KRP203 AS A DESIRABLE IMMUNO-MODULATOR FOR ISLET TRANSPLANTATION

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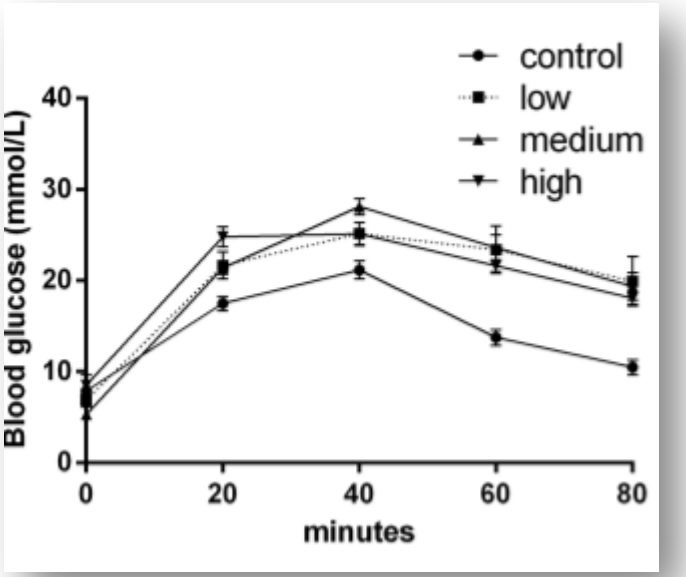
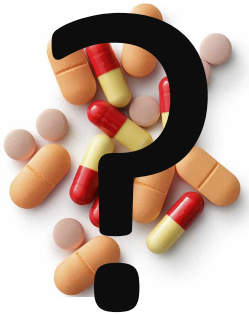
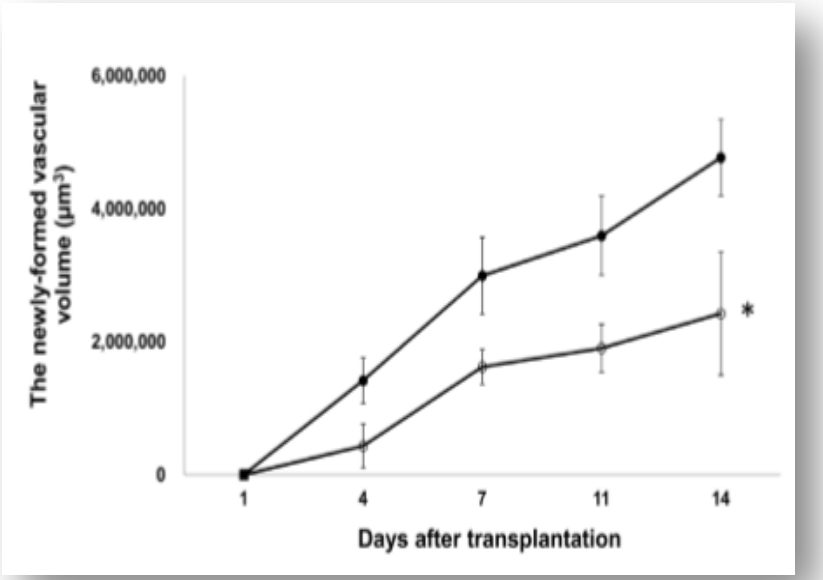
Drawbacks of current immunosuppressives



