

2017 Banff Pancreas Session

Summary Report

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University of Maryland School of Medicine



Department of Surgery

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Celebrating 50 Years of Pancreas Transplantation: Discovery, Innovation, and Advancement

Honoring pioneers and celebrating 50 years of achievements since the first pancreas transplant. The first pancreas transplant patient, a young woman with advanced diabetic complications, immediately became normoglycemic and insulin-independent. The transplant was performed on December 16-17, 1966 by Drs. William D. Kelly and Richard C. Lillehei. Since then, over 30,000 pancreas transplants have been performed worldwide benefiting seriously ill diabetic patients with to without kidney failure.

John S. Najarian Lecture Panel Speakers:

- Jean-Michel (Max) Dubernard, MD, University of Lyon, France
- Frederick Merkel, MD, Loyola University and Rush University, Chicago, Illinois
- Hans W. Sollinger, MD, University of Wisconsin, Madison, Wisconsin
- David E.R. Sutherland, MD, University of Minnesota, Minneapolis, Minnesota



Dr. Lillehei in the operating room. (1969)

Progress in Pancreas Tx:

- **Required significant refinement of surgical Techniques.**
- **Pathology advances where rapid initially, but studies where based primarily on failed grafts.**
 - R. Sibley
 - R. Nakhle
 - H. Carpenter

Important leap forward

Allen RD, Wilson TG, Grierson JM, Greenberg ML, Earl MJ, Nankivell BJ, Pearl TA, Chapman JR.

Percutaneous biopsy of bladder-drained pancreas transplants.

Transplantation. 1991 Jun;51(6):1213-6.

Percutaneous Pancreas Bx: 1991

- 1995 Pancreas discussions in Banff Conference
- 1997 Maryland Grading Schema

Transplantation. 1997 Jun 15;63(11):1579-86.

Evaluation of pancreas transplant needle biopsy: reproducibility and revision of histologic grading system.

Drachenberg CB¹, Papadimitriou JC, Klassen DK, Racusen LC, Hoehn-Saric EW, Weir MR, Kuo PC, Schweitzer EJ, Johnson LB, Bartlett ST.

American Journal of Transplantation 2008; 8: 1237–1249
Blackwell Munksgaard

2008

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Transplantation and the American Society of Transplant Surgeons*

doi: 10.1111/j.1600-6143.2008.02212.x

Banff Schema for Grading Pancreas Allograft Rejection: Working Proposal by a Multi-Disciplinary International Consensus Panel

American Journal of Transplantation 2011; 11: 1792–1802
Wiley Periodicals Inc.

2011

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Transplantation and the American Society of Transplant Surgeons*

doi: 10.1111/j.1600-6143.2011.03670.x

Special Article

Guidelines for the Diagnosis of Antibody-Mediated Rejection in Pancreas Allografts—Updated Banff Grading Schema

Meeting Report

doi: 10.1111/ajt.14107

The Banff 2015 Kidney Meeting Report: Current Challenges in Rejection Classification and Prospects for Adopting Molecular Pathology

A. Loupy^{1,*†}, M. Haas^{2,†}, K. Solez³, L. Racusen⁴,
D. Glotz⁵, D. Seron⁶, B. J. Nankivell⁷,
R. B. Colvin⁸, M. Afrouzian⁹, E. Akalin¹⁰,
N. Alachkar¹¹, S. Bagnasco⁴, J. U. Becker¹²,
L. Cornell¹³, C. Drachenberg¹⁴, D. Dragun¹⁵,
H. de Kort¹⁶, I. W. Gibson¹⁷, E. S. Kraus¹¹,
C. Lefaucheur⁵, C. Legendre¹, H. Liapis¹⁸,
T. Muthukumar¹⁹, V. Nickleit²⁰, B. Orandi¹¹,
W. Park¹³, M. Rabant¹, P. Randhawa²¹,
E. F. Reed²², C. Roufosse²³, S. V. Seshan²⁴,
B. Sis³, H. K. Singh²⁰, C. Schinstock²⁵,
A. Tambur²⁶, A. Zeevi²⁷ and M. Mengel³

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¹⁷Department of Pathology, University of Manitoba, Winnipeg, Canada

¹⁸Department of Pathology & Immunology, Washington University, St. Louis, MO

¹⁹Division of Nephrology and Hypertension, Department of Medicine, New York Presbyterian Hospital-Weill Cornell Medicine, New York, NY

²⁰Department of Pathology and Laboratory Medicine, University of North Carolina, Chapel Hill, NC

²¹Division of Transplantation Pathology, The Thomas E Starzl Transplantation Institute, University of Pittsburgh, Pittsburgh, PA

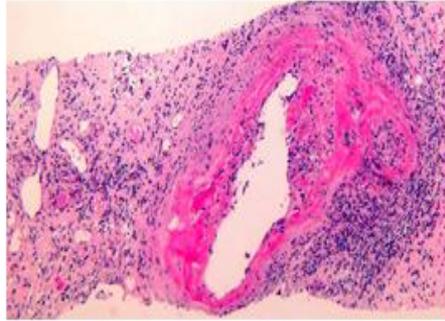
²²Department of Pathology, University of Pittsburgh, Pittsburgh, PA

