HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

Long-term rejection free renal allograft survival with Fc-modified anti-CD154 antibody monotherapy in nonhuman primates.

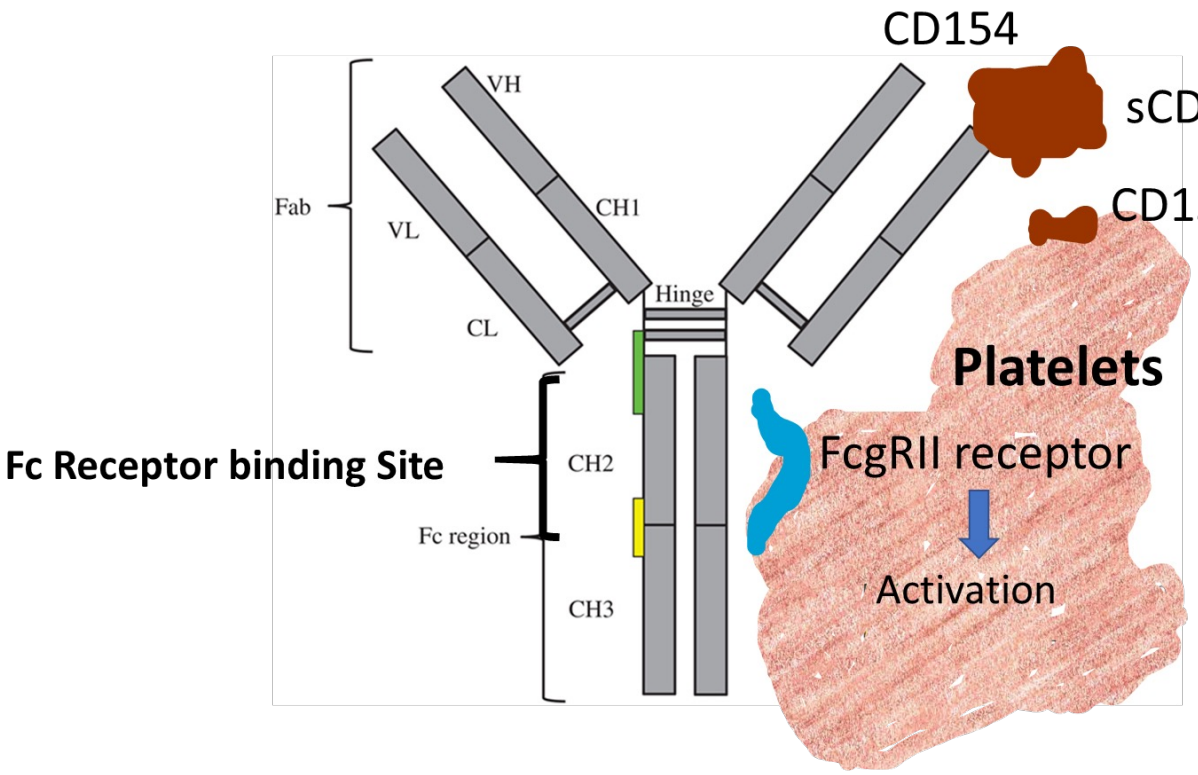
Grace Lassiter, MD

Center for Transplantation Sciences
Massachusetts General Hospital

MASSACHUSETTS
GENERAL HOSPITAL
CENTER FOR
TRANSPLANTATION SCIENCES

Background

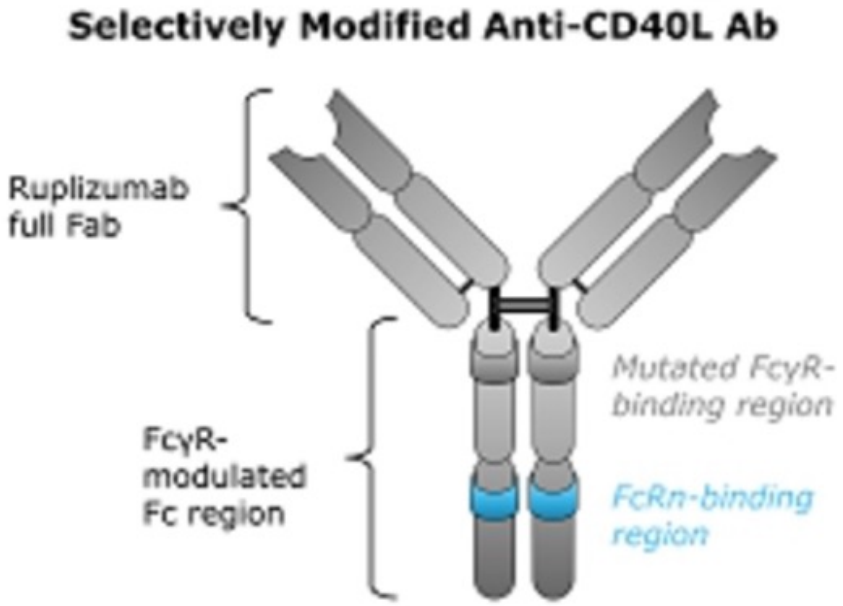
CD154 mAb-sCD154 immune complex can activate platelets



