



Fig 1s

Figure 1s. Inflammatory status before and after syngeneic islet transplantation in mouse.

Panel A. C57BL/6 islets (500/ml) from seven preparations were cultured for 24 h in the absence (unstimulated, white box) or in the presence (gray box) of 10 ng/ml IL-1 β , and the chemokine/cytokine concentrations in the supernatant were measured by a multiplex sandwich ELISA. Data are represented as box plots indicating median, interquartile range (boxed areas), 5 and 95% limits (whiskers). Statistical analysis was performed by Mann Whitney U test. * $p \leq 0.05$; ** $p \leq 0.01$ unstimulated vs. IL-1 β treated. *Panel B.* After 24h culture, 350 islets from each preparation (unstimulated, n=7; IL-1 β treated, n=7) were infused in 14 syngeneic diabetic C57BL/6 mice through the portal vein. Chemokine and cytokine concentrations in serum before and 24h after islet infusion were measured as above. Data are expressed as fold increase (24h versus basal). The mean basal concentrations (pg/ml) are given in the lower panel. Each point on the scatter plot represents one recipient. Statistical analysis was performed by Mann Whitney U test. * $p \leq 0.05$; ** $p \leq 0.01$ 24h vs. basal. *Panel C.* After 24h culture, 350 unstimulated islets from three of seven preparations were transplanted in 6 diabetic mice and local liver inflammatory status before and 4h-24h after intrahepatic islet infusion was evaluated using RNase protection-based assays for detecting cytokine and chemokine transcripts. Data are expressed as fold increase versus basal. Each point on the scatter plot represents one recipient. nt=not tested

Supplementary Tables

Table 1s. Intrahepatic leukocyte populations after islet transplantation

| | Maximum Fold increase (time) ^a | | | Delta AUC ^b | | |
|------------|---|-------------------|----------------|------------------------|-------------------|-----------------|
| | Vehicle | CXCR1/2 inhibitor | p ^c | Vehicle | CXCR1/2 inhibitor | p ^c |
| Syngeneic | | | | | | |
| PMN | 4.9 (1d) | 3.2 (1d) | <0.05 | 1,307 | 530 | 0.27 |
| NKT cells | 4.8 (1d) | 1.9(1d) | 0.12 | 2,259 | -1,265 | <0.05 |
| Allogeneic | | | | | | |
| PMN | 18.4 (5d) | 9.3 (5d) | <0.05 | 18,314 | 9,913 | <0.05 |
| NKT cells | 9.9 (7d) | 3.4(5d) | <0.05 | 9,107 | 2,378 | <0.05 |

Data are reported as median

^a Value and time of the maximum fold increase versus basal after islet infusion

^b Incremental area under the number of cell time curve after islet transplantation

^c Mann-Whitney Test

Table 2s. Characteristics of islet preparations, donors and recipients

| | ATG/RAPA/MMF + Steroid and IL1Ra (N=8) | ATG/FK506/MMF (N=3) |
|---------------------------------------|--|---------------------|
| Donor/islet | | |
| Sex (M/F) | 3/5 | 2/1 |
| Age | 56±5 | 47±11 |
| Pancreas Weight (g) | 136±51 | 162±32 |
| Equivalent islet (x10 ³) | 342,951±50,122 | 436,961±112,068 |
| Isolation index | 0.96±0.26 | 0.88±0.18 |
| Purification (%) | 53±21 | 48±9 |
| Volume (ml) | 2.8±1.12 | 3.3±1.2 |
| Pre Tx culture (h) | 35±12 | 50±17 |
| Recipient | | |
| Sex (M/F) | 3/5 | 2/1 |
| Age | 38.7±5.1 | 45±4 |
| Diabetes duration (Years) | 22±12 | 31±12 |
| Pre TX Insulin requirement (U/kg/die) | 0.50±0.09 | 0.53±0.17 |
| Pre Tx HbA1c (%) | 8.4±1.04 | 9.56±1.72 |
| Creatinine (mg/dl) | 0.74±0.14 | 0.93±0.22 |
| Weight (kg) | 60±9.8 | 58±10.1 |
| IEQ/kg | 5,809±1,199 | 7,486±1,134 |

Table 3s. Characteristics of donor and islet preparations transplanted in reparixin islet transplant trial: first infusion

| Patient | Donor Age/sex | Donor BMI | Total IEQ ^a | Purity (%) | Viability (% negative) | PI | Pre Tx culture time (h) | Pellet volume (ml) | IEQ/kg expected ^a | IEQ/kg infused ^b |
|---------------------------------|---------------|-----------|------------------------|------------|------------------------|----|-------------------------|--------------------|------------------------------|-----------------------------|
| CTRL | | | | | | | | | | |
| #1 | 19/F | 30.1 | 301,500 | 50 | 90 | | 45 | 2 | 6,030 | 4,075 |
| #4 | 22/M | 19.3 | 244,500 | 55 | 90 | | 38 | 1,5 | 7,067 | 4,690 |
| | 54/F | 25.4 | 229,000 | 20 | 90 | | 15 | 3 | | |
| #6 | 63/M | 34 | 361,425 | 55 | 90 | | 18 | 3 | 6,178 | 4,820 |
| TOT | 39.5±11.1 | 27.2±3 | 284,106±60,238 | 45±16 | 90±0 | | 29±7 | 2.4±0.4 | 6,425±323 | 4,528±229 |
| REPA | | | | | | | | | | |
| #2 | 52/M | 22.7 | 89,550 | 85 | 90 | | 70 | 1 | 6,972 | 4,176 |
| | 50/F | 18.4 | 328,750 | 40 | 90 | | 21 | 3 | | |
| #3 | 58/M | 23.4 | 311,183 | 50 | 90 | | 42 | 2 | 6,621 | 4,199 |
| #5 | 35/F | 19 | 153,102 | 35 | 95 | | 25 | 1 | 6,506 | 4,095 |
| | 60/F | 26 | 295,549 | 60 | 95 | | 22 | 2 | | |
| #7 | 42/F | 22.3 | 408,341 | 55 | 90 | | 18 | 4 | 6,586 | 5,589 |
| TOT | 49±4 | 21.9±1.3 | 264,412±48,641 | 54±7.2 | 91±2.6 | | 33±8 | 2.2±0.5 | 6,671±103 | 4,514±358 |
| After protocol has been amended | | | | | | | | | | |
| #8 | 46/F | 25 | 314,799 | 53 | 90 | | 24 | 1.5 | 7,914 | 6,251 |
| | 48/M | 51.4 | 160,000 | 60 | 95 | | 0 | 0.5 | | |
| #9 | 48M | 51.4 | 386,425 | 60 | 90 | | 18 | 2.5 | 7,830 | 5,154 |

^a Islet equivalents counted at the end of isolation

^b Islet equivalents counted after culture immediately before infusion