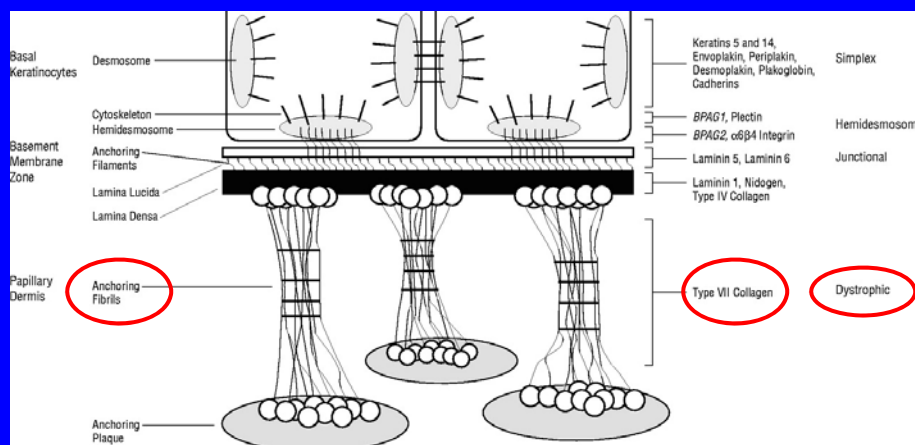


Transplantation for Extracellular Matrix Disorders: Problems, Premises, and Promises

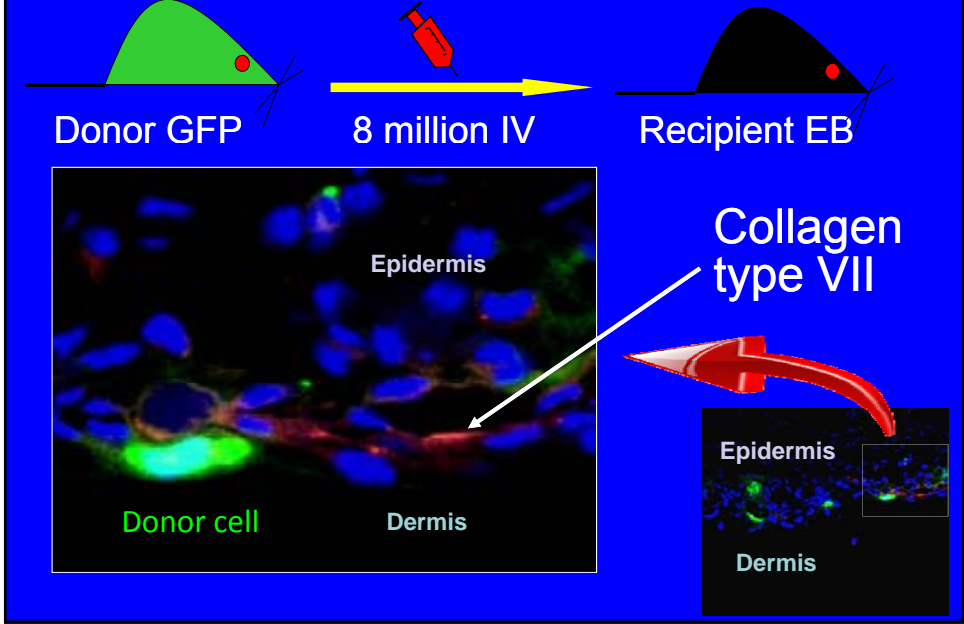
Jakub Tolar, MD, PhD
Blood and Marrow Transplantation
University of Minnesota

Hypothesis

Systemically administered stem cells
correct collagen type VII deficiency.



