



HARVARD MEDICAL SCHOOL
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Long-Term (>1 year) Rejection Free Survival of Kidney Xenografts with Triple Xenoantigen Knockout and Multiple Human Transgenes in Cynomolgus Monkeys

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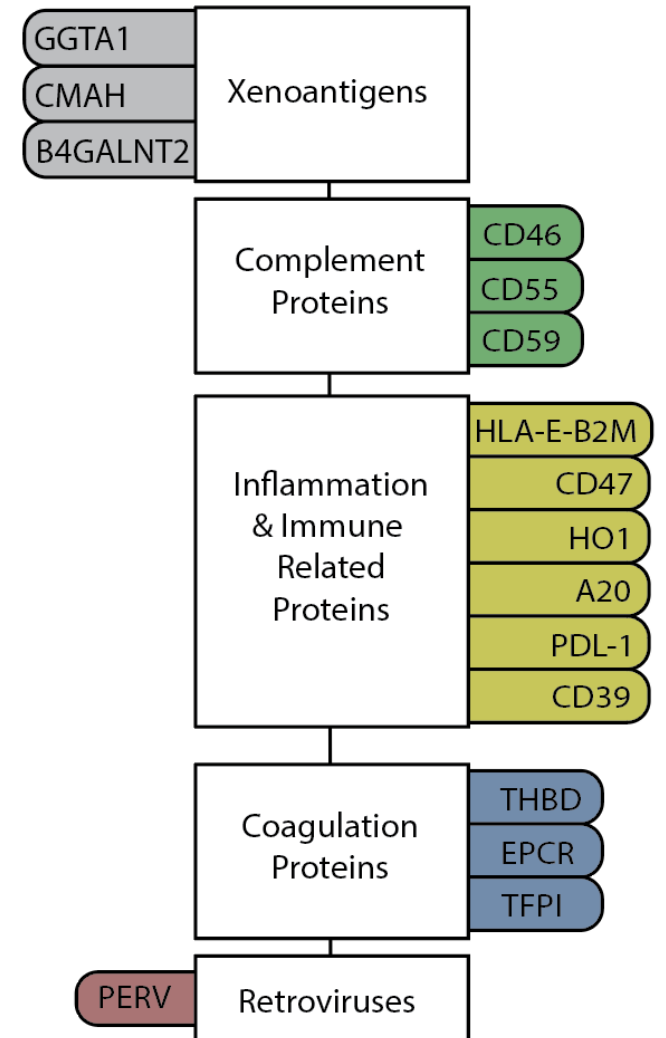