Carry-over projects from 2015

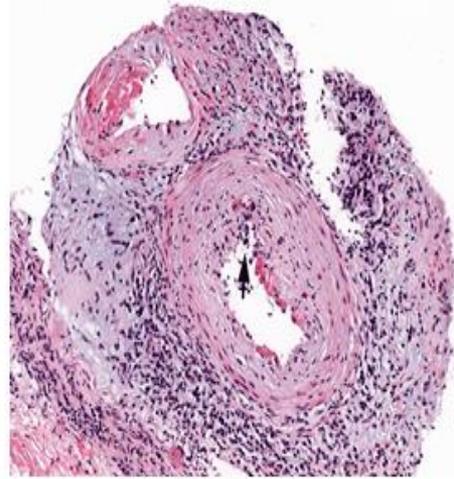
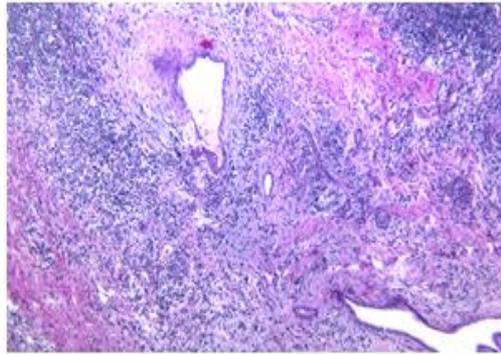
- Candice Roufousse: NanoString pilot study of pancreas allograft biopsies.



- Danni Holanda: Transplant duodenal cuff as a surrogate of pancreas allograft biopsies.



MIXED ACTIVE CHRONIC TCMR AND AMR



The University of Wisconsin Diagnosis and Treatment Algorithm *

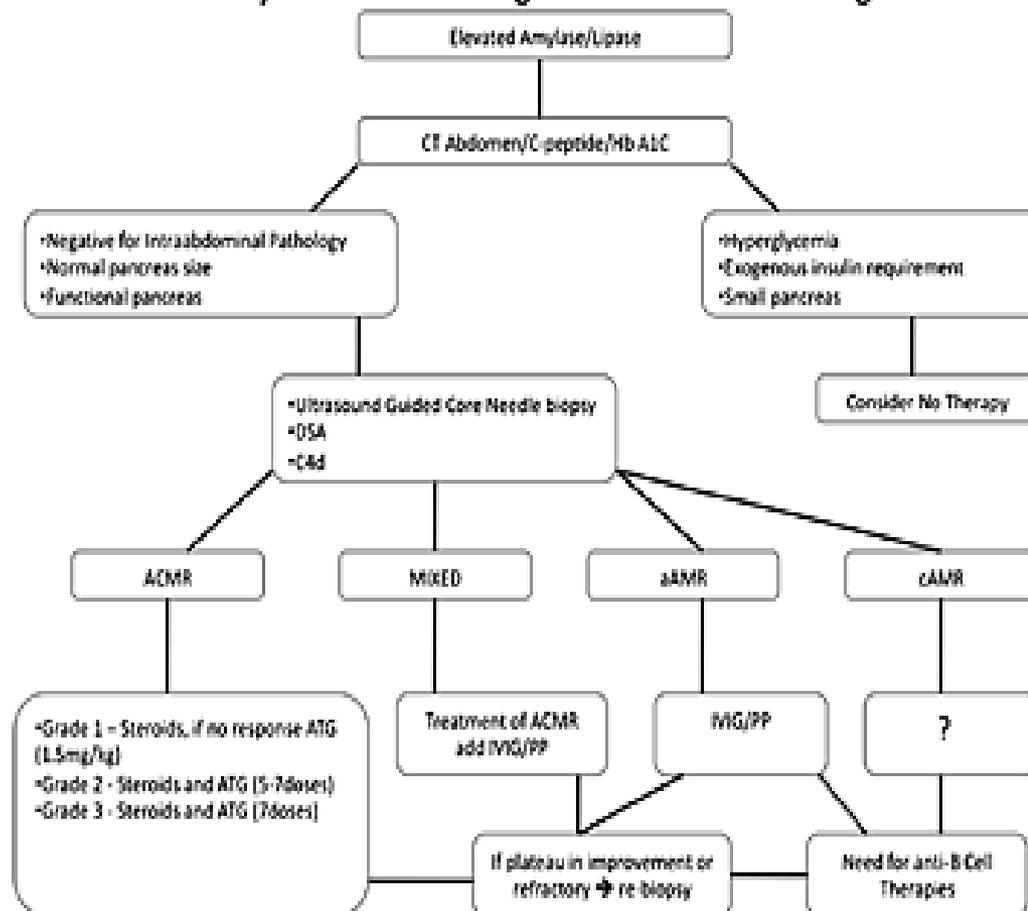


Fig. 2 The University of Wisconsin Diagnosis and Treatment Algorithm
Abbreviations: DSA donor-specific antibody, ACMR acute cell-mediated rejection, aAMR acute antibody-mediated rejection, cAMR chronic

antibody-mediated rejection, ATG anti-thymocyte globulin, IVIG intravenous immunoglobulin, PP plasmapheresis. [Published in Trends in Transplantation, © Permanyer Publications 2].