Proof of Concept: Preclinical Model



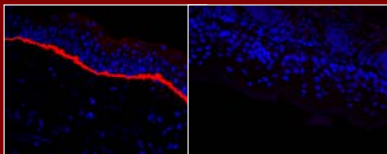
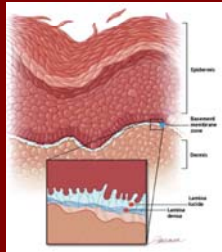
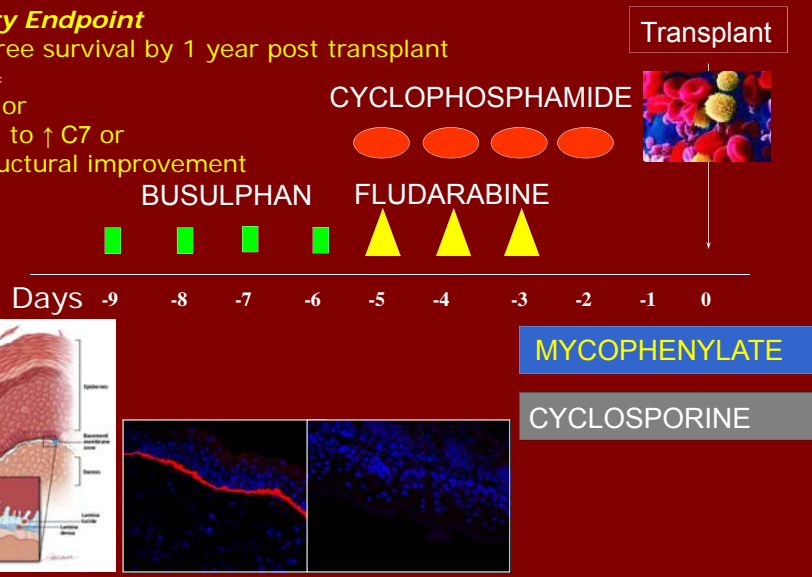
Clinical Trial

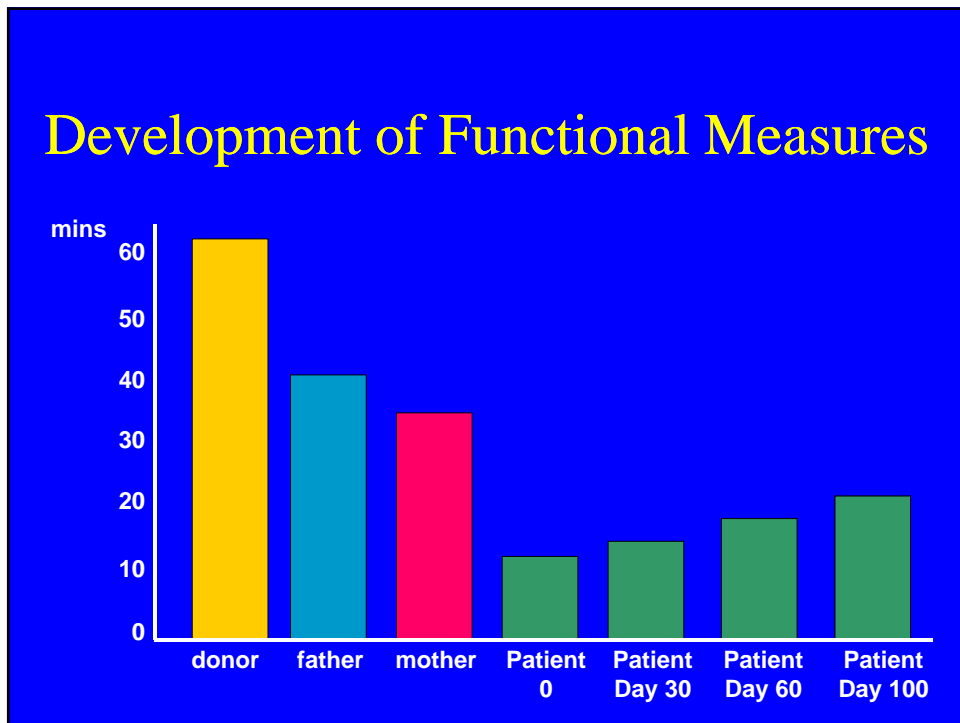
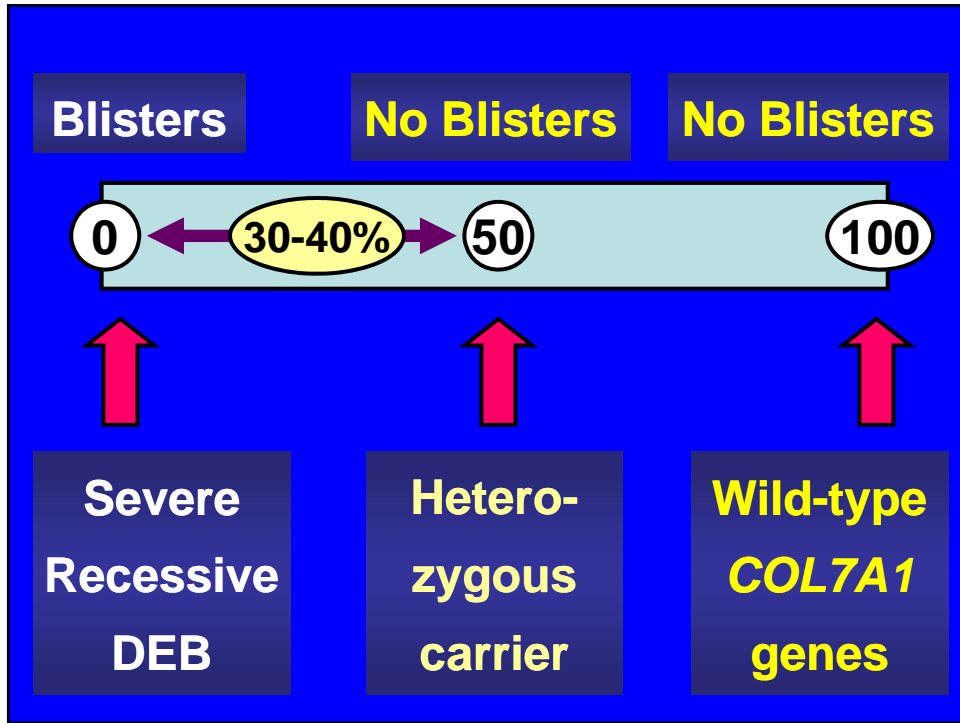
Primary Endpoint