Li Z, *et al*. PloS One. 2015





Nishimura R,..Goto M. PLoS One. 2013

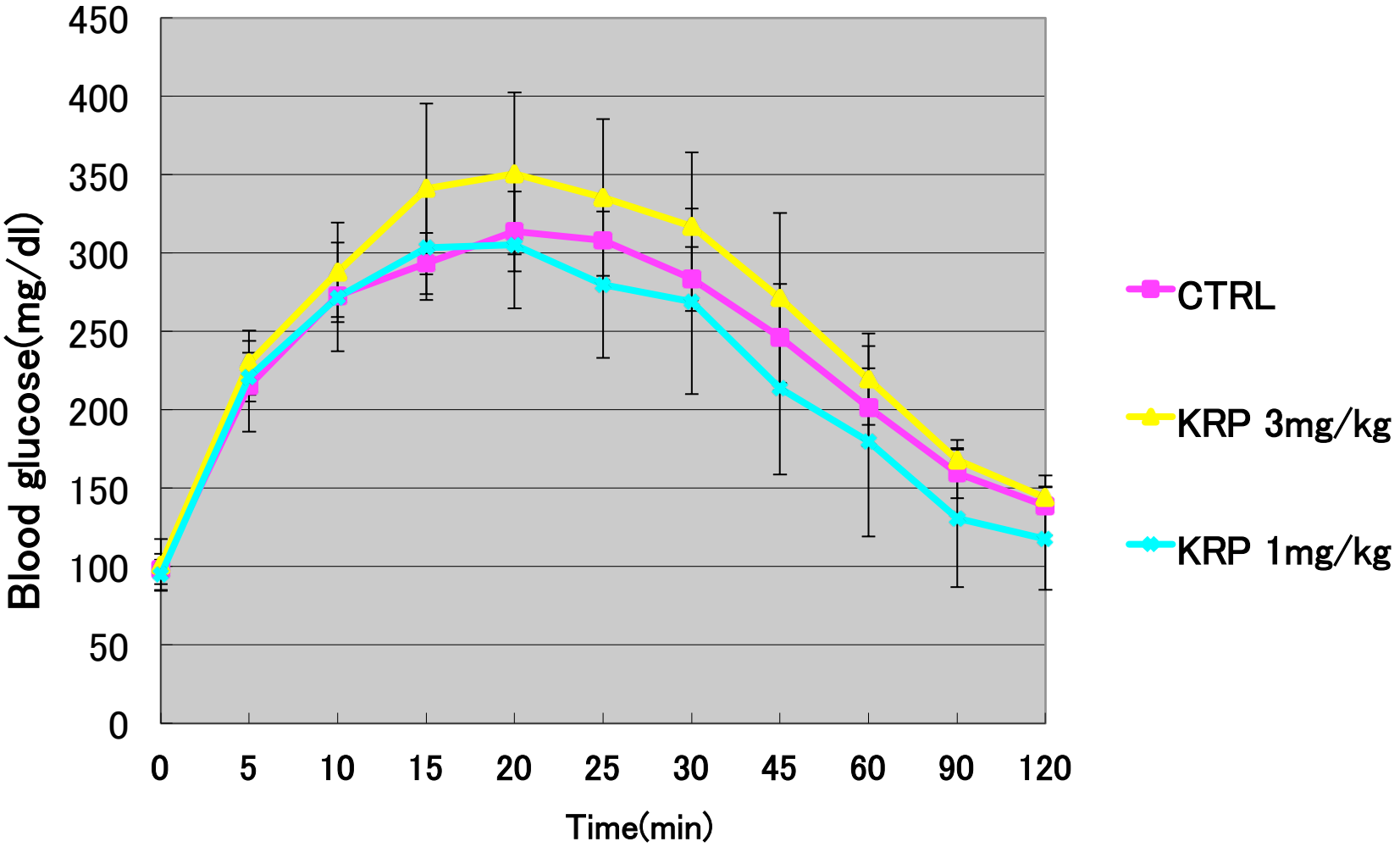
Aim

1. Examine the effect of KRP203 on blood glucose levels, glucose tolerance, and islet function.

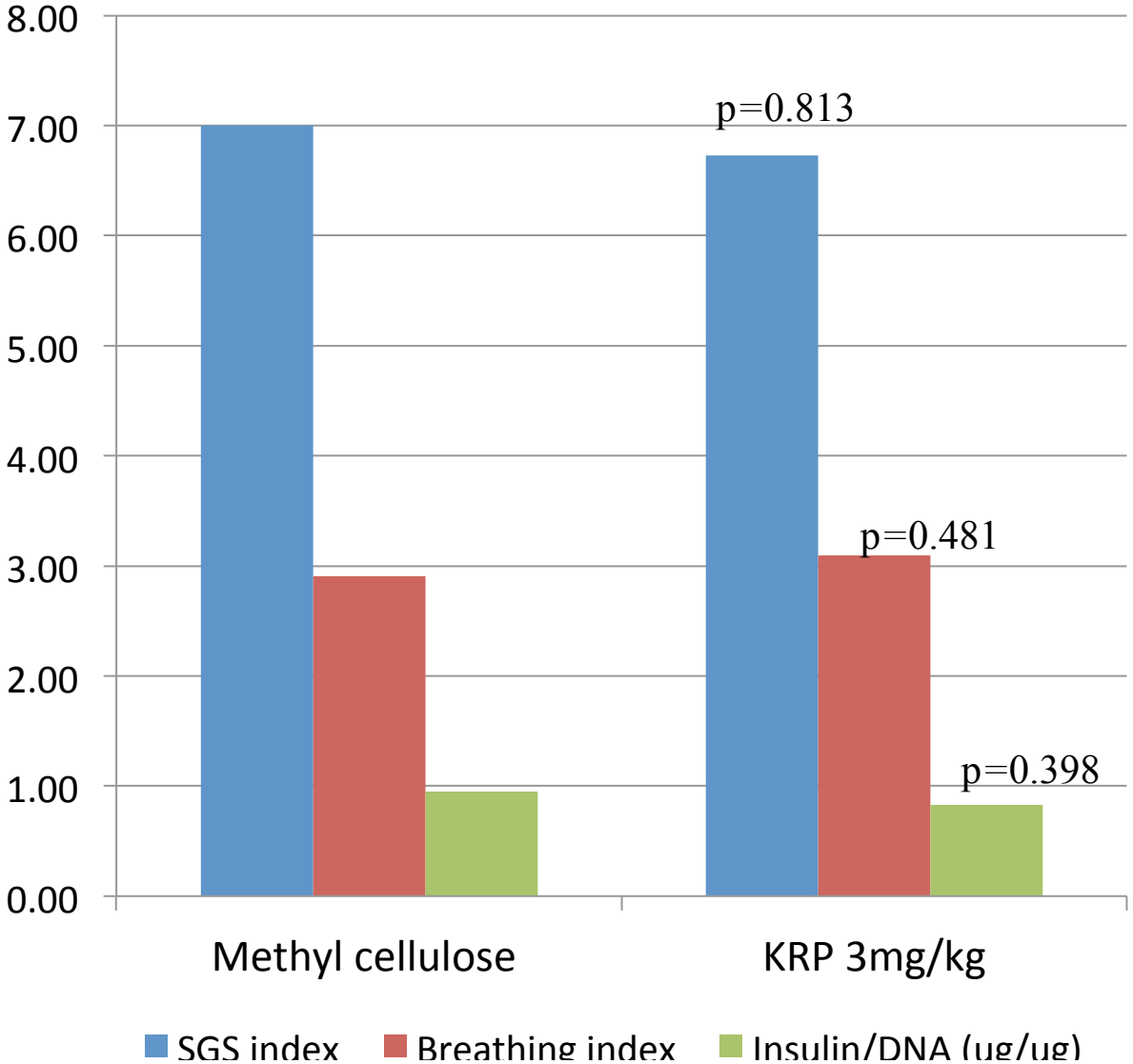
2. Examine the effect of KRP203 on *in-vivo* islet vascularity.

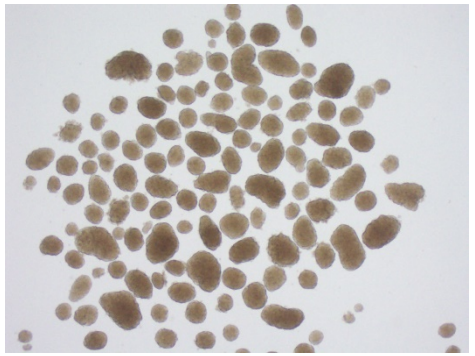
3. Explore the possibility of omitting calcineurin-inhibitors in KRP203 based regimen for islet allo-transplantation.