A Single-center Experience on the Value of Pancreas Graft Biopsies and HLA Antibody Monitoring After Simultaneous Pancreas-Kidney Transplantation

L.E. Becker^{a,*}, P. Hallscheidt^b, S.M. Schaefer^a, K. Klein^a, L. Grenacher^b, R. Waldherr^c, S. Macher-Goepfing^c, P. Schemmer^d, A. Mehrabi^d, C. Suesal^e, M. Zeier^a, and C. Morath^a

^aDivision of Nephrology, University of Heidelberg, Heidelberg, Germany; ^bDiagnostic and Interventional Radiology, University of Heidelberg, Heidelberg, Germany; ^cInstitute of Pathology, University of Heidelberg, Heidelberg, Germany; ^dDepartment of General, Visceral and Transplant Surgery, University of Heidelberg, Heidelberg, Germany; and ^eInstitute of Immunology, University of Heidelberg, Heidelberg, Germany

ABSTRACT

Background. In simultaneous pancreas-kidney transplantation (SPKT), monitoring of the pancreas allograft is more complex than the kidney allograft due to difficulties in obtaining pancreas histology and weak clinical evidence supporting the role of donor-specific antibodies (DSA).

Methods. We performed a single-center retrospective analysis of all 17 SPKT recipients who underwent a total of 22 pancreas allograft indication biopsies from October 2009 to September 2012. Fifteen patients had at least 2 DSA measurements: pretransplantation and at the time of biopsy.

Results. All 7 patients (100%) with post-transplantation DSA-positivity (de novo: n = 6; persistent: n = 1) at biopsy had at least 1 rejection episode either of the pancreas (n = 4) or the kidney (n = 3), with 3 antibody-mediated rejections (AMR). In contrast, only 4 of 8 patients (50%) without post-transplantation DSA had evidence of rejection, with 1 AMR. Findings during pancreas allograft biopsy procedures led to a change of immunosuppressive therapy in 11 of 15 (73%) patients. Patient survival, graft survival, and function were not adversely affected by the presence of post-transplantation DSA. One major and 2 minor procedure-related complications occurred during the pancreas biopsies.

Conclusions. In this small retrospective analysis, pancreas allograft histology provided the most therapeutically relevant information, rather than the kidney histology or DSA monitoring.

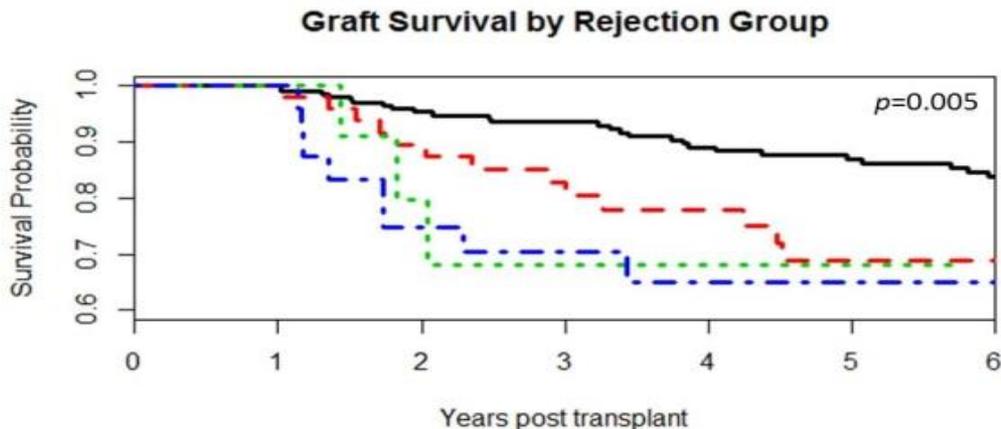
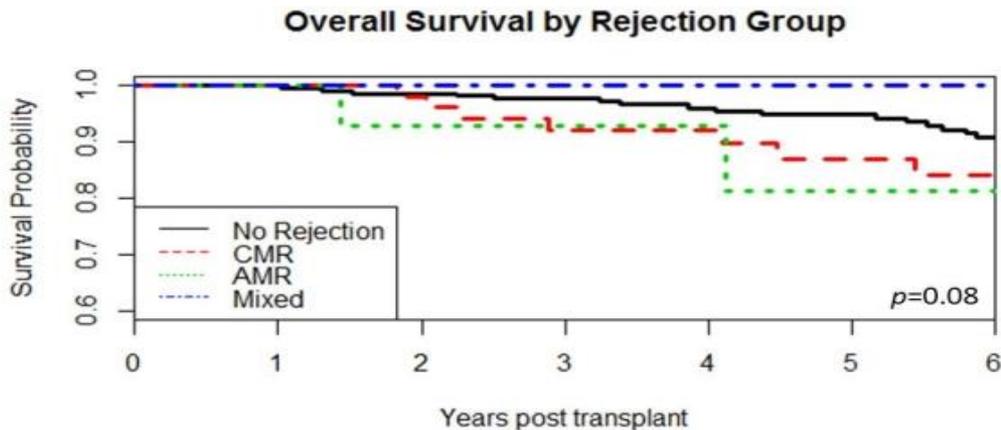


Figure 1. Overall Patient (A) and Graft (B) Survival for Patients with AMR, CMR, Mixed Rejection, or No Rejection.

