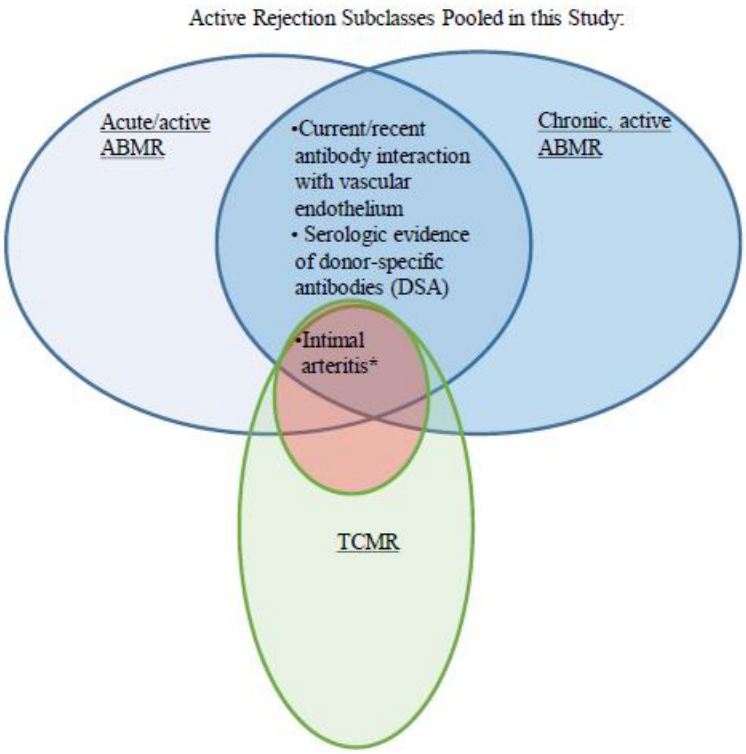
SUPPLEMENTAL MATERIALS for Bloom et al., Cell-Free DNA and Active Rejection in Kidney Allografts



Supplemental Figure 1. Diagram illustrating the three rejection subclasses included in the primary analysis and the overlapping elements of the Banff Working Group's histologic criteria for diagnosis of TCMR, acute/active ABMR and chronic active ABMR. * Intimal arteritis or transmural intimal arteritis are TCMR (types IIA, IIB, and III) and are also criteria for acute/active ABMR.

Supplemental Table 1. Patient Characteristics

Clinical Characteristic	All DART Patients	DART Study Cohort	Active Rejection Group	No Active Rejection Group	Renal Transplant Patients in U.S. (2015)[a]
Number of Patients	384	102	27	75	17,878
Race					
Black or African American	133 (35%)	36 (35 %)	13 (48 %)	23 (31 %)	5012 (28%)
White	187 (49%)	54 (53 %)	13 (48 %)	41 (55 %)	8232 (46%)
Native Hawaiian or Other Pacific Islander	2 (15)	1 (1 %)	1 (4 %)	0 (0 %)	79 (0.4%)
Hispanic/Latino	32 (8%)	4 (4 %)	0 (0 %)	4 (5 %)	3119 (17%)
Asian	7 (2%)	1 (1 %)	0 (0 %)	1 (1 %)	1141 (6%)
Other	23 (6%)	6 (6 %)	0 (0 %)	6 (8 %)	295 (1.7%)
Male Sex	220 (57%)	61 (60 %)	16 (59 %)	45 (60 %)	10877 (61%)
Age at Enrollment	49 ± 13	51 ± 14	46 ± 16	53 ± 13	Not Available
Days Post Transplant	553 ± 1262	1131 ± 1391	968 ± 1107	1189 ± 1482	Not Available
CMV Serologic Status					
D-/R+	86 (22%)	17 (17 %)	4 (15 %)	13 (17 %)	24% (deceased donor), 20.5% (living donor)
D+/R+	125 (33%)	29 (28 %)	5 (19 %)	24 (32 %)	43.1% (deceased donor), 34.4% (living donor)
D-/R-	52 (14%)	19 (19 %)	3 (11 %)	16 (21 %)	12.4 % (deceased donor), 23.2% (living donor)
D+/R-	44 (11%)	13 (13 %)	4 (15 %)	9 (12 %)	18.6 % (deceased donor), 15.8% (living donor)
Unknown	77 (20%)	24 (24 %)	11 (41 %)	13 (17 %)	[b](Ref SRTR)
Donor Type					
Deceased donor	248 (65%)	62 (61 %)	20 (74 %)	42 (56 %)	12,250 (69%)
Living unrelated	72 (19%)	26 (25 %)	2 (7 %)	24 (32 %)	2972 (17%)
Living related	63 (16%)	14 (14 %)	5 (19 %)	9 (12 %)	2656 (15%)
Child	13 (3%)	5 (5 %)	2 (7 %)	3 (4 %)	744 (4.1%)
Sibling	26 (7%)	6 (6 %)	2 (7 %)	4 (5 %)	1024 (6%)
Parent	8 (2%)	1 (1 %)	0 (0 %)	1 (1 %)	462 (2.6%)
Half Sibling	1 (0%)	0 (0 %)	0 (0 %)	0 (0 %)	55 (0.3%)
Other Biological Blood relation	15 (4.1%)	2 (2%)	1 (4 %)	1 (1 %)	362 (2%)
Creatinine	2.2 ± 1.6	2.4 ± 1.3	2.5 ± 1.0	2.4 ± 1.4	Not Available
EGFR		35 ± 19	32 ± 12	36 ± 21	Not Available

