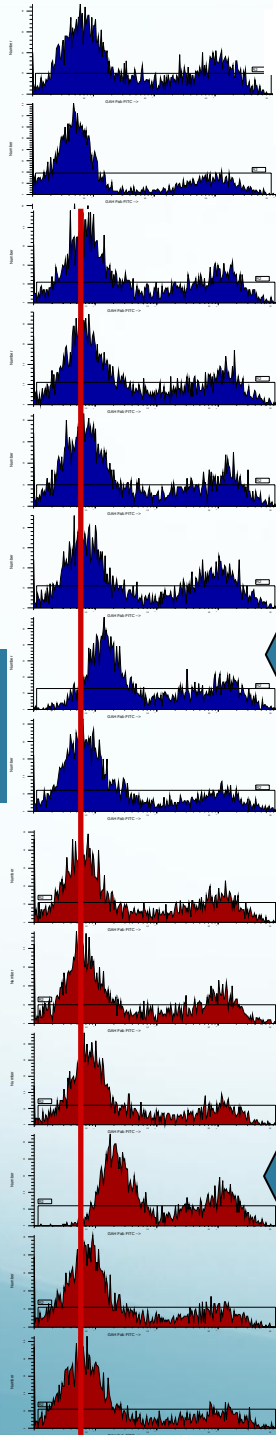


Pos Control

Low anti-allo IgM response

B266

Neg Control



Anti-Allo
IgM FACS

Day 0

Day 4

Day 7

Day 14

Day 21

Day 30

Day 41

Day 45

Day 48

Day 55

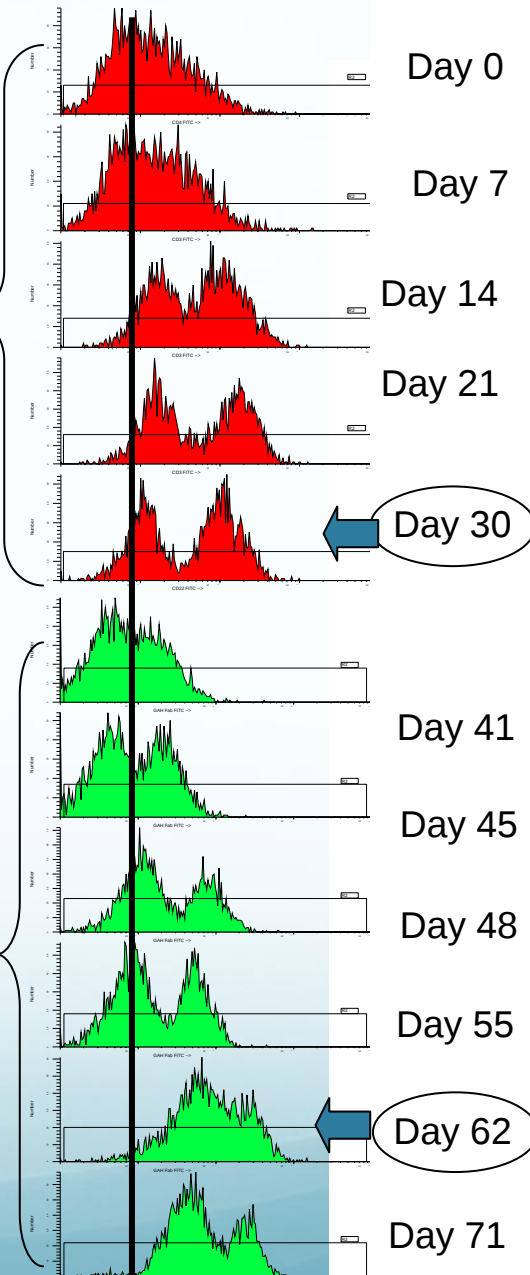
Day 62

Day 71

I set of Skin Grafts

II set of Skin Grafts

Page 129



Day 0

Day 7

