groups show proof-of-concept efficacy for biopolymers in SCI
- Proof of concept in rat hemisection SCI

Hydrogel for Controlled Local Drug Delivery



Formation of a crosslinked network under physiologic conditions.



Injectable hydrogel for sustained release of methylprednisolone sodium succinate (Pritchard et al., 2011, Biomaterials)

- Thiol-acrylate poly(ethylene glycol) (PEG)-based hydrogel
- Meets a unique combination of design requirements
- No volume increase during equilibration
- Resilient mechanical properties that match human tissues of interest
- Mesh size adequate for diffusion-controlled release of hydrophilic small molecule drugs
- Tunable gelation kinetics
- Ability to functionalize the material with biological motifs to guide cellular interactions.

InVivo Founded in 2005

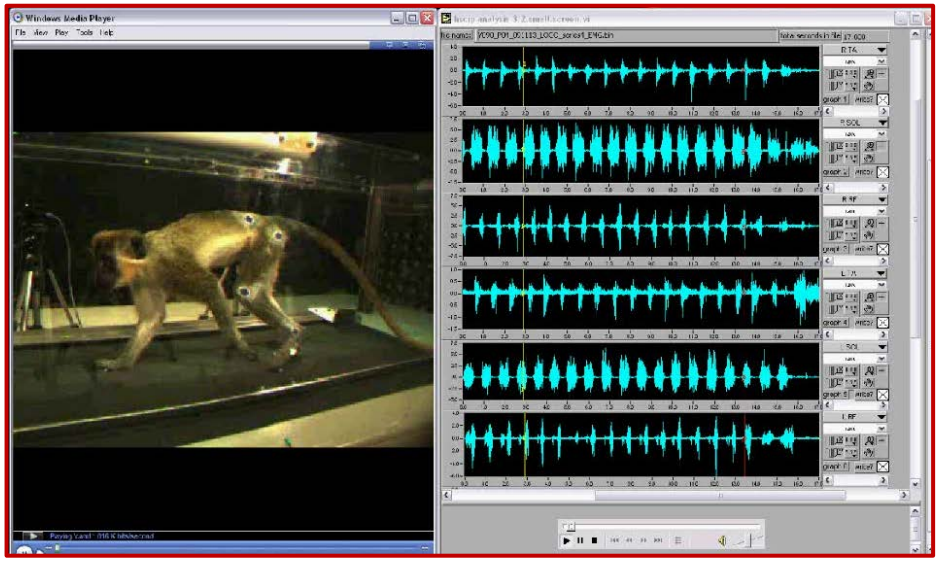
- Frank Reynolds
- Founder, CEO, CFO
- Former Director of Global Business Development at Siemens Corporation
- Suffered an SCI in 1992
- Met Dr. Langer while earning an MBA in the Sloan Fellows Program at MIT
- Took InVivo public in 2010

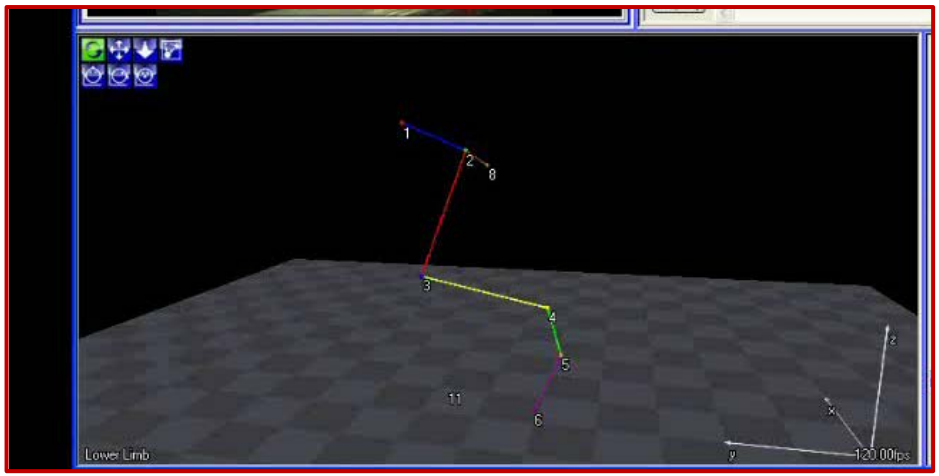
InVivo Therapeutics Mission Statement

Provide society with superior neurological products and services by delivering novel approaches to the treatment of disease that will improve the quality of life and satisfy the needs of those who live with spinal cord injury.

Efficacy & Safety in Nonhuman Primates

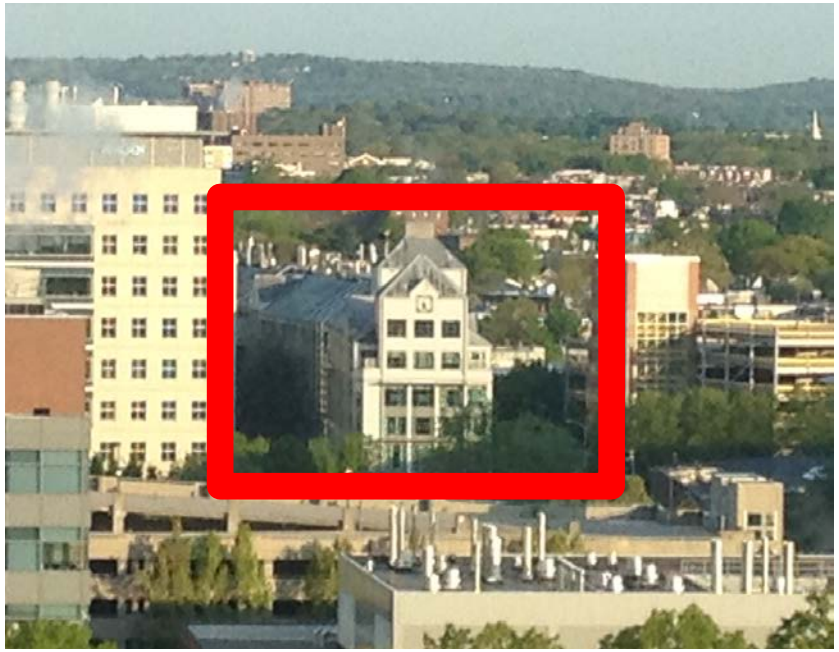
- Pilot study in 2008 (published in J. Neurosci. Methods, 2010)
- Two additional studies in 2009, 2011
  - T9-T10 lateral hemisection
  - Evaluation of both PLGA-PLL scaffold and hydrogel + MPSS
  - Rigorous locomotor evaluation including behavior, wireless EMG and kinematic analyses
  - All assessments were blinded
  - No scaffold-related adverse events
  - Data analysis of 2011 study in progress





Translation to Clinical Trials

- IDE submitted in July 2011
- Met with FDA in April 2012
  - Anticipate HUD/HDE clinical pathway
- Evaluation of PLGA-PLL scaffold and hydrogel + MPSS in rat contusion model underway
- Moving to new facility to speed polymer development & testing and to add GMP manufacturing capability



INVIVO THERAPEUTICS

THANK YOU