Antibody-Mediated Rejection in Pancreas Transplantation.

O. Serrano,¹ D. Vock,² E. Finger,¹ R. Kandaswamy,¹ D. Sutherland,¹ T. Dunn.¹

¹Surgery, Univ. of Minnesota, Minneapolis, MN

²Biostatistics, University of Minnesota, Minneapolis, MN.

Meeting: [2016 American Transplant Congress](#)

Abstract number: 485

2017 Banff Pancreas Session

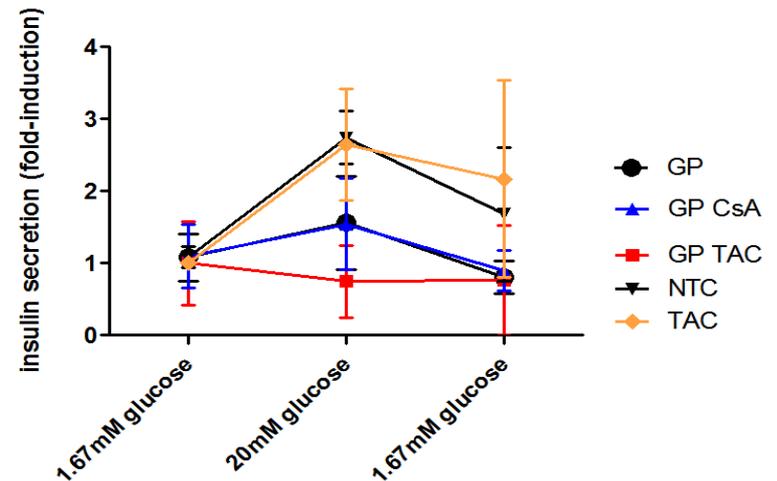
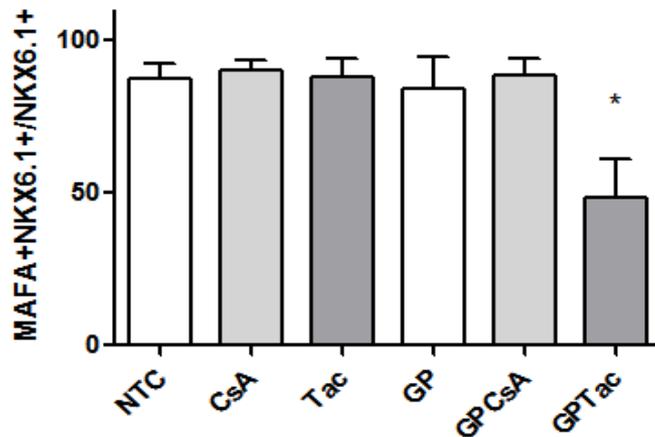
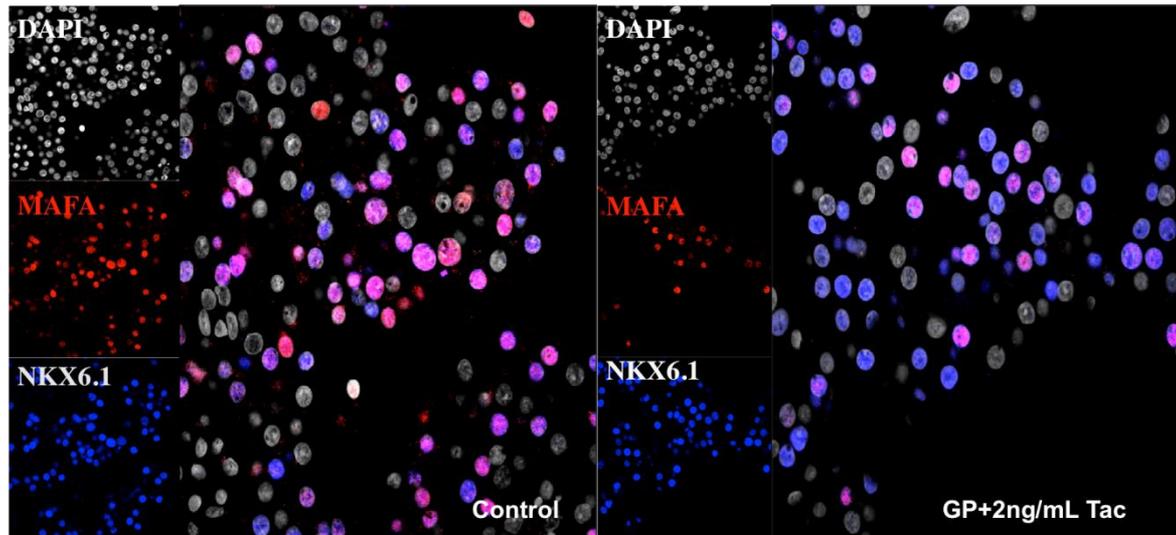
- Julien Branchereau, Nantes, France
 - Pancreas perfusion with hypothermic machine:
Pancreas and duodenal histology up to 24 hours.