Event-free survival by 1 year post transplant

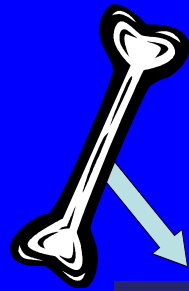
Event =

- death or
- failure to \uparrow C7 or
- no structural improvement

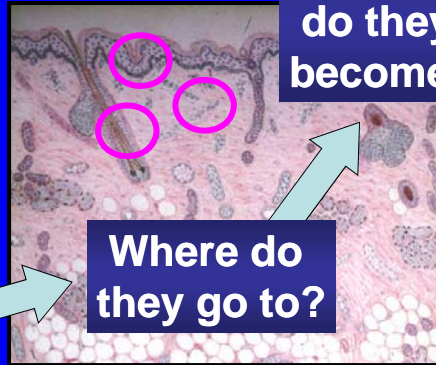




Which Specific Bone Marrow-derived Cells Benefit the Skin?



Which cells?



What do they become?

Where do they go to?

Patient: XX Female

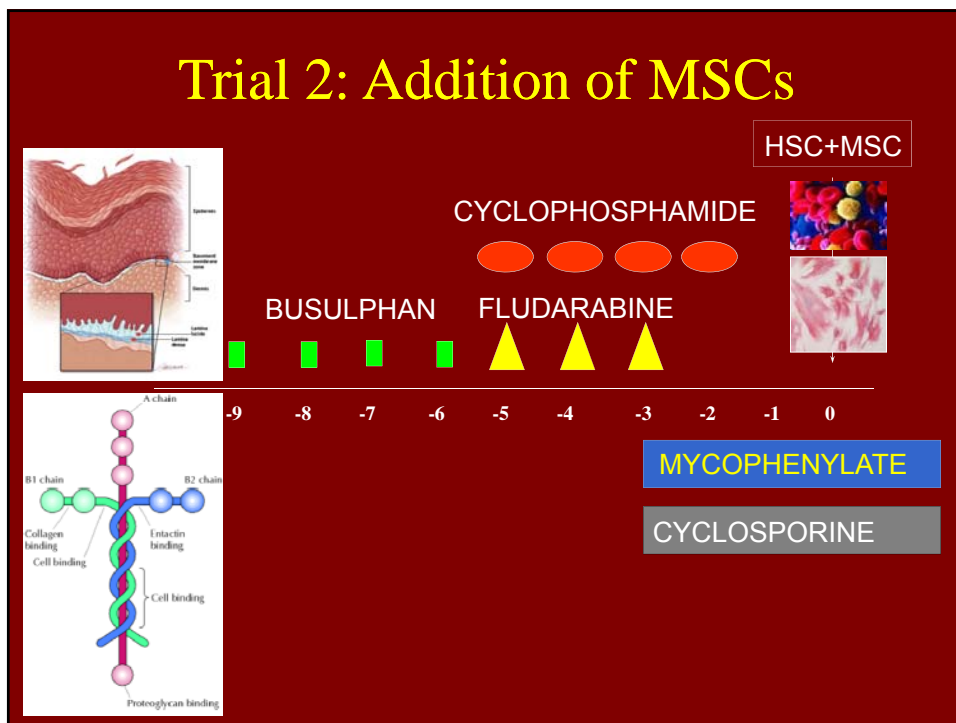
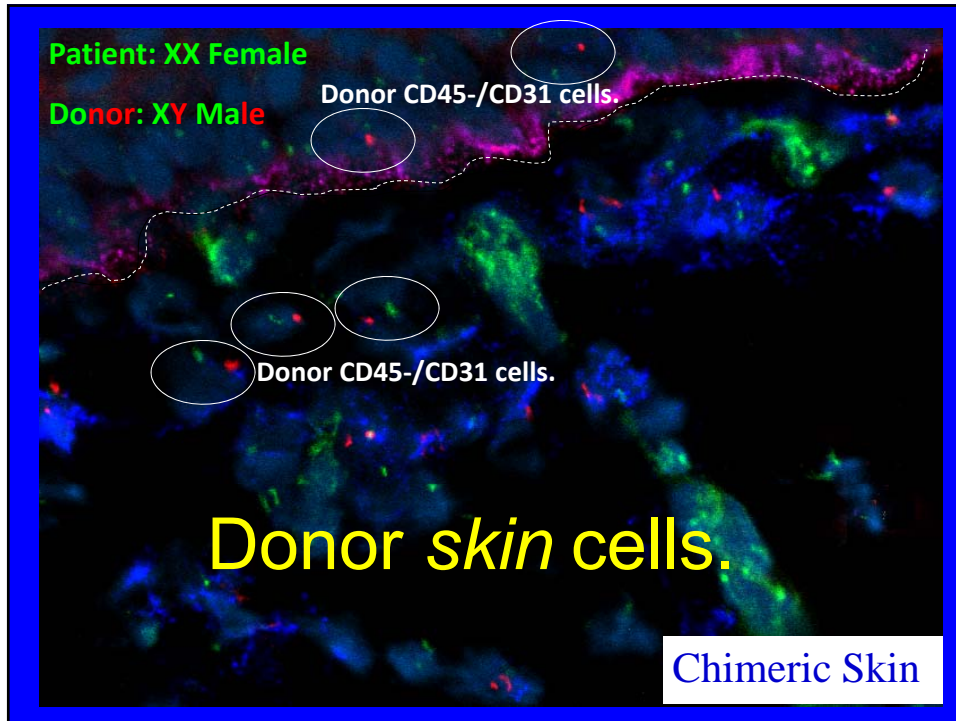
Donor: XY Male