IPGTT

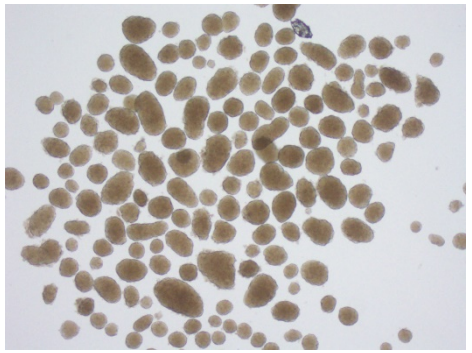

Blood glucose(mg/dl)
450
400
350
300
250
200
150
100
50
0
0
5
10
15
20
25
30
45
60
90
120
Time(min)
CTRL
KRP 3mg/kg
KRP 1mg/kg

Functional assays



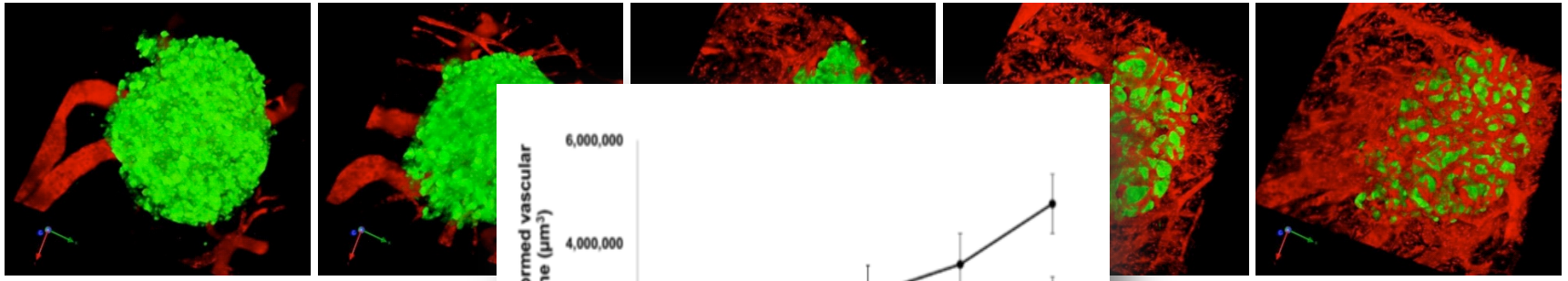


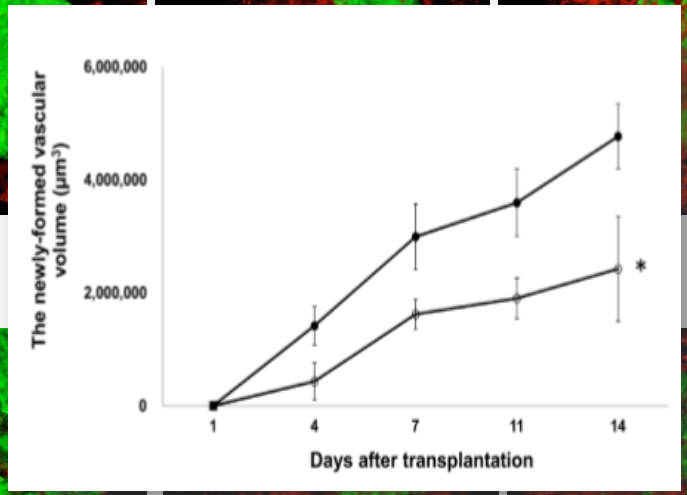
KRP 3mg/kg