Novel, well developed protocol and technique with excellent tissue preservation: normal appearing gross and microscopic morphology.

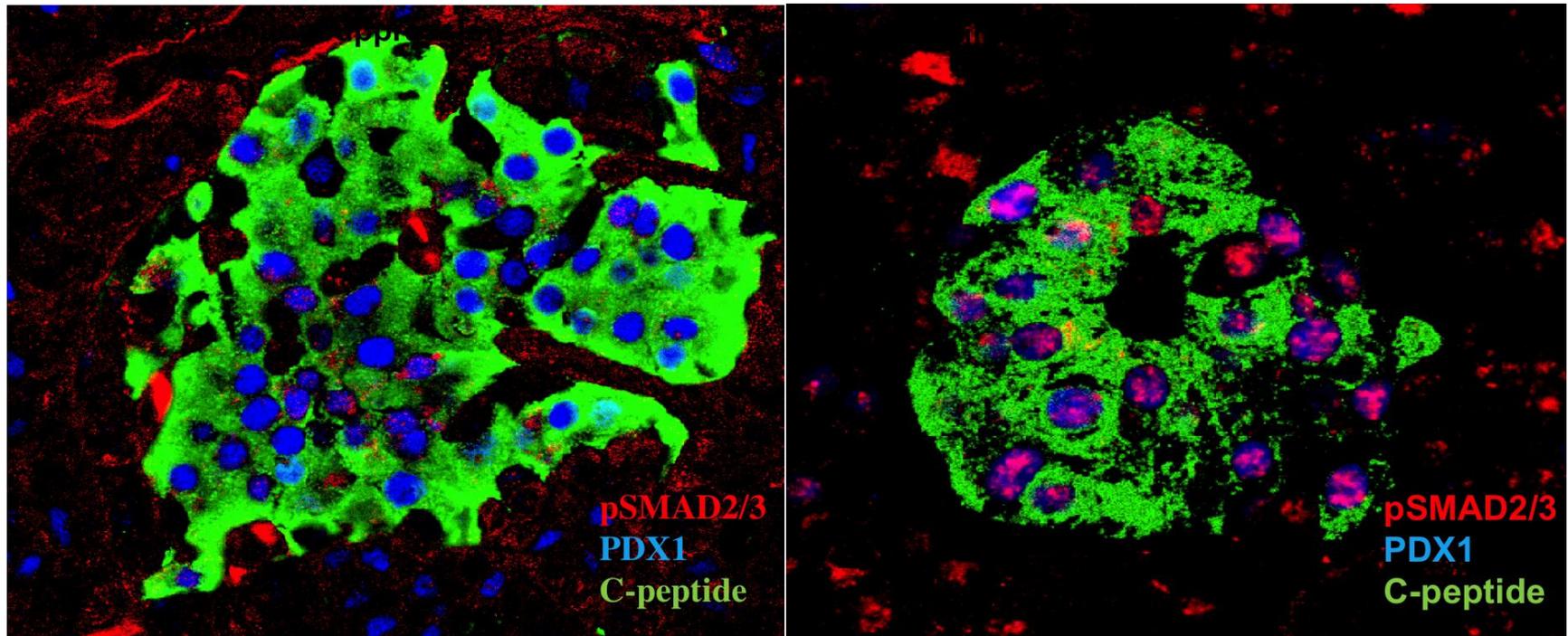
Javier Trinanes Ramos, Leiden, The Netherlands

- Effect on immunosuppressive therapies on transplanted islets and pancreas.
 - Studies of transcription factors related to Beta cell differentiation and insulin secretion

1. Nuclear levels of the transcription factor MAFA in β -cells as an early marker of cell dysfunction.
2. Tacrolimus-induced β -cell failure may be related to this loss besides calcineurin inhibition



Tacrolimus-based immunotherapies induce a higher activation of the TGF β pathways, related with cytostatic responses and de-differentiation.



This mechanism rather than toxicity and apoptosis could be the cause of Tac-related β -cell dysfunction.