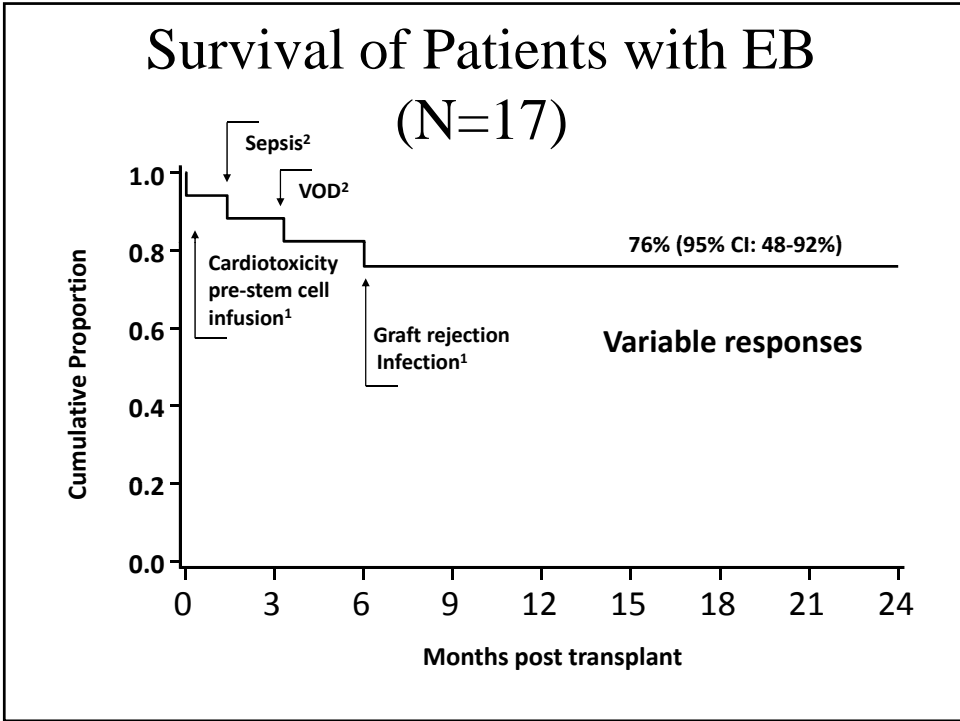
Donor-derived CD45+ cells.

Host-derived CD31+ cells

Donor blood cells.