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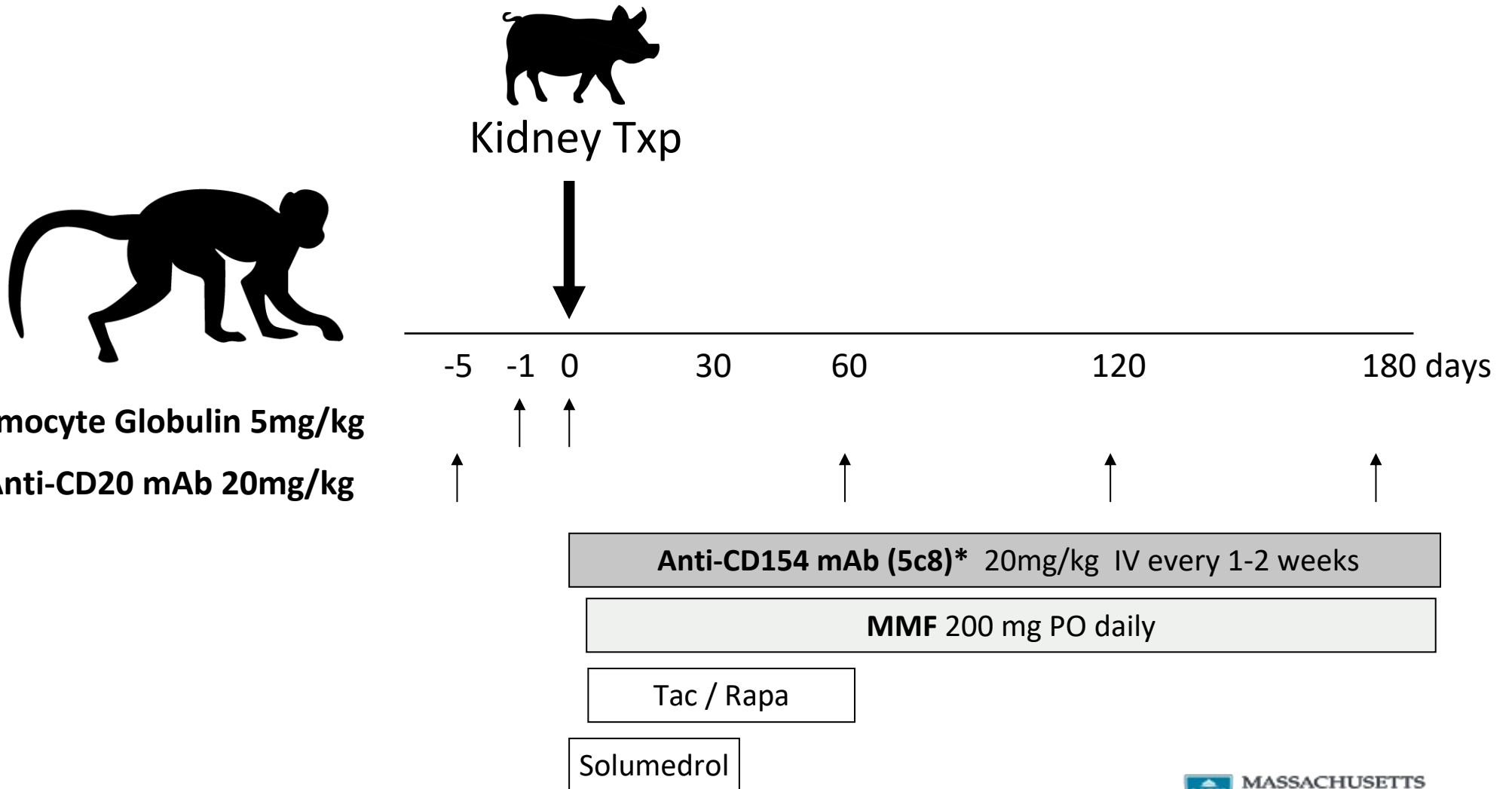
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Background – Xenotransplantation Barriers & Strategies to Overcome

- Xenotransplantation has three major barriers to overcome prior to making it clinically available
 - Hyperacute Rejection (overcome by deletion of 3 carbohydrate xenoantigens)
 - Longevity/Chronic Rejection
 - Zoonotic crossover
- Using *Cynomolgus Macquaces* as a non-human primate preclinical model we studied the importance of multiple human transgene insertion into the TKO xenograft



