Title

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Saved life-years for DD KTA recipients were 30,581 years; for SPK recipients, 113,942 years; for PAK 20,668 years, and for PTA recipients, 9,670 years. This resulted in 7.8 life–years that were saved for every type 1 diabetic recipient of a pancreas and/or kidney transplant. The average observed number of life-years saved for DD KTA recipients was 6.8years; for SPK recipients, 8.9 years; for PAK 5.4 years and PTA recipients, 3.4 Years. The difference was highly significant ($p < 0.0001$).

Conclusions: Our analysis demonstrates the following: (1) Waiting list mortality was highest for patients with end-stage-renal disease (KTA, SPK). Patient survival was highest after SPK, PTA; the lowest patient survival rate was noted in DD KTA; (3) At 5-years, patient mortality rates from time of listing for transplanted vs. waiting patients was 87% vs 30% for DD KTA and 92% and 22% for SPK recipients (4) More average life-years were saved with SPK than with DD KTA; (5) To date, primary DD pancreas and/or kidney transplants in type 1 diabetics have saved almost 300,000 life-years.

313.4

The tissue common response module (tCRM) score predicts treatment response for acute cellular rejection following pancreas transplant

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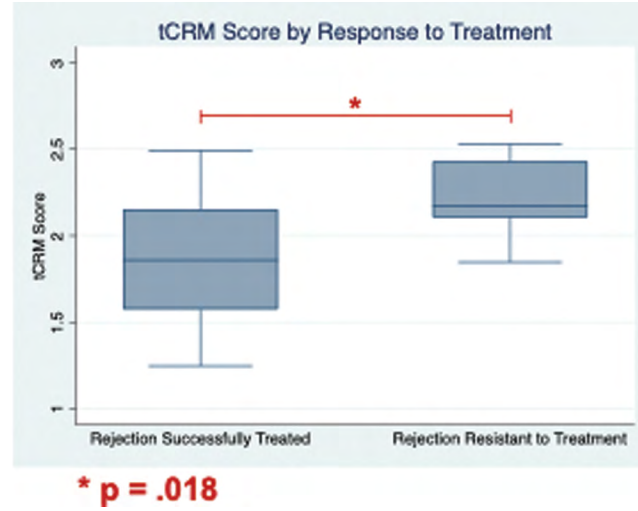
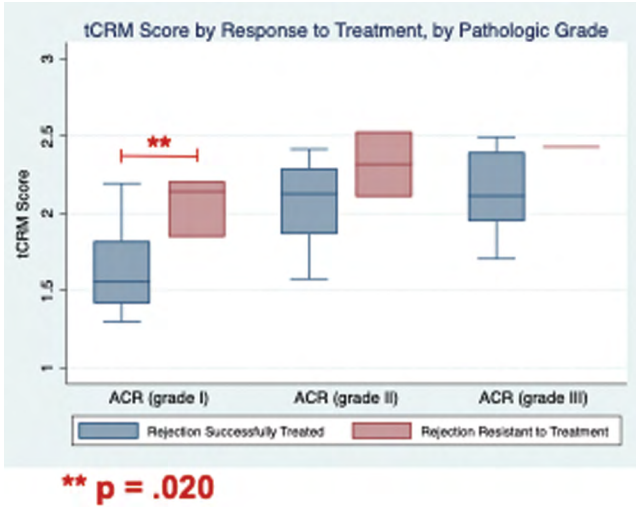
Introduction: The tissue Common Response Module (tCRM) score, which is based on the expression levels of 11 genes (BASP1, ISG20, PSMB9,RUNX3, TAP1, NKG7, LCK, INPP5D, CXCL9, CD6, CXCL10), was developed using genomics data from heart, liver, lung, and kidney tissue with acute cellular rejection (ACR). Using our institution's repository of pancreas transplant specimens, we sought to validate the tCRM score in pancreas samples with ACR and to determine whether it correlates with treatment response.

Methods: Fifty one formalin fixed paraffin embedded pancreas biopsy specimens: 14 normal, 14 Grade 1 (G1) ACR, 14 Grade 2 (G2) ACR, and 9 Grade 3 (G3) ACR were analysed using multiplex RNA sequencing. Differential gene expression and pathway analyses were performed using a panel of 804 unique genes, including the genes that make up the tCRM score. Whole transcriptome spatial RNA analysis is ongoing to further investigate patterns of gene expression in distinct regions and cell populations.

Results: Significant differences in gene expression were seen in G2 and G3 ACR, but not G1 ACR, when compared with normal pancreas samples. Pathway analyses demonstrated that the genes enriched in G2 and G3 ACR were associated with inflammatory pathways like interferon signalling, antigen processing and presentation, and phagocytosis. A statistically significant difference was found in the tCRM scores for G2 ACR and G3 ACR, when compared to the tCRM score for normal pancreas tissue. Patients with rejection that was resistant to treatment (defined as recurrent rejection within 2 months of the initial rejection episode) had significantly higher tCRM scores (Figure 1). This difference remained significant for patients with G1 ACR, but was not significant for patients with G2 or G3 ACR (Figure 2).