HLA Class 1 No. of Mismatches (A, B)		2.6 ± 1.4	2.7 ± 1.4	2.6 ± 1.4	[c](Ref SRTR)
HLA Class 2 No. of Mismatches (DR)		1.1 ± 0.7	1.2 ± 0.6	1.1 ± 0.8	[c](Ref SRTR)
Weight (kg)		84 ± 20	85 ± 19	84 ± 21	Not Available
Height (cm)		171 ± 9	170 ± 10	171 ± 8	Not Available

[a] Information from the Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients Report (http://www.srtr.org) as of August 2016.

[b] D Unk/R+: 0.2% (deceased donor), 1.9% (living donor), D Unk/R-: 0.1% (deceased donor), 1.4% (living donor), D Unk/R Unk: 0% (deceased donor), 0.4% (living donor).

[c] Number of patients with A, B and DR mismatches: 0 Mismatches: 1235, 1 Mismatch: 368, 2 Mismatches: 1257, 3 Mismatches: 2720, 4 Mismatches: 4059, 5 Mismatches: 4811, 6 Mismatches: 2488, Unknown Mismatches: 160

Supplemental Table 2: Renal allograft biopsies and histology-based diagnoses of rejection

	For-Cause		Surveillance		Rejection Follow-Up		Total	
	Patients	Biopsies	Patients	Biopsies	Patients	Biopsies	Patients	Biopsies
Active Rejection	**52**	**58**	**1**	**1**	**1**	**2**	**53**	**61**
ABMR or mixed	**27**	**29**	**0**	**0**	**0**	**0**	**27**	**29**
Chronic, active ABMR	16	17	0	0	0	0	16	17
Acute/active ABMR	**12**	12	0	0	0	0	12	12
TCMR only	**27**	**29**	**1**	**1**	**1**	**2**	**28**	**32**
Type IA	**9**	9	1	1	0	0	**10**	10
Type IB	**12**	13	0	0	1	1	**12**	14
Type IIA	**5**	5	0	0	0	0	**5**	5
Type IIB	**0**	0	0	0	1	1	**1**	1
Type III	**2**	2	0	0	0	0	**2**	2
No Rejection**	**123**	**146**	**32**	**33**	**2**	**2**	**149**	**181**
Total	**170**	**204**	**33**	**34**	**3**	**4**	**206**	**242**

A total of 206 patients had 242 biopsies. 5 biopsies had findings of TCMR in addition to ABMR; these mixed forms of rejection are included among the ABMR class. ** The biopsy findings in the no rejection group are described in figure 7.

Supplemental Table 3, Participating Sites.

Clinical Site Name	**Principal Investigators/ Co-Investigators**
Baylor Research Institute, Dallas	Bernard Fischbach, MD
Baylor Scott&White Memorial Hospital, Temple	Mohanram Narayanan, MD
Cedars-Sinai Medical Center, Los Angeles	Stanley C. Jordan, MD
Cleveland Clinic Foundation, Cleveland	Emilio Poggio, MD/ Ziad Zaky, MD
Columbia University Medical Center, New York	David J. Cohen, MD/ Jae Chang, MD
Indiana University, Indianapolis	Asif Sharfuddin, MD
University of Alabama, Birmingham, Birmingham	Shikha Mehta, MD/ Rosalyn Mannon, MD
University of California, Los Angeles, Los Angeles	Suphamai Bunnapradist, MD
University of Maryland, Baltimore	Jonathan S. Bromberg, MD, PhD/ Matthew Weir, MD
University of Minnesota, Minneapolis	Arthur Matas, MD
University of Pennsylvania Health System, Philadelphia	Roy D. Bloom, MD
University of Pittsburgh Medical Center, Pittsburgh	Puneet Sood, MD/ Sundaram Hariharan, MD
Vanderbilt University, Nashville	Anthony Langone, MD
Washington University, St. Louis	Daniel C. Brennan, MD/ Rowena Delos Santos, MD