Immunosuppressive Regimen

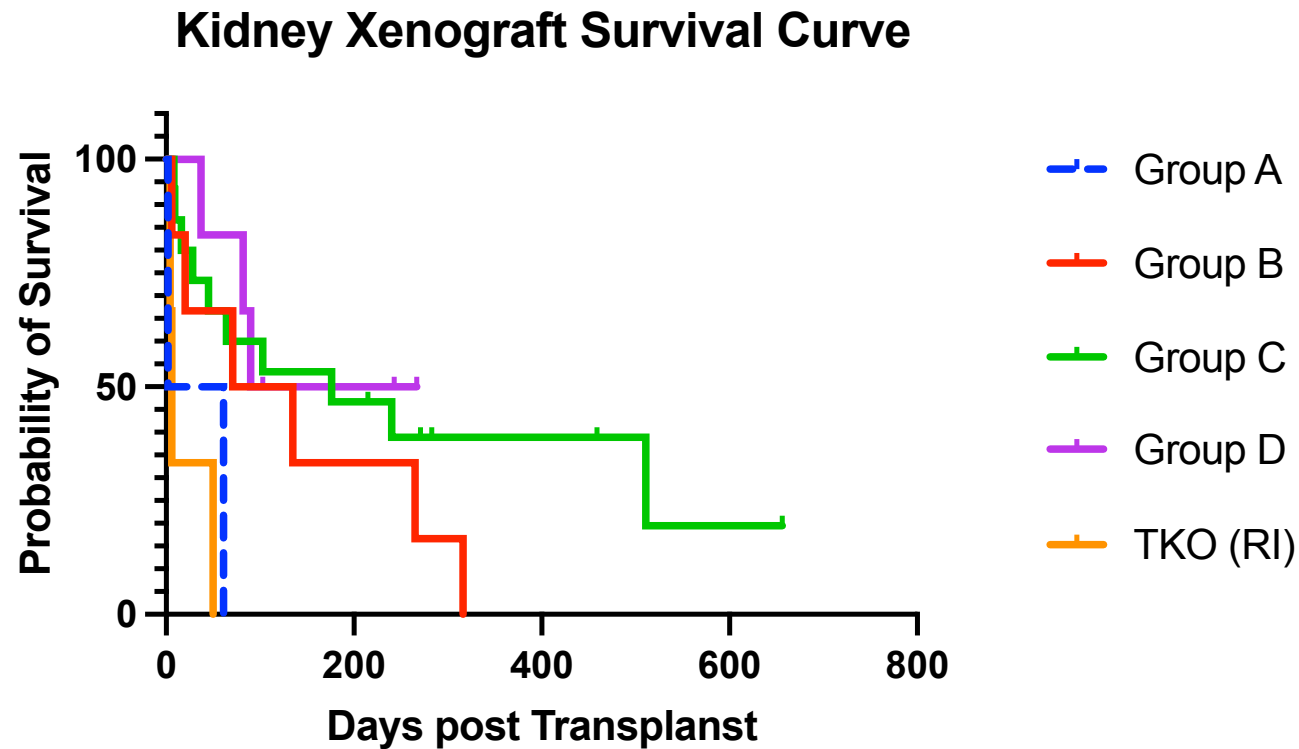


*Combination of NHPs treated with hu5c8 and TNX-1500. TNX-1500 is an investigational new biologic and has not been approved for any indication

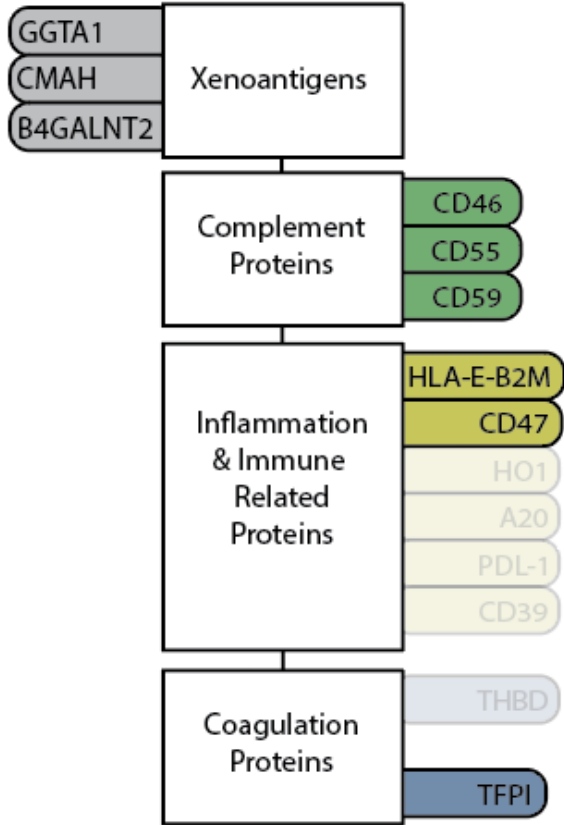
Summary - Clinical Results

Group	Donor	Immunosuppression		Survival Days
		Maintenance	Tac/Rapa (1-2 months)	
TKO	N=4	aCD154, MMF	Tac	50, 6, 4
A	EGEN-2528 (N=2)	aCD154, MMF	1 none/ 1 Rapa	61, 2
B	EGEN-2536 (N=6)	aCD154, MMF	4 Rapa 2 Tac	265, 71, 20, 15 316, 135
C	EGEN-2734/2784 (N=15)	aCD154, MMF	Tac	>656, >459, >271, >215, 511, 283, 240, 176, 103, 64, 45, 25, 16, 9, 8
D	EGEN-2060 (N=6)	aCD154, MMF	Tac	>103, 265, 242, 90, 82, 37

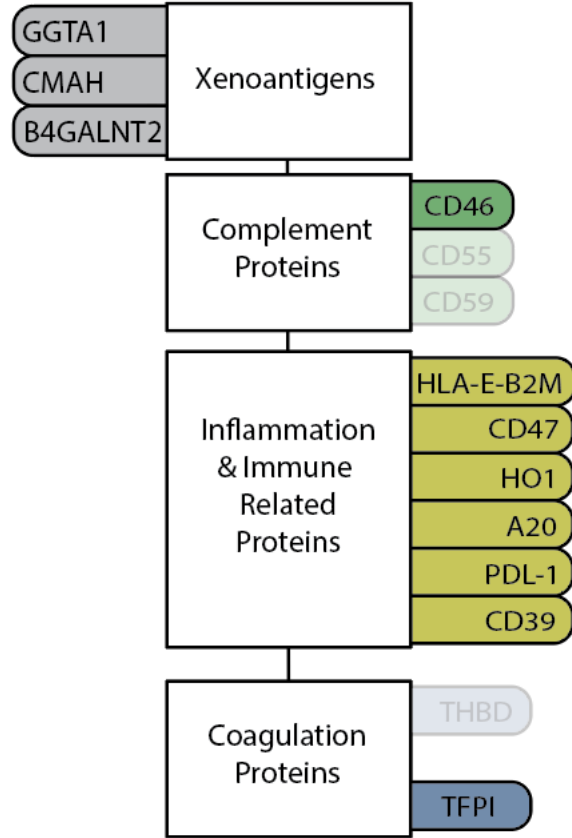
Kaplan-Meier Curve, Group C has Median survival of 176 days