Day 14

Day 21

Day 30

Day 41

Day 45

Day 48

Day 55

Day 62

Day 71

Anti-Allo
IgG FACS

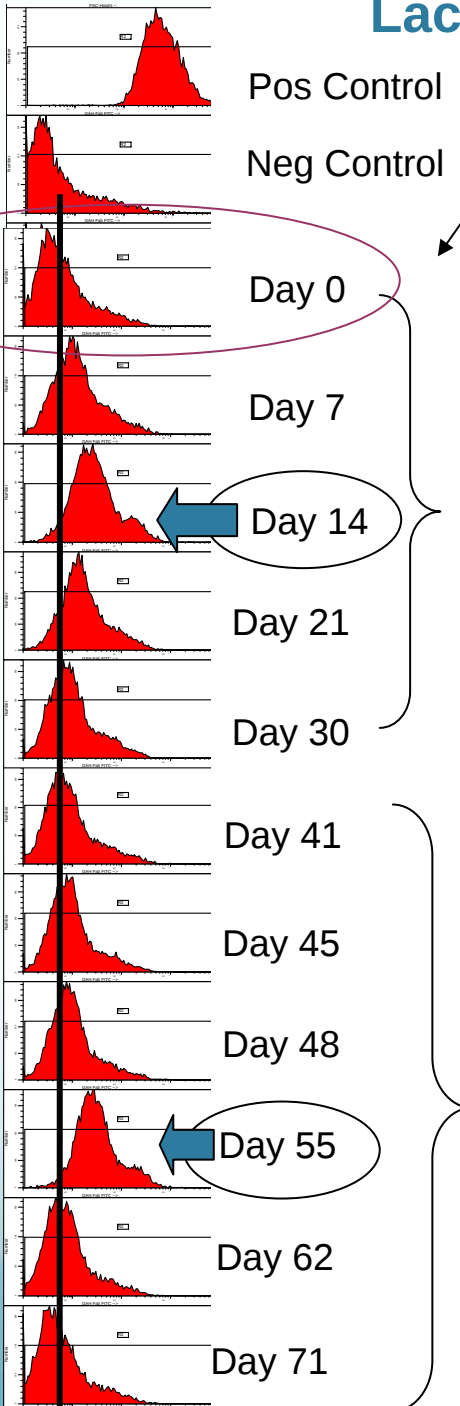
B266

Lack of Anti-non-Gal Ab before TX

Presence of Anti-non-Gal Ab after TX

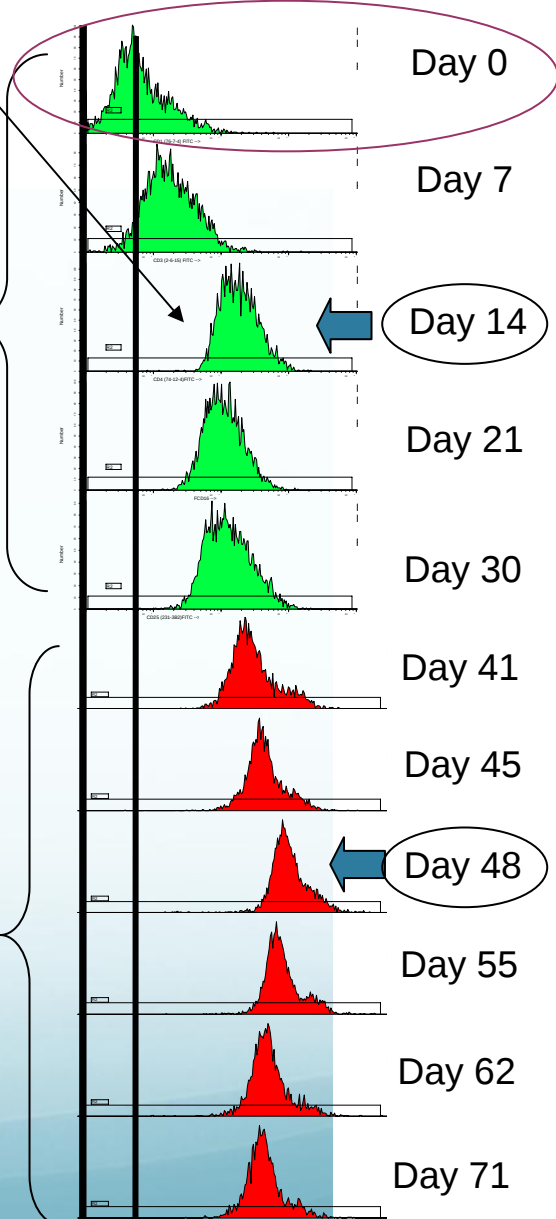
Anti-non-Gal IgM FACS (Gal KO cells)

Anti-non-Gal IgG FACS (Gal KO cells)