Conclusions: We found that the tCRM score not only correlates with commonly used histologic grading criteria, but also identifies patients with ACR who are at risk for treatment resistant rejection and thus may warrant more aggressive initial treatment with lymphodepleting agents. Further work using spatial transcriptomics, including whole transcriptome differential expression analysis and spatial deconvolution is underway to better elucidate the regions and cell populations involved in the development of acute pancreas rejection.

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313.5

Pancreas After Kidney Transplantation Outcomes Over the Past 20 Years in the USA

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Introduction: The number of pancreas transplants performed each year has been variable since 1988 when the Organ Procurement Transplant Network (OPTN)/Scientific Registry of Transplant Recipients (SRTR) began tracking transplant data. The most recent OPTN/SRTR data shows a 9.1% increase in pancreas after kidney (PAK) transplants.

Material and methods: We performed a retrospective registry analysis utilizing the OPTN/UNOS database for pancreas transplants after kidney transplants performed in the United States from January 2001 to December 2020 to assess transplant outcomes. The data was collected directly from the de-identified information contained within the database. Pancreas transplants without outcomes data were excluded.

Results: 3706 allograft recipients were included in the study. 2892 (78%) transplants were done from 2001 to the end of 2010. 814 (22%) transplants were done from 2011 to the end of 2020. Table 1 summarises the demographic characteristics of each group. Although the BMI and recipient sex comparison shows a statistically significant difference, the differences are not clinically significant. The overall 5-year allograft survival rate was 55.95% in the 2001-2010 group, which significantly increased to 63.67% in the 2011-2020 group (P=0.001) (Fig 1). The allograft survival difference increased significantly after 10 years of follow-up (39.58% vs. 51.41%, P<0.001). The overall 5-year patient survival rate was 83.12% in the 2001-2010 group, which increased to 84.88% in the pancreas after kidney transplants from 2011 to 2020 (P=0.41) (Fig 2). The 10-year patient survival rate was 61.37% in the 2001-2010 group, and 67.76% in the 2011-2020 group (P=0.14)

Table 1. Worldwide reports of liver transplantation for propionic acidemia associated cardiomyopathy

References	n	Gender	Genetic analysis	Age at diagnosis	Age at LT	Indication for LT	Graft type	Follow-up	Post-LT metabolic decompensation	Post-LT protein restriction	Post-LT cardiomyopathy	Patient outcome
Romano et al. 2010	2	F/F	N/A	10m/3d	6.5y/9y	Dilated CM/MD & Dilated CM	Deceased	0.5y/10y	None	No restriction	Completely normalized	Alive
Amelook et al. 2011	1	M	N/A	8m	16y	Dilated CM	Deceased	70d	None	No restriction	Normal systolic left ventricular function	Alive
Kasahara et al. 2012	1	F	N/A	46d	2.2y	MD & Dilated CM	Living	3.4y	None	Mild	Normal cardiac function	Alive
Arrizza et al. 2015	1	M	Heterozygous mutations in the *PCCA* gene	26m	22y	Dilated CM	Deceased	10y	None	No restriction	Normal cardiac function	Alive
Charbit-Henrion et al. 2015	3	M/F/F	N/A	N/A	7.1y/6.7y/8.3y	MD & Dilated CM/Dilated CM/Dilated CM	Deceased	253d/8y/1y	None	Mild	Fully recovered	Dead/Alive/Alive
Silva et al. 2017	2	M/F	N/A	N/A	12.5y/5.5y	Dilated CM	Living	4y/5y	None	Mild	Progressive resolution	Alive
Critelli et al. 2018	1	M	Homozygous mutation in the *PCCB* gene	7d	8.7y	Dilated CM	Living	2.5y	None	Mild	Improved cardiac function	Alive
Shanmugam et al. 2019	1	M	N/A	N/A	4.6y	MD & Dilated CM	Living	4.2y	None	No restriction	No progress	Alive
Berry et al. 2020	1	M	N/A	5m	10.1y	Dilated CM	Deceased	8.9y	None	N/A	Cardiogenic shock and heart failure	Dead
Tuchmann-Durand et al. 2020	1	M	Homozygous mutation in the *PCCB* gene	at birth	15y	MD & Dilated CM cardiomyopathy	Deceased	0.02y	None	N/A	Normal electro-encephalography	Alive
Hejazi et al. 2022	1	M	Homozygous mutation in the *PCCB* gene	newborn screening	8.8y	MD & Dilated CM	Living	6y	None	No restriction	Severely dilated left ventricle with severe systolic dysfunction	Alive (Received cardiac transplant)
Present case	1	F	Homozygous mutation in the *PCCA* gene	0.6m	2.7y	MD & Dilated CM	Living	3.5y	None	No restriction	Improved	Alive

CM, cardiomyopathy; F, female; LT, liver transplantation; M, male; MD, metabolic decompensation; N/A, not available.