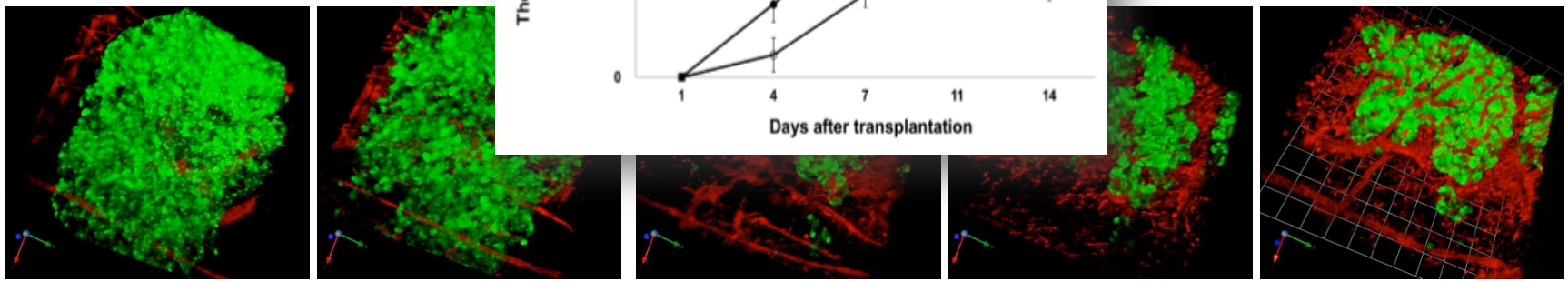
0.5% Methyl cellulose

Control





Tacrolimus



Day1 **Day4** **Day7** **Day11** **Day14**

Nishimura R, Goto M et al. PLOS ONE:8 (4):e56799: 2013