I set of Skin Grafts

II set of Skin Grafts



Day 0

Day 7

Day 14

Day 21

Day 30

Day 41

Day 45

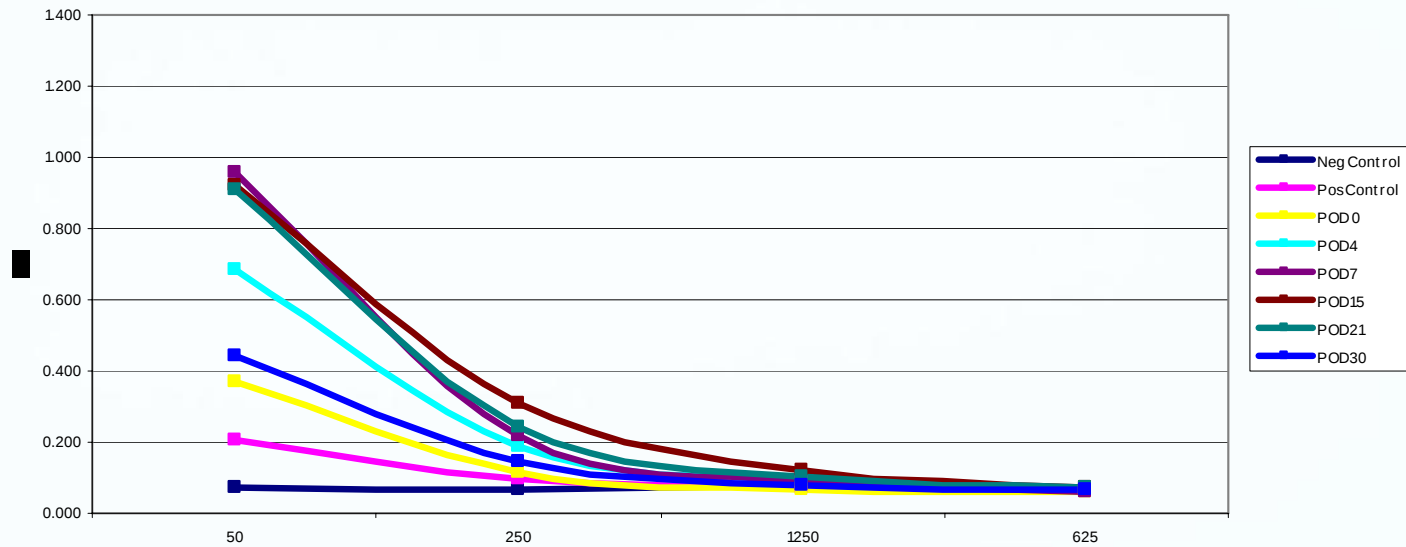
Day 48

Day 55

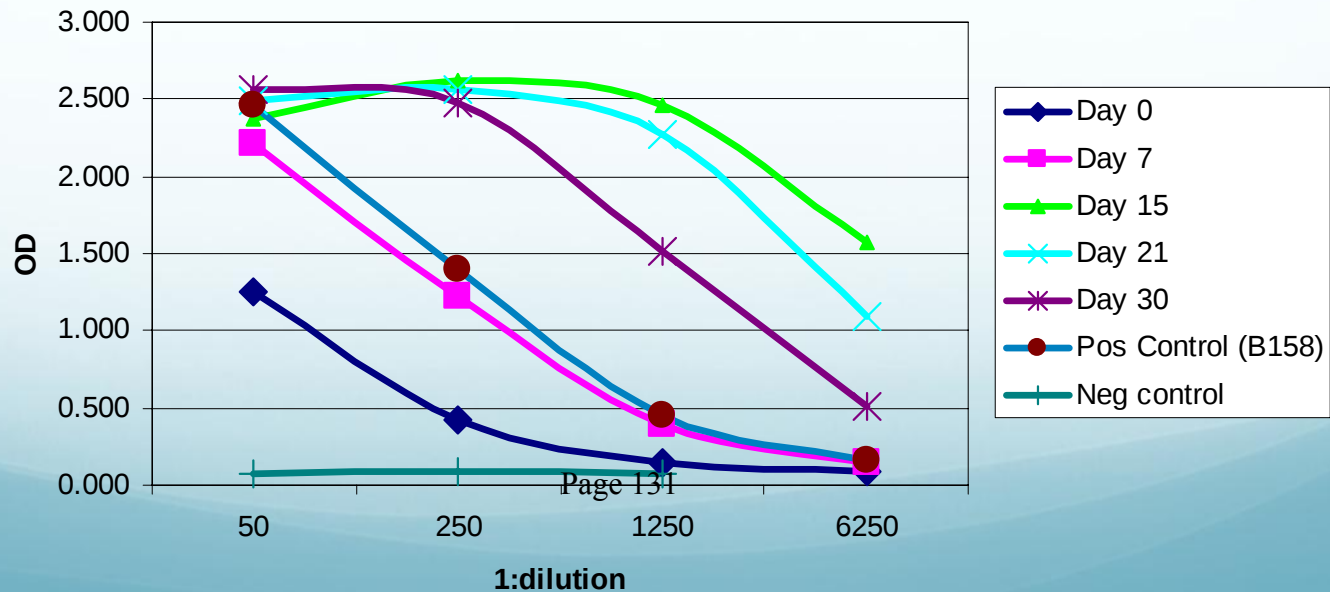