- Steve Bartlett, Baltimore, MD USA

Outcome of pancreas transplantation alone with portal venous drainage vs. systemic venous drainage

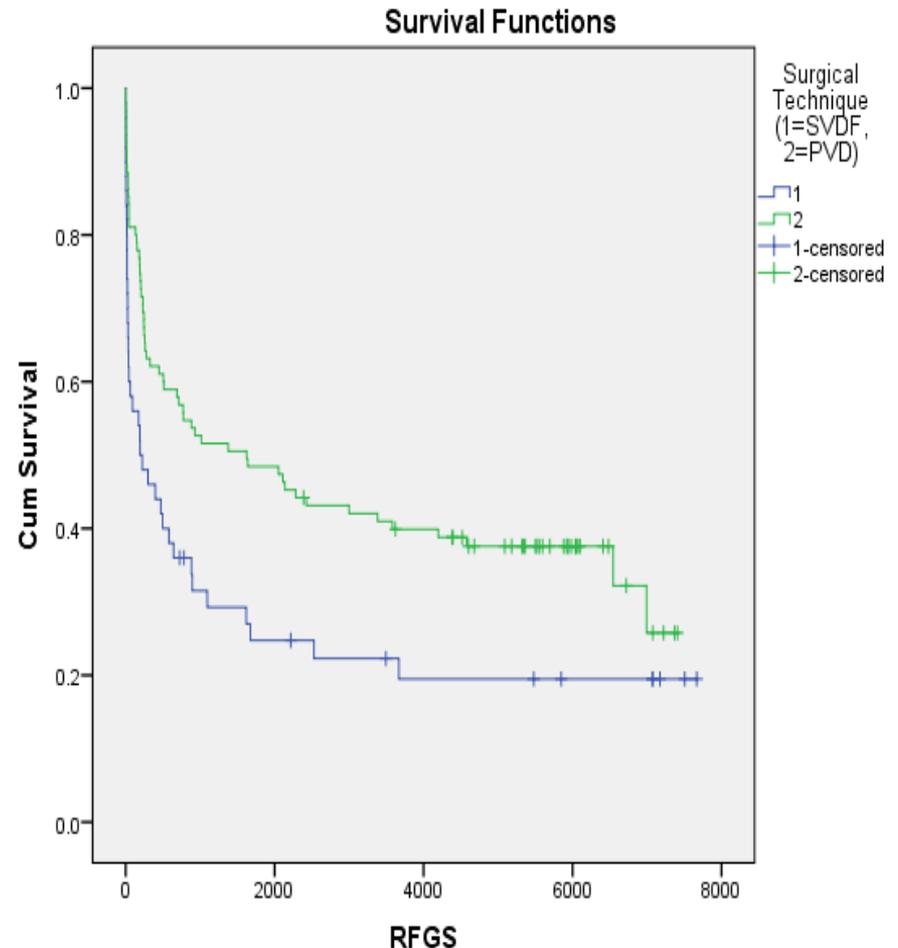
Rejection free graft

survival:

1 year:

SVD: 46%

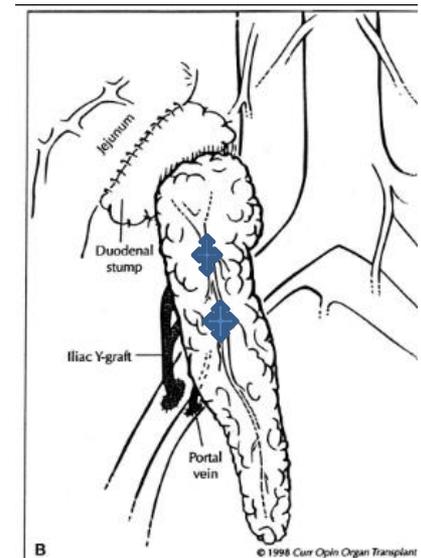
PVD: 62%



- Steve White
New Castle, United Kingdom

Vascular remodeling following whole pancreas transplantation

CT scans at 3 months post transplantation demonstrate significant and abrupt narrowing of the vascular lumina of larger vessels with no thrombosis.