Robles-Carrillo L et al. J Immunol 2010

MASSACHUSETTS GENERAL HOSPITAL
CENTER FOR TRANSPLANTATION SCIENCES

Background



- To date, there has not been a fully human or humanized aCD154 antibody that can effectively prevent transplant rejections, inflammatory conditions or autoimmune conditions with an acceptable level of side effects

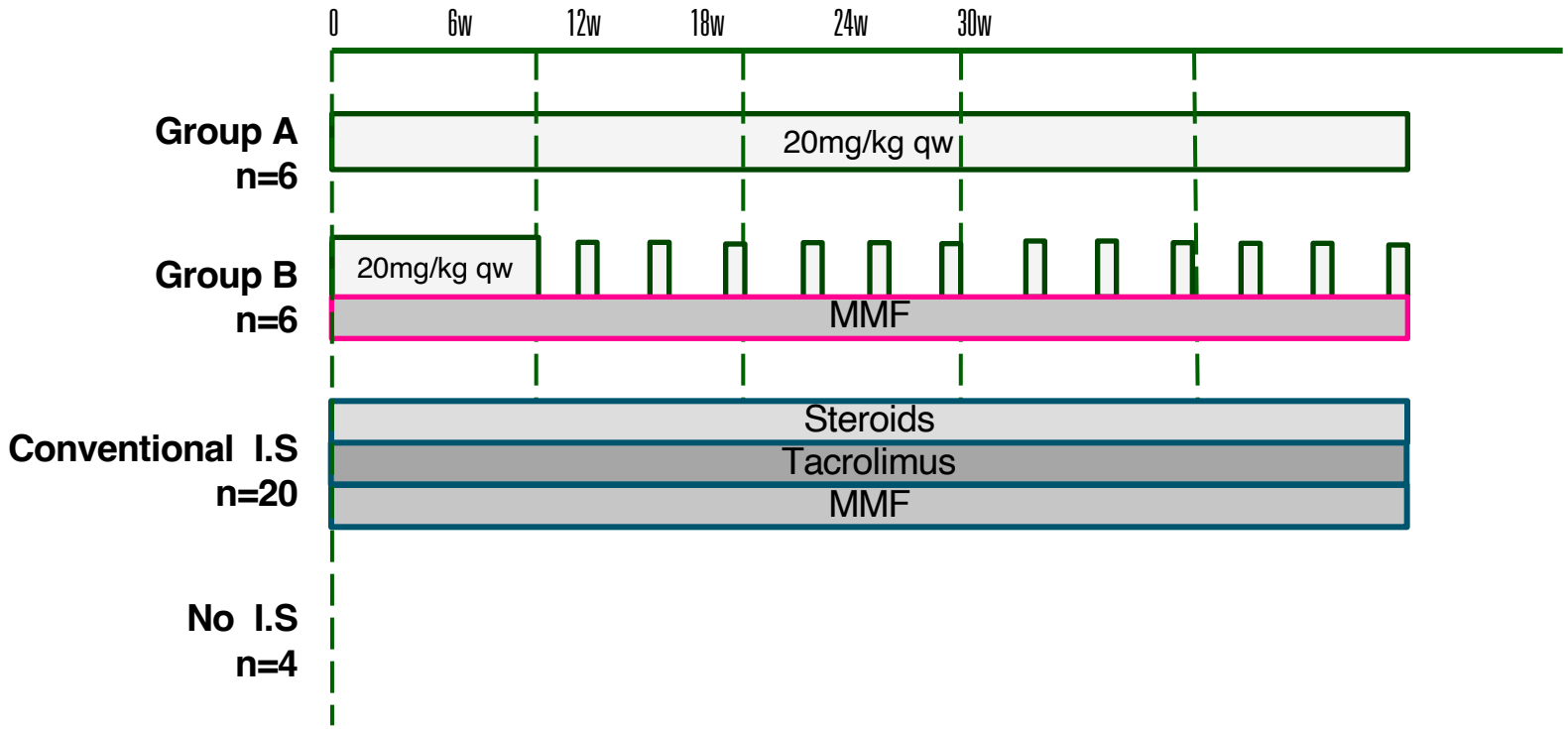
- Tonix Pharmaceuticals Inc. has developed an Fc-Modified aCD154 with low binding to FcγRIIa (TNX-1500)