Day 62

Day 71

B266 Anti-Gal IgM ELISA (s/p 1st set of grafts)

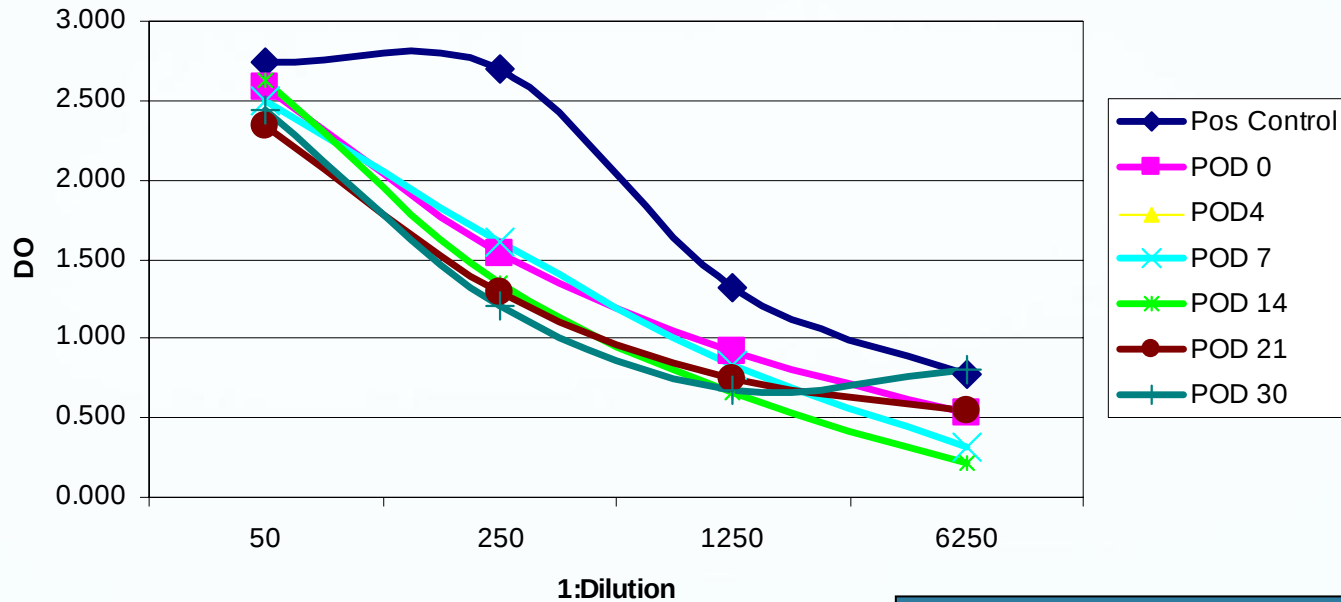


B266 Anti-Gal IgG ELISA (s/p 1st set of grafts)