Islet Vascularity

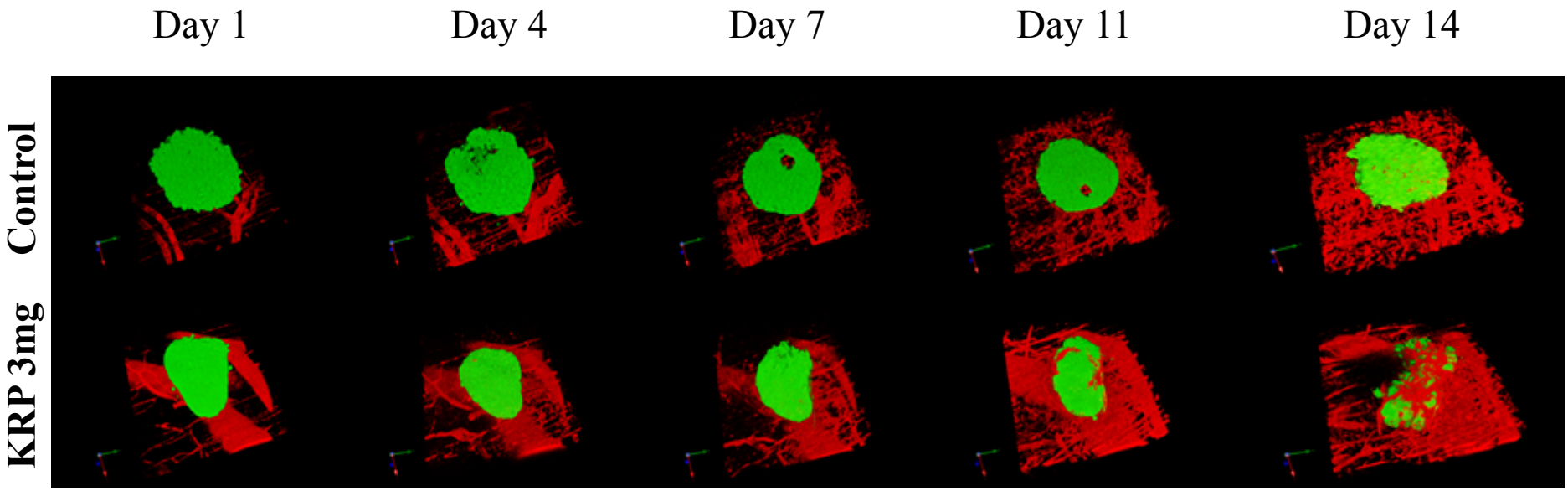
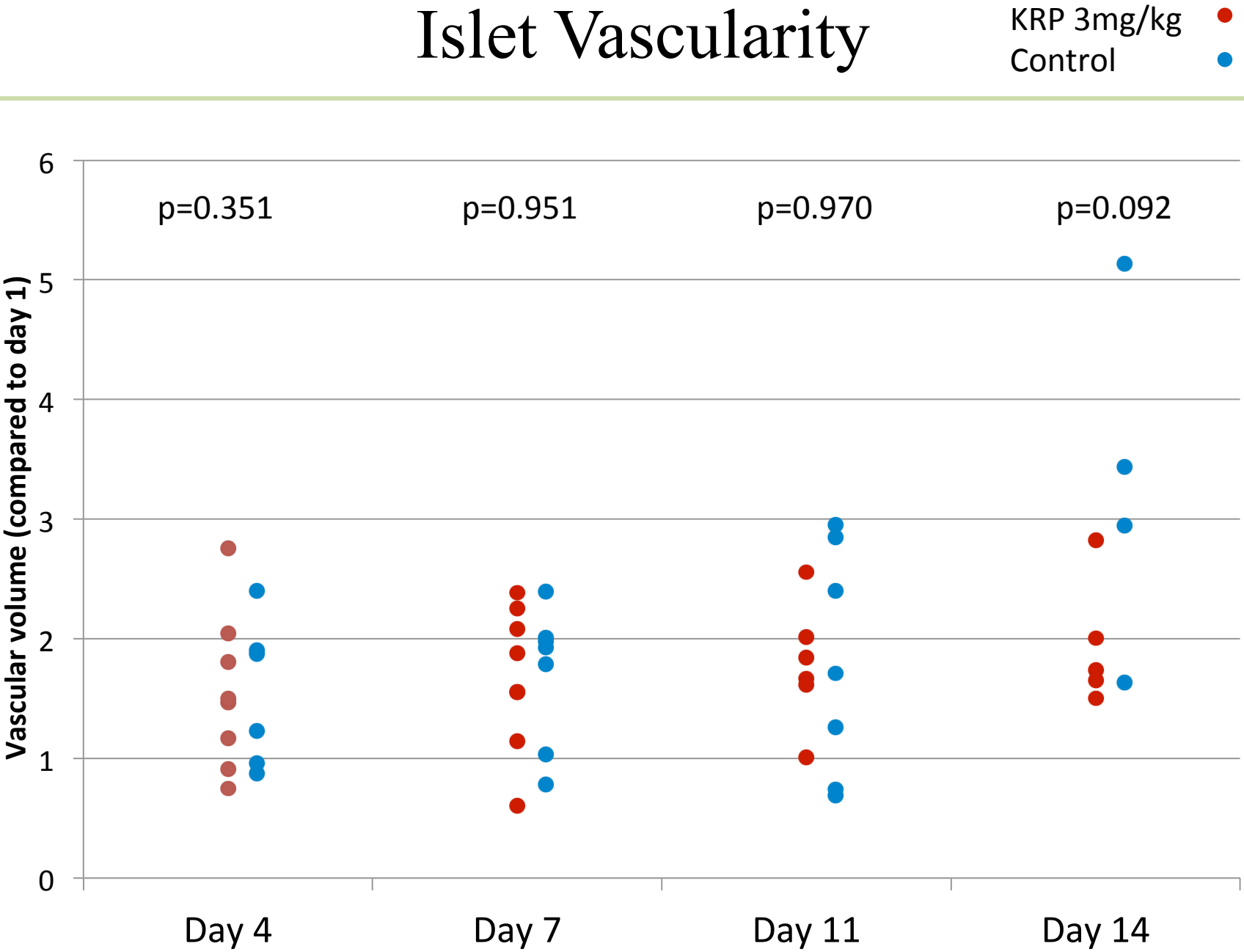
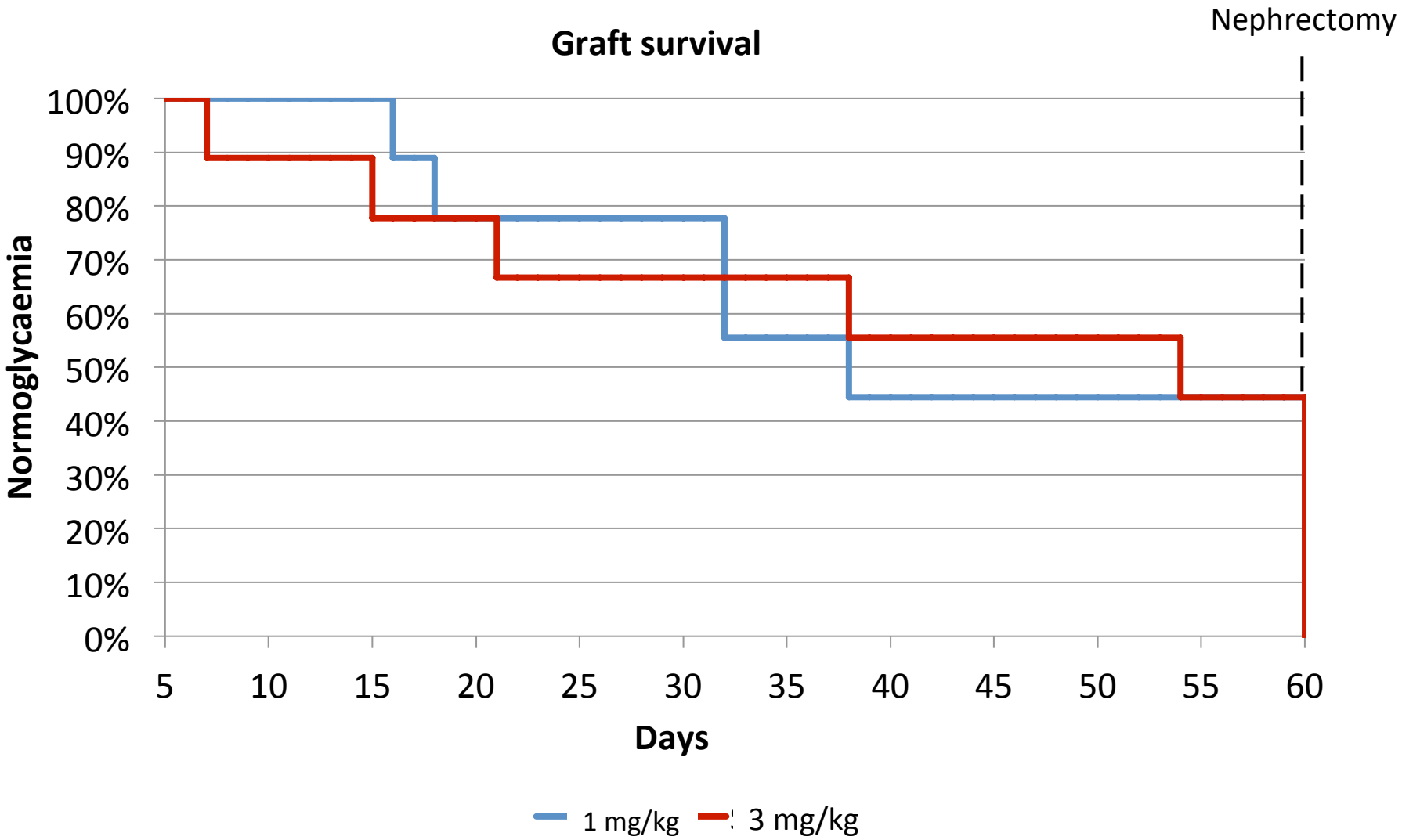