Chimeric Skin





Hurdles

1. No funding for POC→family support
2. Uncertainty of mechanism
3. Some children died waiting in a queue
4. Insurance→exp tx as a standard HCT
5. Investigator-

-clinician conflict;
External
Advisory
Panel

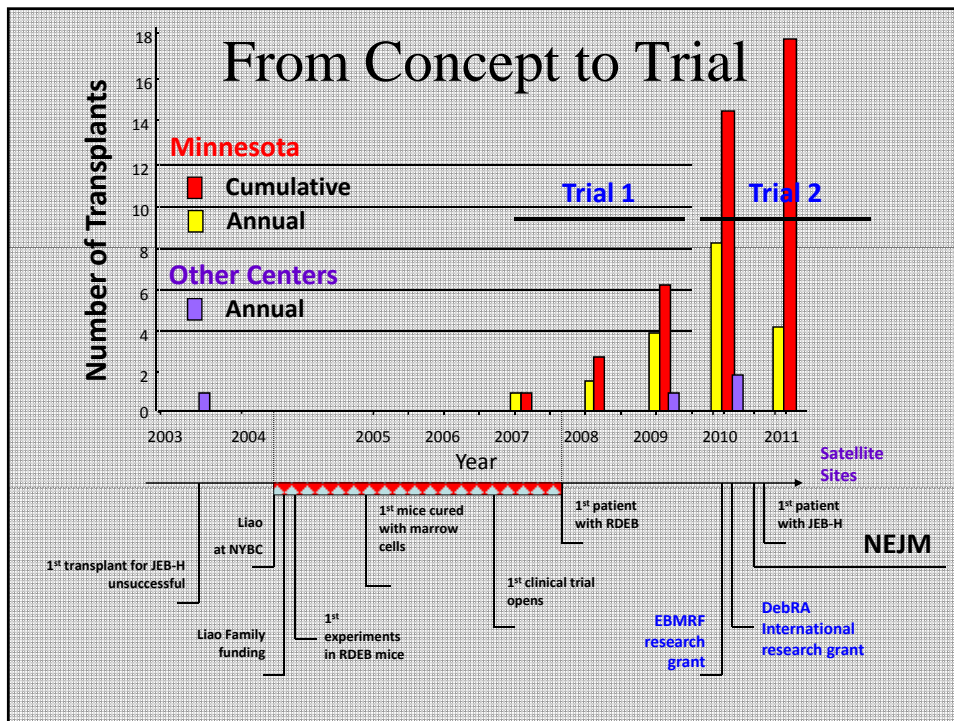


Experts in Epidermolysis Bullosa

John A. McGrath, MD
Alain Hovnanian, MD
Hiroshi Shimizu, MD

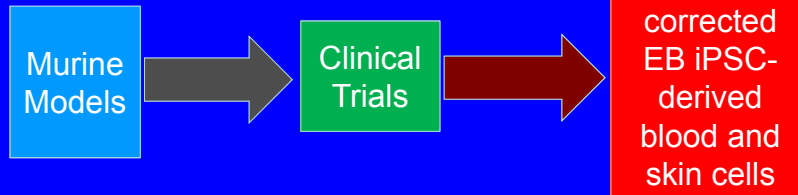
Hype, Harm, and Hope

1. Decrease suffering or prolong misery?
2. Treat infants with severe phenotype or adults with mild form of the same ds?
3. How much preliminary data is enough to substantiate clinical trial?
4. When is exp tx no longer experimental?
5. Vulnerable population c unknown risks?
6. Wait for alternative tx? How long?

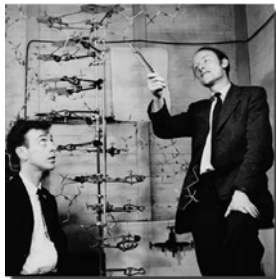


Lessons Learned

1. Need funds to shorten the start-up phase
2. Need proof-of-concept, mechanisms
3. Need objective oversight, EAP
4. Need to collect data in the same way
5. Need family support group



- University of Minnesota
 - John E. Wagner
 - Bruce R. Blazar
 - Mark J. Osborn
 - Maria Hordinsky
 - Ana Junqueira Bertin
 - Megan J. Riddle
- St. John's, London, UK
 - John A. McGrath
- Osaka University, Japan
 - Katsuto Tamai
- Shriners, Portland, OR
 - Douglas R. Keene
- USC, Los Angeles, CA
 - David Woodley
 - Mei Chen
- INSERM, Paris, France
 - Alain Hovnanian



“New ideas need
new facts.”



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