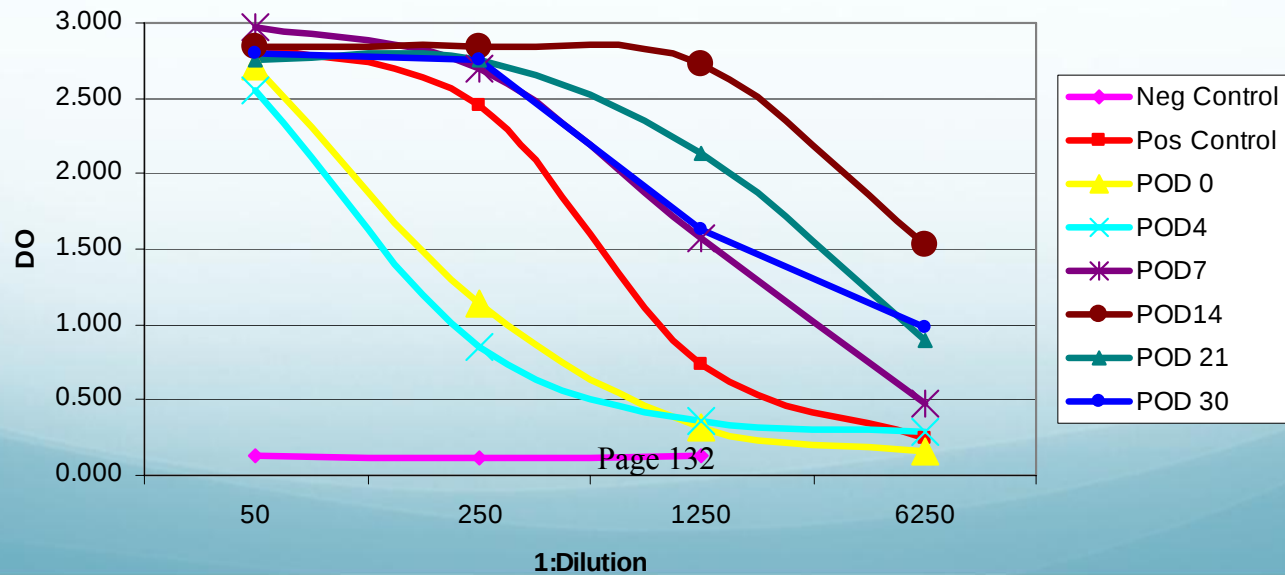
B268 Anti-Gal IgG ELISA

GalT-KO skin graft only



B269 Anti-Gal IgG ELISA

GalT + skin graft only



Experimental Observations

1st graft

2nd graft

GalT +

**Preformed
Ab
Response**



White Graft

GalT-KO

**No
preformed
Ab**



Sensitization



Post regrafting

Allo

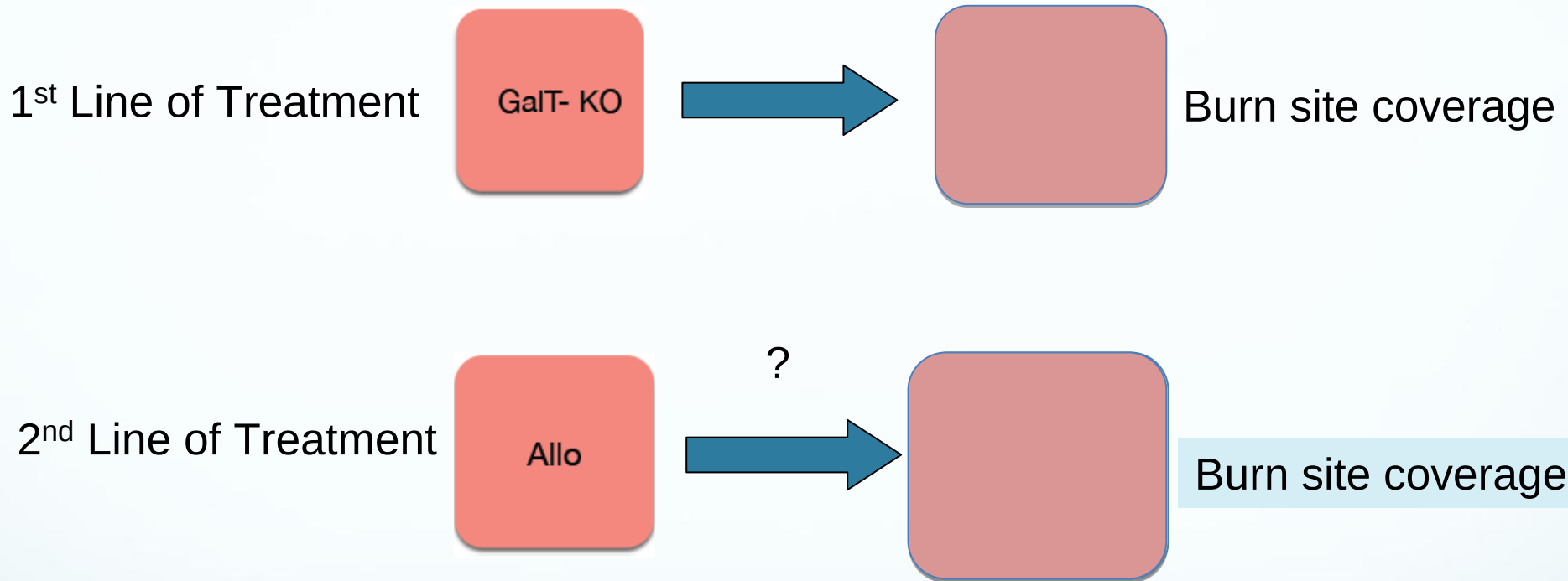
**No
preformed
Ab**



Sensitization



Possible Clinical Treatment Strategy (currently being studied)