Image acquisition: *FluoView FV1000MPE; OLYMPUS, Tokyo, Japan.*
Vascular volume analysis: *Volocity 3D system, PerkinElmer, Waltham, MA, USA*

Islet Vascularity



Islet allotransplantation (Balb/c to B/6)

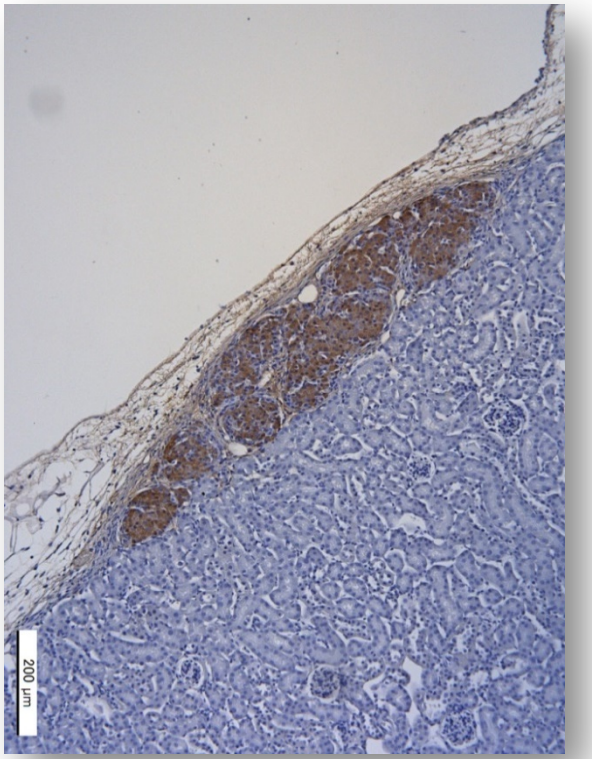


Immunohistochemistry (Anti-insulin)

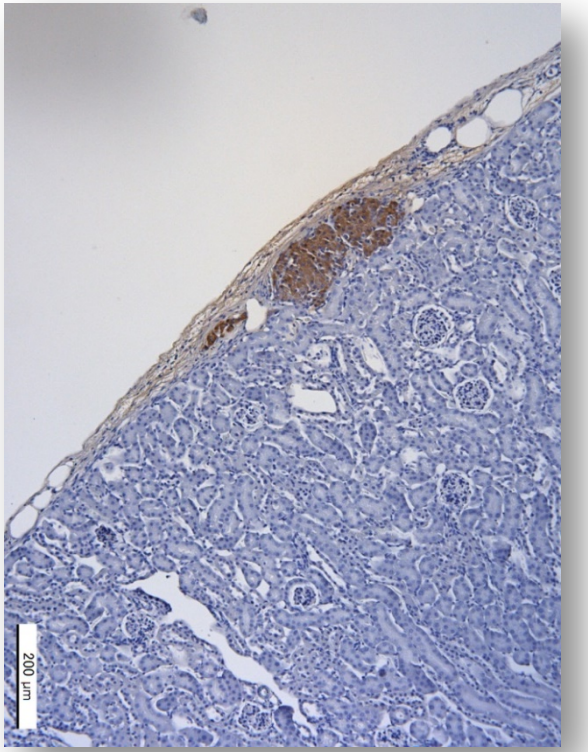
NO REJECTION

REJECTION

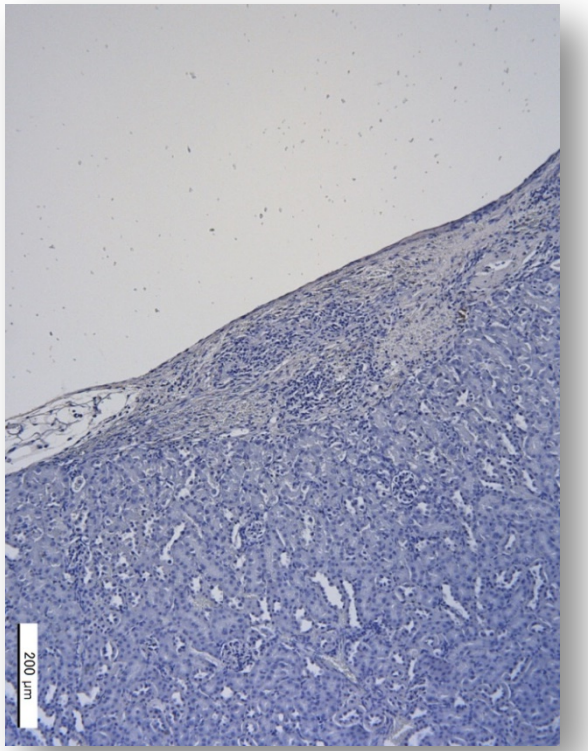
KRP 1 mg/kg



KRP 3 mg/kg



KRP 1 mg/kg



Co-stimulatory blockade + KRP203

Daily KRP203 (1mg/kg)

+

Anti-LFA1α
(100 μg from day 0 to day 6)

No rejection beyond 50 days of follow-up (2/2 mice)

Conclusions

KRP203 is a desirable immunomodulator for islet transplantation

- Preserving endocrine function
- Preserving revascularization of transplanted islet grafts.

Therefore, KRP203 in combination with co-stimulatory blockade *could be* an attractive alternative to current standard immunosuppressive regimen.