MASSACHUSETTS GENERAL HOSPITAL
CENTER FOR TRANSPLANTATION SCIENCES

TNX-1500 is an investigational new biologic and has not been approved for any indication

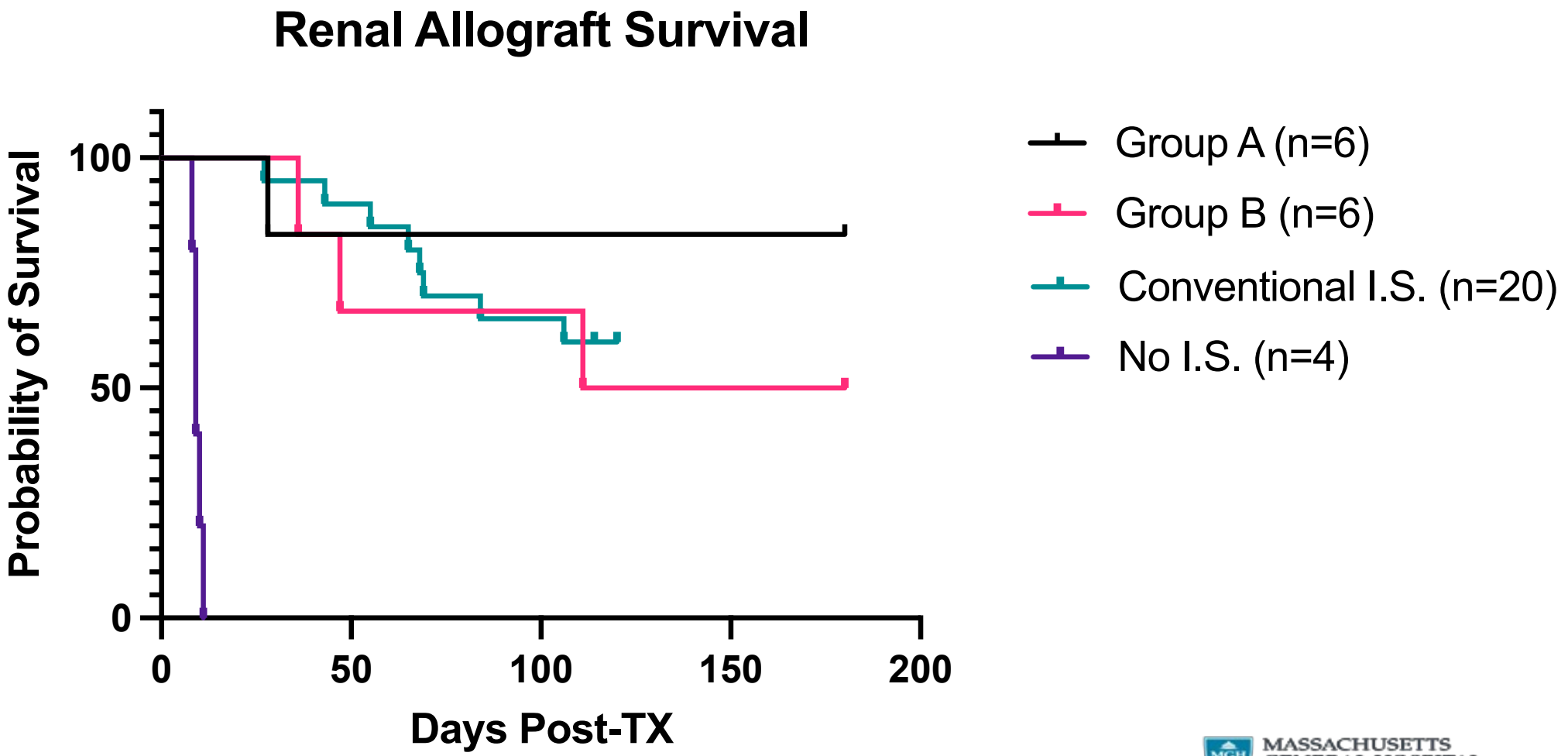
Study Overview

Twelve Transplants have been Completed & Compared with Historical Results



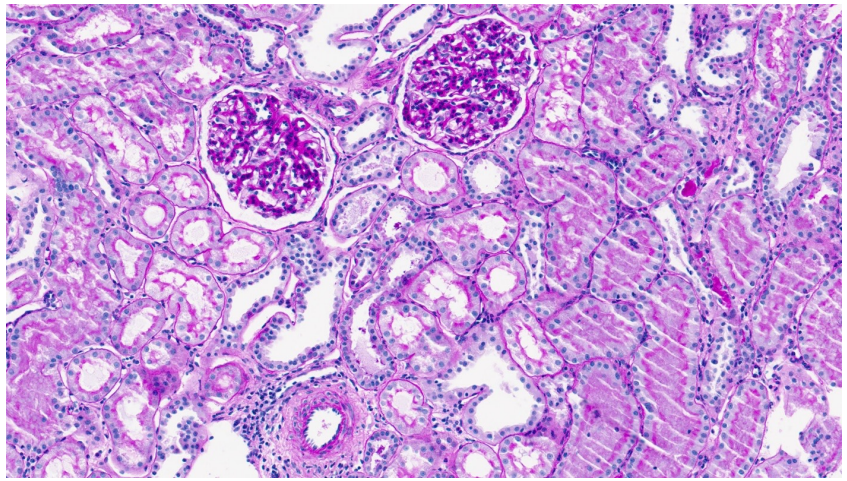
MASSACHUSETTS GENERAL HOSPITAL