Day 0

~ Day 10

Xeno

Summary

- GalT-KO skin xenografts exhibit comparable survival to allografts (Xenografts = Allografts)
- GalT-positive skin is rejected in a Hyperacute fashion, presumably due to preformed antibodies (White Graft)
- No differences in survival of fresh vs frozen GalT-KO skin was observed following re-transplant

Summary

- GalT-KO skin can be used as a **temporary** skin substitute in severe burns in lieu of Allografts or Biomaterials
- Current studies: Can **Xeno** skin be used as a **first line** skin substitute to allow for subsequent successful use of Allografts and prolong wound coverage?

Acknowledgments



Transplantation Biology Research Center (TBRC)

- Curtis L. Cetrulo Jr, M.D.
- Radbeh Torabi
- Fan Liang, M.D.
- David H. Sachs, M.D.

- TBRC Staff

Harvard Plastic Surgery

- Jay Austen, M.D.
- Michael Yaremchuk, M.D.
- Mark Randolph, M.S.

DOD Grant: W81XWH-09-1-0419



Subcommittee on Research Animal Care
Massachusetts General Hospital
149 13th Street
Charlestown, MA 02129
Tel: (617) 726-3495
Fax: (617) 724-2475

Notification of IACUC Review

Protocol #: 2009N000062 / 6

Date: March 31, 2010

To: David H. Sachs, MD
MGH, Surgery
CNY 149 9019

From: Diane McCabe, IACUC Manager
Research Management

Title of Protocol:	Genetically-modified Porcine Skin Grafts for Treatment of Severe Burn Injuries (Swine)
Sponsor:	ARMY-DOD
Species / Number:	Swine / 264
Annual Review #:	1
Approval Date:	03/31/2010
Expiration Date:	05/20/2012
Annual Report Due:	03/31/2011

This Annual Report has been reviewed and approved by the MGH Subcommittee on Research Animal Care (SRAC) – OLAW Assurance # A3596-01. The protocol as submitted and reviewed conforms to the USDA Animal Welfare Act, PHS Policy on Humane Care and Use of Laboratory Animals, the "ILAR Guide for the Care and Use of Laboratory Animals" and other applicable laws and regulations. The protocol is approved for a three-year period, subject to submission of annual reports.

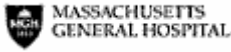
Please note that if a SRAC member had a conflict of interest with regard to the review of this protocol, that member left the room during the discussion and the vote on this project.

As Principal Investigator you are responsible for the following:

1. Compliance with MGH SRAC/CCM Policies governing the care and use of animals.
2. Submission in writing of changes to this project for SRAC review and approval prior to initiation of the change.
3. Submission of annual progress reports to the SRAC for review and approval.
4. Submission of a copy of this approval to CCM when ordering animals.

The SRAC can and will terminate projects that are not in compliance with these requirements. Direct questions, correspondence and forms to Diane McCabe, the IACUC Manager, Tel: (617) 724-9718, Fax: (617) 724-2475.





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Fax: (617) 724-2475

Notification of IACUC Review

Protocol #: 2009N000063 / 1

Date: August 25, 2009

To: David H. Sachs, MD
MGH, Surgery
CNY 149 9019

From: Diane McCabe, IACUC Manager
Rese arch Management

Title of Protocol: Genetically-modified Porcine Skin Grafts for Treatment of Severe Burn Injuries (Baboons)

Sponsor: ARMY-DOD

Species / Number: Monkeys - Baboon / 137

Approval Date: 07/15/2009

Effective Date: 08/25/2009

Expiration Date: 07/15/2012

Annual Report Due: 07/15/2010

This Protocol has been reviewed and approved by the MGH Subcommittee on Research Animal Care (SRAC) – OLAW Assurance # A3596-01. The protocol as submitted and reviewed conforms to the USDA Animal Welfare Act, PHS Policy on Humane Care and Use of Laboratory Animals, the “ILAR Guide for the Care and Use of Laboratory Animals” and other applicable laws and regulations. The protocol is approved for a three-year period, subject to submission of annual reports.

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