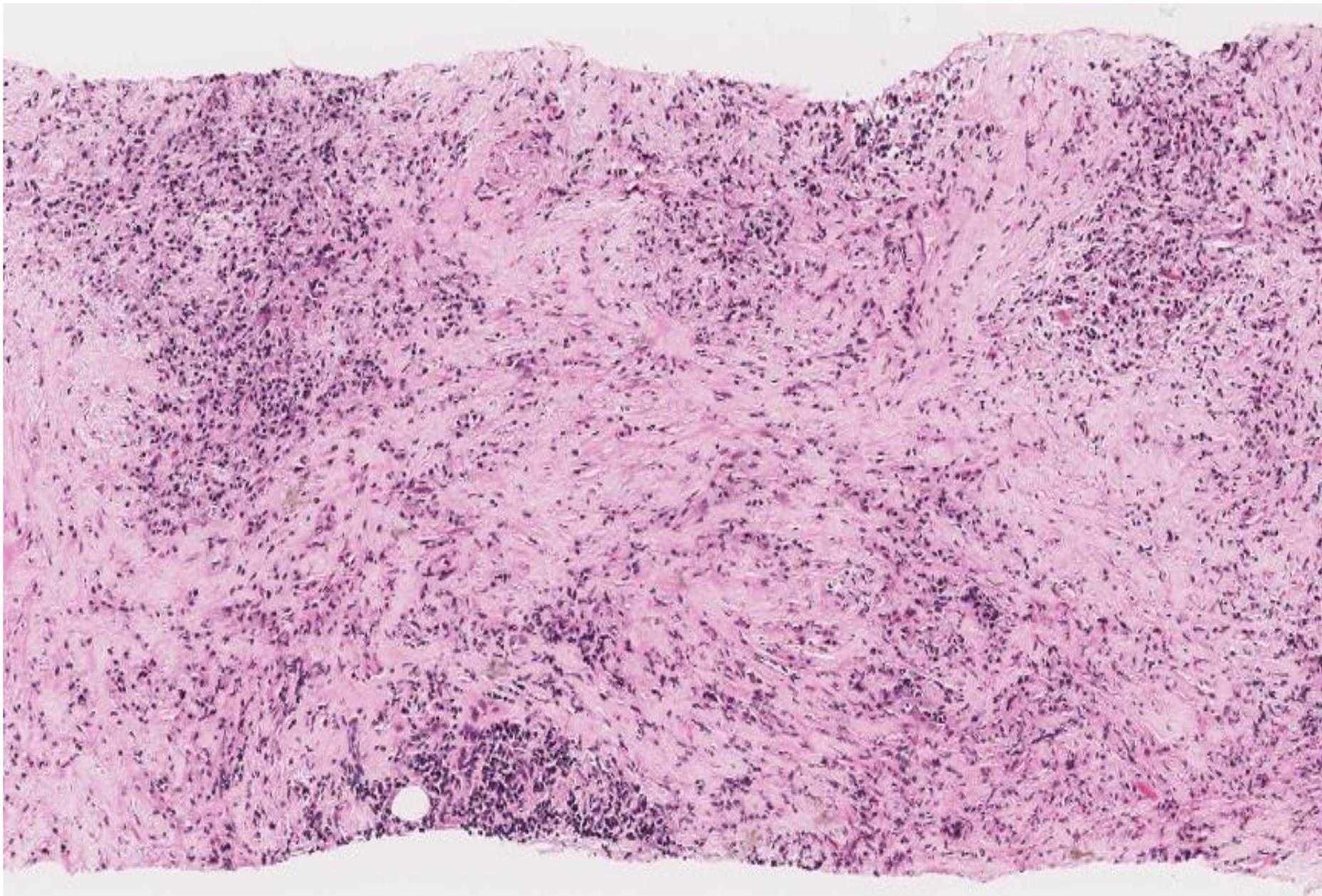
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John Papadimitriou, Baltimore MD