CENTER FOR TRANSPLANTATION SCIENCES

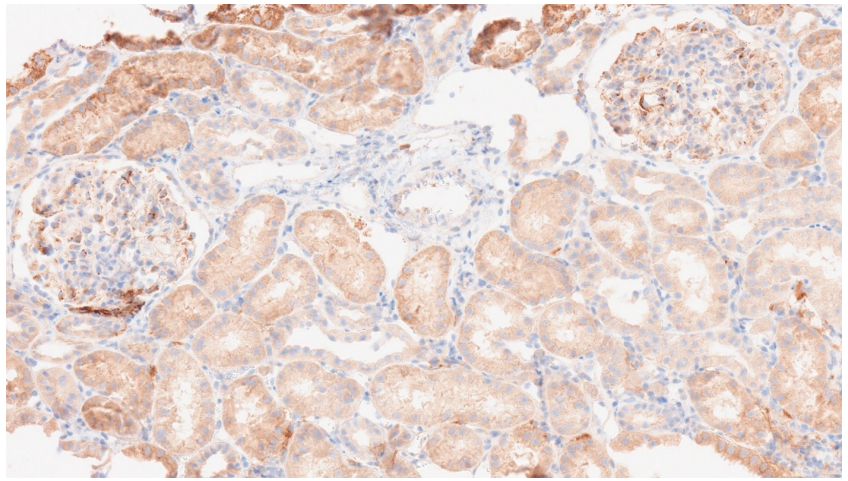
Results: Kaplan-Meier Survival Curve



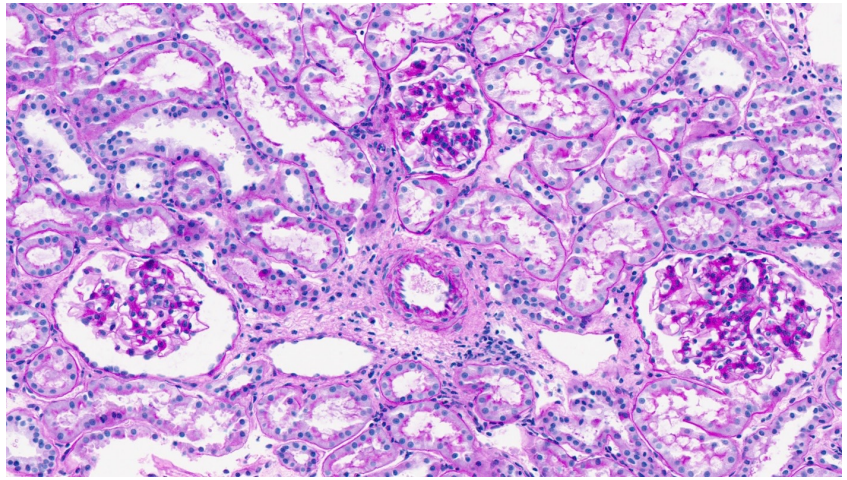
MASSACHUSETTS GENERAL HOSPITAL
CENTER FOR TRANSPLANTATION SCIENCES

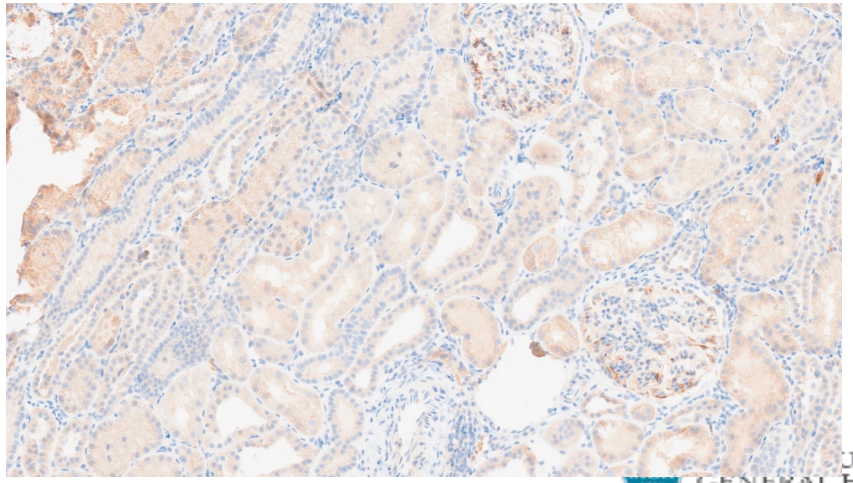
Results: Histopathology





Group A NHP (1) biopsy at day 180 post transplant C4d negative

