Supplementary Table S1. Participating Centers

Location	Principal investigators	Samples contributed
Birmingham, AL, USA	Roslyn Mannon	28
Barcelona, Spain	Daniel Serón and Joana Sellarés	71
Bronx, NY, USA	Enver Akalin	33
Manchester, UK	Declan de Freitas and Michael Picton	39
Baltimore, MD, USA	Jonathan Bromberg and Matt Weir	72
Berlin, Germany	Klemens Budde and Timm Heinbokel	12
Hannover, Germany	Gunilla Einecke	67
Harrisburg, PA, USA	Harold Yang and Seth Narins	12
Detroit, MI, USA	Milagros Samaniego-Picota	1
Paris, France	Carmen Lefaucheur, Alexandre Loupy	212
Poland	Marek Myslak and Agnieszka Perkowska-Ptasinska	2
San Antonio, TX, USA	Adam Bingaman	83
St Louis, MO, USA	Daniel Brennan and Andrew Malone	20
Minneapolis, MN, USA	Bertram Kasiske	6
Edmonton, AB, CA	Philip F Halloran	487
Minneapolis, MN, USA	Arthur Matas	76
Madison, WI, USA	Arjang Djamali	10
Vienna, Austria	Georg Böhmig and Farsad Eskandary	198
Richmond, VA, USA	Gaurav Gupta	250
TOTAL		**1679**

Supplementary Table S2. Patient demographics and biopsy data

Patient Demographics		**All patients (N=1381)**	**All archetype TCMR patients (N=161)**
Mean recipient age (range)		51 (8 – 91)	47 (10 – 78)
Recipient Gender Male (% male)		702 (51%)	100 (69%)
Ethnicity	Caucasian	607	79
	Black	171	24
	Other	147	23
	Not available[a]	456	35
Primary Disease	Diabetic nephropathy	211	24
	Hypertension / large vessel disease	94	16
	Glomerulonephritis / vasculitis	47	49
	Interstitial nephritis / pyelonephritis	26	10
	Polycystic kidney disease	125	9
	Others	767	21
	Unknown etiology	111	32
Mean donor age (range)		44 (0.03 – 85)	42 (1 – 80)
Donor gender (% male)		386 (28%)	48 (40%)
Donor type (% deceased donor transplants)		889 (64%)	98 (65%)
Latest kidney status (% of total)	Patient alive – graft functioning	1001 (80%)	101 (69%)
	Patient death - graft failure	231 (18%)	43 (29%)
	Patient death – cause other than graft failure	20 (2%)	3 (2%)
	Mean (median) follow-up (functioning grafts) in days	720 (405)	734 (393)
Clinical characteristics at time of biopsy		**All biopsies (N=1679)**	**All archetype TCMR biopsies (N=175)**
Median time of biopsy post-transplant (TxBx) in days (range)		650 (1 day – 34 years)	360 (6 days – 26 years)
Early biopsies (< 1 year) (% total)		709 (42%)	88 (50%)
Late biopsies (≥ 1 year) (% total)		966 (57%)[b]	87 (50%)
Indication for biopsy (% of total)	Primary non-function	10 (1%)	1 (1%)
	Rapid deterioration of graft function	292 (17%)	63 (36%)
	Slow deterioration of graft function	307 (18%)	33 (19%)

Stable impaired graft function	92 (5%)	11 (6%)
Investigate proteinuria/rejection/BK/creatinine	247 (15%)	30 (17%)
Delayed graft function	74 (4%)	6 (3%)
Others	617 (37%)	27 (15%)
Indication unknown	40 (2%)	4 (2%)

[a] Some centers preferred not to identify ethnicity

[b] Four biopsies had no date of transplant

Abbreviations: TxBx – time of biopsy posttransplant

Supplementary Table S3. List of transcript sets used in this paper[a]

Transcript set	Abbreviation	Description of the transcripts
TCMR-related	TCB	T cell burden (1)
	QCAT	Cytotoxic T cell associated (2)
ABMR-related	DSAST	DSA selective (3)
	NKB	NK cell transcript burden (1)
	ENDAT	Endothelial cell associated (4)
	GRIT	Interferon gamma-inducible (5)
Expressed in macrophages	QCMAT	Quantitative constitutive macrophageassociated (6)
	AMAT	alternative macrophage activationassociated (6)
Increased after recent injury	IRRAT	Injury-repair response associated (7)
	FICOL	Fibrillar collagen transcripts (8)
	IRITD3	Injury-repair induced transcripts, day 3 (9)
	IRITD5	Injury-repair induced transcripts, day 5 (9)
Atrophy-fibrosis	IGT	Immunoglobulin transcripts (10)

[a] https://www.ualberta.ca/medicine/institutes-centres-groups/atagc/research/gene-lists

Abbreviations: AMAT – alternative macrophage activation transcripts; DSAST - donor-specific antibody (DSA) selective transcripts; ENDAT – endothelial cell-associated transcripts; GRIT – interferon gamma-inducible transcripts; IGT – immunoglobulin transcripts; IRRAT – AKI transcripts; NKB – NK cell burden transcripts; QCAT - Cytotoxic T cell associated transcripts; QCMAT – quantitative constitutive macrophage-associated transcripts; TCB – T cell burden transcripts