- Histology of refractory pancreas rejection

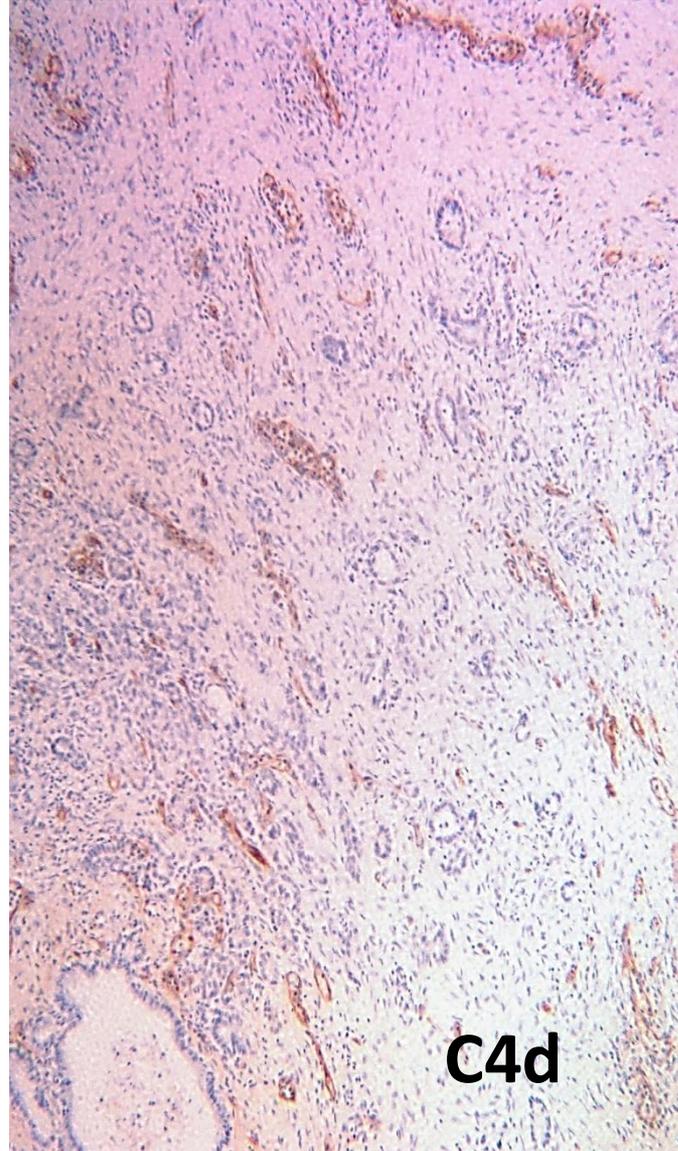
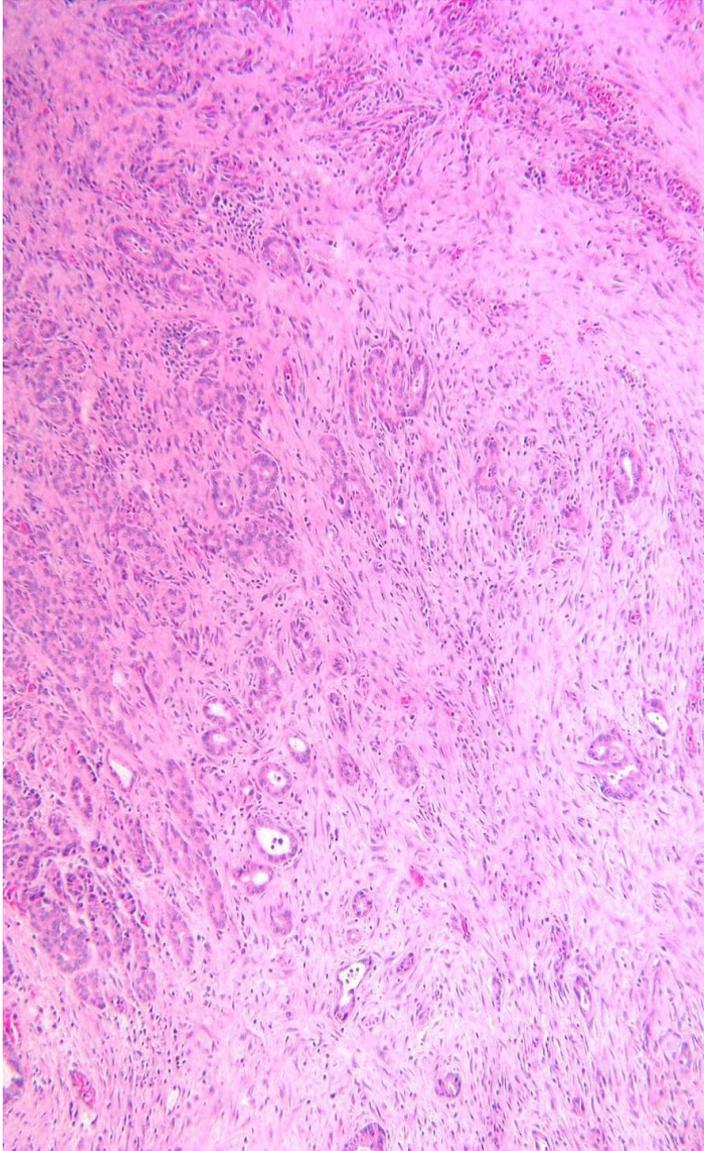
Persistent/refractory rejection

- Features of active rejection
- Features of evolving, chronic tissue damage



Chronic active TCMR

Chronic active AMR



- Pablo Uva (Buenos Aires Argentina)
 - Comparison between rejection in pancreas and kidney biopsies in SPK patients with graft dysfunction (in one or both organs)
 - Discordance between the Pancreas and the Kidney with respect to the presence and grade of rejection is seen in up to 30% of cases.

Maria Fernanda Toniolo (Buenos Aires Argentina)

- Impact of BK nephritis in pancreas transplant recipients

PVN occurred in 6% of patients with SPK and IS reduction was complicated also with pancreas allograft rejection. With early diagnosis there was no graft loss related to PVN or rejection.

Diego Cantarovich, Nantes, France

Co-chair

- Case Study: SPK recipient with acute loss of glycemic control 6 years post-transplantation

Recurrence of autoimmune diabetes

Clinical

Serological

Histological studies

Good response to aggressive IS treatment

Igls, Austria



Igls classification of β -cell graft function

Draft (M. Rickels, P. Stock, J. Odorico) for IPITA and EPITA

Functional Status	HbA1c (%)	Severe Hypoglycemic Events	Insulin requirements	C-peptide	Success
Optimal	≤ 6.5	None	No	>Baseline	Yes
Good	< 7.0	None	<50% Baseline	>Baseline	Yes
Marginal	≥ 7.0	<Baseline (footnotes)	$\geq 50\%$ Baseline (footnotes)	>Baseline	No (footnotes)
Failure	Baseline	Baseline (footnotes)	Baseline	Baseline (Footnotes)	No

Future Opportunities and Challenges

- Pathology studies - outcomes should use the current definitions of graft function/failure (upcoming Iglis classification).
- Define the pathological basis for the various functional states after whole pancreas transplants.
 - Define the impact of TCMR and AMR on the islets

Future Opportunities and Challenges

- Acknowledge similarities with islets in islet Tx including Beta cell stresses and exhaustion.
 - Islet transplantation
- Familiarize ourselves with the advances and challenges of pancreas and islet tissue engineering and attempt to bridge traditional and innovative technologies for the benefit of both areas.
 - Islet encapsulation

- Thank you!

- Gràcies!

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