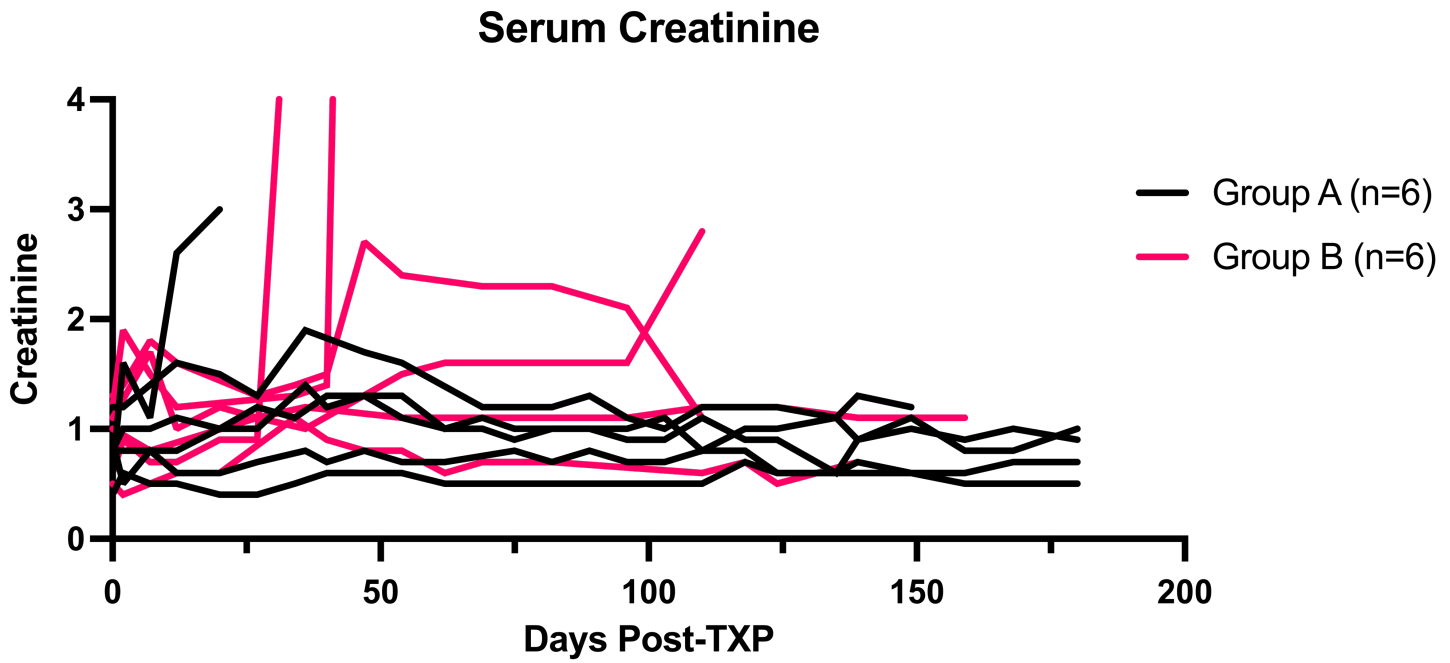




Group A NHP (2) biopsy at day 169 post transplant C4d negative

Results: Adverse Effects

- No increased incidence of thrombosis seen
- No other evidence of end organ damage noted on Necropsy



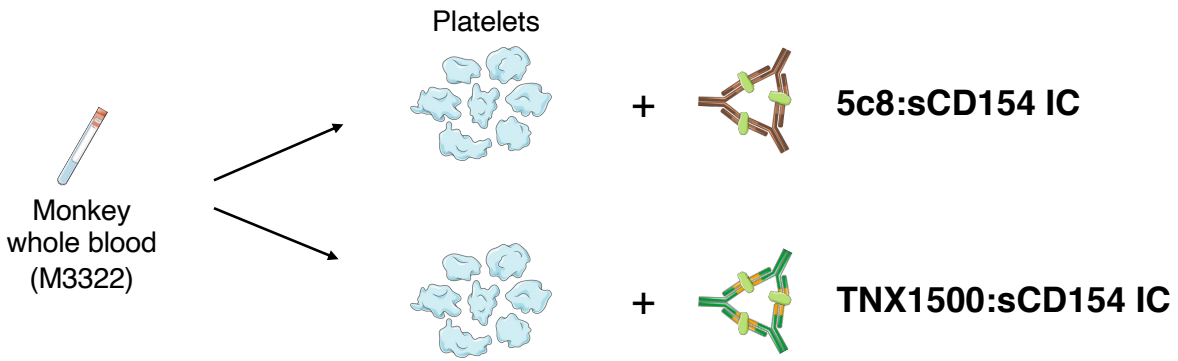
MASSACHUSETTS GENERAL HOSPITAL
CENTER FOR TRANSPLANTATION SCIENCES

Results: Platelet Activation

220829

METHODS

Flow cytometric analysis for platelet activation after anti-CD154:soluble-CD154 immune complex (IC) stimulation



Antibody	Conc. 1	Conc. 2	Conc. 3	Conc. 4	Conc. 5
5c8	500	500	-	-	-
TNX1500	-	-	500	500	-
Soluble CD154	1500	-	1500	-	1500 nM

*Antibody and soluble CD154 were mixed and incubated for 1h at RT.