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Supplementary Table S4. Relating MMDx signout diagnoses to archetype assignments in 1679 biopsies

	Archetype group assignments						***Row Totals***
MMDx signout assignments	**1 NR**	**2 TCMR1**	**3 TCMR2**	**4 EABMR**	**5 FABMR**	**6 LABMR**	
ABMR	70	0	5	192	175	67	*509*
Mixed	2	44	13	2	7	1	*69*
NR	898	0	0	6	0	1	*905*
pABMR	43	0	0	7	0	2	*52*
pTCMR	9	0	10	2	0	0	*21*
TCMR	18	31	72	1	0	1	*123*
Column Totals	*1040*	*75*	*100*	*210*	*182*	*72*	*1679*

pABMR, possible ABMR.
pTCMR, possible TCMR.

Supplementary Table S5. Top 20 genes by Spearman correlation decreased (negatively correlated) with time post-transplant within molecular TCMR biopsies >1 year (archetypes TCMR1/2, N=86)

Gene Symbol	Gene Name	PBT	Spearman correlation with time posttransplant [A]
SIGLEC11	sialic acid binding Ig-like lectin 11	(inflammation)	-0.45
CD8A	CD8a molecule	QCAT,TCMR-RAT	-0.42
ANKRD22	ankyrin repeat domain 22	GRIT3,TCMR-RAT	-0.42
ST8SIA5	ST8 alpha-N-acetyl-neuraminide alpha-2,8sialyltransferase 5		-0.42
LAG3	lymphocyte-activation gene 3	TCMR-RAT	-0.41
HLA-F	major histocompatibility complex, class I, F	GRIT3,TCMR-RAT	-0.39
NUSAP1	nucleolar and spindle associated protein 1	IRITD5,QCAT, endothelium	-0.39
HLA-F	major histocompatibility complex, class I, F	ABMR-RAT,GRIT3,RAT,Rej-RAT,TCMR-RAT	-0.38
NUSAP1	nucleolar and spindle associated protein 1	IRITD5,IRRAT950,LivGST_UP,QCAT	-0.38
CALCA	calcitonin-related polypeptide alpha		-0.37
MYRFL	myelin regulatory factor-like		-0.37
GMNN	geminin, DNA replication inhibitor		-0.37
UBE2T	ubiquitin-conjugating enzyme E2T (putative)	IRRAT950	-0.37
ATP6AP1	ATPase, H+ transporting, lysosomal accessory protein 1		-0.36
HLA-B	major histocompatibility complex, class I, B	GRIT1, Rej-RAT	-0.36
EOMES	eomesodermin	TCMR-RAT	-0.35
EOMES	eomesodermin	TCMR-RAT	-0.35
MAP3K15	mitogen-activated protein kinase kinase kinase 15	Dendritic cells	-0.35
GBP4	guanylate binding protein 4	GRIT3, Rej-RAT	-0.35
ZNF672	zinc finger protein 672		-0.35

[A] All P values<0.001

Abbreviations: PBTs are listed on our home page https://www.ualberta.ca/medicine/institutes-centres-groups/atagc/research/gene-lists

Supplementary Table 6. Top 20 genes increased (positively correlated) with time post-transplant within molecular TCMR biopsies >1 year (archetypes TCMR1/2, N=86)

Gene Symbol	Gene Name	PBT	Spearman correlation with time posttransplant[A]
COL23A1	collagen, type XXIII, alpha 1		0.42
IGHA1	immunoglobulin heavy constant alpha 1	IGT	0.39
RTN4RL2	reticulon 4 receptor-like 2		0.39
NFIA	nuclear factor I	HT1	0.38
IGHA1	immunoglobulin heavy constant alpha 1	IGT	0.38
IGH	immunoglobulin heavy locus	IGT	0.38
IGH	immunoglobulin heavy locus	IGT	0.37
MAP1LC3C	microtubule-associated protein 1 light chain 3 gamma		0.37
MOGAT2	monoacylglycerol O-acyltransferase 2	CT1	0.37
IGH	immunoglobulin heavy locus	IGT	0.37
PCSK1	proprotein convertase subtilisin		0.37
CLU	clusterin	IRITD5	0.37
SNAP91	synaptosomal-associated protein, 91kDa		0.37
NALCN	sodium leak channel, non-selective		0.36
IGH	immunoglobulin heavy locus	IGT	0.36
ABI3BP	ABI family, member 3 (NESH) binding protein	ENDAT	0.36
ADRA2C	adrenoceptor alpha 2C		0.36
CCDC122	coiled-coil domain containing 122	LT1	0.36
SLC6A1	solute carrier family 6 (neurotransmitter transporter, GABA), member 1		0.36
DEFB113	defensin, beta 113		0.36

[A] All P values<0.001

Abbreviations: PBTs are listed on our home page https://www.ualberta.ca/medicine/institutes-centres-groups/atagc/research/gene-lists