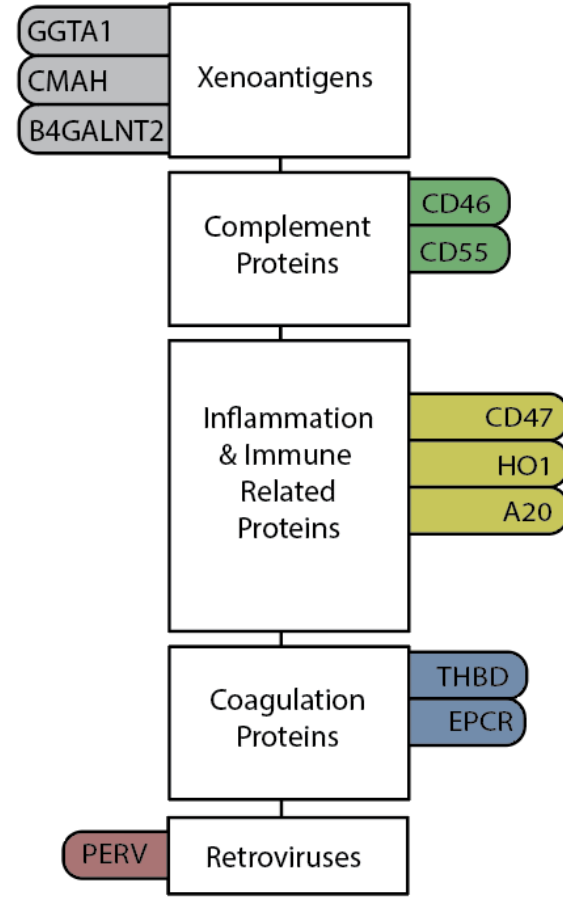
Group A



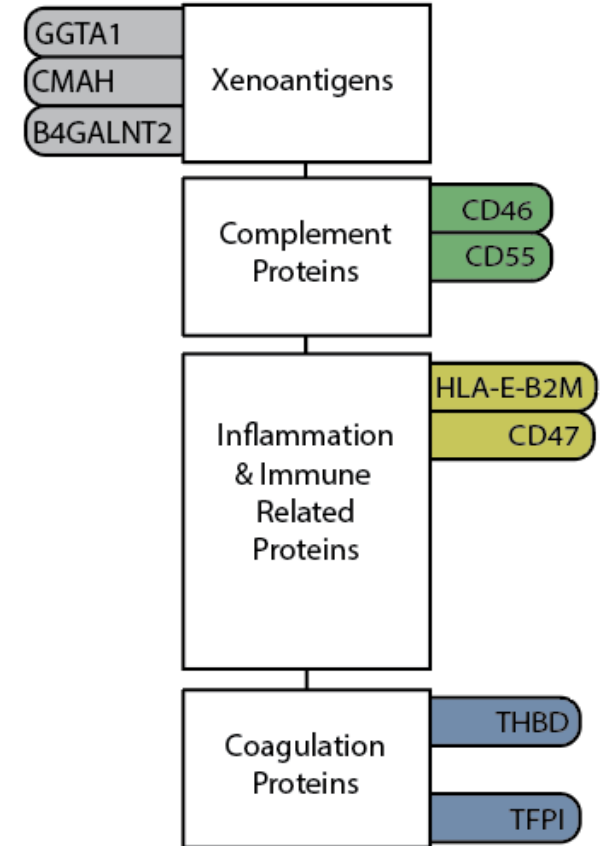
Group B



Group C



Group D



Conclusion

- We consider human transgene insertion to be critical for longterm success of xenotransplantation of kidneys
- The role of specific human transgenes, including THBD and EPCR, in preventing xenograft rejection remains to be defined by longer-term observation in more recipients

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