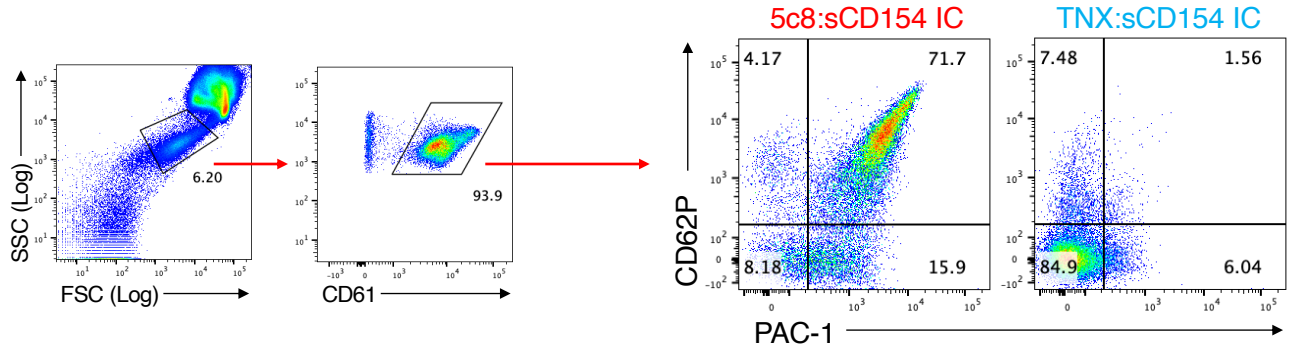
MASSACHUSETTS GENERAL HOSPITAL
CENTER FOR TRANSPLANTATION SCIENCES

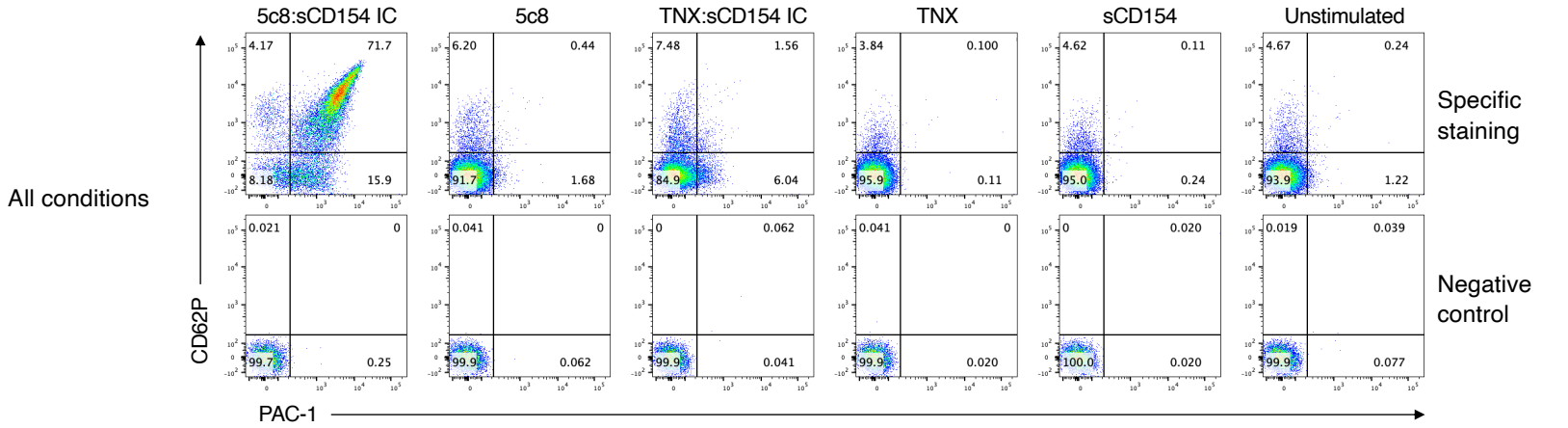
Results: Platelet Activation

220829

RESULTS

Platelet activation status after incubation with CD154:sCD154 IC





MASSACHUSETTS GENERAL HOSPITAL
CENTER FOR TRANSPLANTATION SCIENCES

Conclusion

- Fc-Modified aCD154 is well tolerated and can be an effective alternative to conventional immunosuppression therapy in nonhuman primates.
- TNX-1500 in combination with MMF resulted in an increased rate of graft failure compared to monotherapy
- Optimal dosage remains to be defined

MASSACHUSETTS GENERAL HOSPITAL
CENTER FOR TRANSPLANTATION SCIENCES

Questions?

Special Thanks to these wonderful people

Takayuki Hirose
Ryo Otsuka
Ahmad Karadagi
Toshi Tomosugi
Kohei Kinoshita
Abbas Dehnadi
Cindy Miller
Jane O
Franzi Pollok
R.N. Pierson, III
A.Benedict Cosimi
Tatsuo Kawai

Knight Surgery Research Laboratory
Jessica Burke
Anet Calisir
Nick Deluca
Nelson Marquez Carvajal
Eli Smith
Michael Duggan

MGH Pathology
Ivy Rosales
Robert Colvin
Catherine Stevens

MASSACHUSETTS GENERAL HOSPITAL
CENTER FOR TRANSPLANTATION SCIENCES