SUPPLEMENTARY MATERIALS

New Appendix #1: Brief description of the Joslin Kidney Study

The Joslin Kidney Study (JKS) is a longitudinal observation that aims to investigate the determinants and to describe the natural history of PRD in T1D. Results from this study and protocols used were previously published (8, 29-31). Participants were recruited from among 3,500 adults with T1D, 95% Caucasian, who attended the Joslin clinic between 1991 and 2009. According to the median values of ACR from 2 or more consecutive urine samples obtained during the 2-year period preceding enrollment (baseline), 3 study groups were assembled: Macro-Albuminuria (ACR ≥300 mg/g) (*n*= 526), Micro-Albuminuria (30≤ ACR <300 mg/g) (*n*= 563), and Normo-Albuminuria (ACR <30 mg/g) (*n*= 795). All participants were followed for 7-15 years. They had biannual examinations either during routine clinic visits or were invited for a special visit or were examined at their homes. Biospecimens obtained at examinations were stored in -85 °C. Serum creatinine was used to determine renal function at baseline and its changes during follow-up visits. Protocols to calibrate serum creatinine measurements over time were described previously (31). Estimates of GFR were obtained using the Chronic Kidney Disease Epidemiology Collaboration formula (33). To estimate the slope of eGFR decline, we extracted the linear component of every subject's trajectory with more than 5 measurements of eGFR. All JKS subjects were queried every 2 years against rosters of the United States Renal Data System to ascertain patients who developed ESKD. The last inquiry was conducted in 2015. In the present study PRD (primary outcome) was recognized if individuals' long term eGFR loss greater than or equal to 3 ml/min/1.73m^2/year or they developed ESKD within 7-15 years of follow-up (29-31, 34).

Supplementary Table S1: Effect estimates of tumor necrosis factor (TNF) receptors on risk of PRD in Micro-Albuminuria Study according to two definitions of decliners (eGFR loss ≥3 ml/min/1.73m^2/year and eGFR loss ≥5 ml/min/1.73m^2/year).

		Micro-Albuminuria Study *eGFR loss ≥3 ml/min/year* *n*= 148		**Micro-Albuminuria Study** *eGFR loss ≥5 ml/min/year* *n*= 148	
Gene Name	Protein name	OR	P value	OR	P value
TNF receptors associated with the both outcome					
TNF-R1A	TNF-R1	1.64	0.0015	1.59	0.0038
TNF-R1B	TNF-R2	1.86	0.0001	1.72	0.0009
TNF-R3	LTBR	1.46	0.0140	1.44	0.0210
TNF-R4	OX40	1.64	0.0017	1.52	0.0085
TNF-R6	FAS	1.49	0.0090	1.44	0.0210
TNF-R6B	DcR3	1.56	0.0043	1.52	0.0085
TNF-R7	CD27	1.73	0.0006	1.69	0.0014
TNF-R10A	TRAIL-R1	1.61	0.0024	1.58	0.0047
TNF-R10B	TRAIL-R2	1.40	0.0290	1.46	0.0170
TNF-R11A	RANK	1.43	0.0200	1.43	0.0250
TNF-R14	HVEM	1.60	0.0024	1.63	0.0024
TNF-R21	DR6	1.49	0.0100	1.52	0.0085
TNF-R27	EDA2R	1.45	0.0150	1.38	0.0410
TNF Receptors inconsistent associations					
TNF-R10C	TRAIL-R3	1.22	0.1900	1.22	0.2000
TNF-R11B	OPG	1.36	0.0410	1.24	0.1500
TNF-R12A	TWEAKR	1.24	0.1600	1.31	0.0810
TNF-R13B	TACI	1.30	0.0820	1.36	0.0520
TNF-R19	TROY	1.29	0.0890	1.25	0.1500
TNF-R19L	RELT	1.24	0.1400	1.40	0.0300
Findings for TNF ligands					
TNF-L5	CD40-L	0.93	0.6300	0.89	0.4300
TNF-L6	FASLG	1.13	0.4100	0.94	0.7000
TNF-L7	CD70	1.39	0.0320	1.25	0.1500
TNF-L10	TRAIL	1.36	0.0460	1.16	0.3200
TNF-L13	APRIL	1.18	0.2700	1.14	0.4000
TNF-L13B	BAFF	1.33	0.0580	1.30	0.0840

Revised Supplementary Table S2. Comparison of effect estimates for risk of ESKD according to baseline plasma concentration of TNF receptors measured by SOMAscan, OLINK, and ELISA in 130 individuals with Macro-Albuminuria.

		Tumor necrosis factor (TNF) Receptor Measured:					
		By SOMAscan		By OLINK		By ELISA	
		HR	$-\log_{10}P$	HR	$-\log_{10}P$	HR	$-\log_{10}P$
TNF-R1A	(TNFR1)	1.49	2.80	1.64	3.72	1.40	2.19
TNF-R1B	(TNFR2)	1.82	5.07	1.62	3.85	-	-
TNF-R4	(OX40)	1.36	1.94	1.49	2.82	-	-
TNF-R8	(CD30)	1.15	0.57	-	-	-	-
TNF-R9	(4-1BB)	1.26	1.28	-	-	-	-
TNF-R14	(HVEM)	1.15	0.62	1.73	4.54	-	-
TNF-R19	(TROY)	1.50	2.80	2.15	6.33	-	-
TNF-R19L	(RELT)	1.46	2.51	1.63	4.00	-	-
TNF-R21	(DR6)	1.25	1.10	1.32	1.49	-	-
TNF-R27	(XEDAR)	1.36	1.87	1.63	4.01	-	-
TNF-R3	(LTBR)	1.01	0.03	1.96	5.26	-	-
TNF-R6	(Fas)	-	-	1.32	1.70	-	-
TNF-R6B	(DcR3)	1.27	1.36	1.83	5.40	1.56	2.55
TNF-R7	(CD27)	0.75	1.62	1.60	3.51	1.63	4.09
TNF-R10A	(TRAIL R1)	0.61	4.00	1.56	3.32	-	-
TNF-R10B	(TRAIL R2)	-	-	2.00	6.47	-	-
TNF-R11A	(RANK)	0.90	0.41	1.68	3.96	-	-
TNF-R12A	(Fn14)	1.21	0.90	1.74	3.85	-	-
TNF-R10C	(DcR1)	-	-	1.03	0.10	-	-
TNF-R11B	(OPG)	0.95	0.15	1.00	0.01	-	-
TNF-R13B	(TACI)	1.04	0.12	1.21	0.92	-	-
TNF-R13C	(BAFFR)	0.91	0.34	-	-	-	-
TNF-R17	(BCMA)	0.76	1.59	-	-	-	-
TNF-R18	(GITR)	1.18	0.74	-	-	-	-
TNF-R25	(DR3)	0.87	0.62	-	-	-	-
EDAR	(EDAR)	1.16	0.64	-	-	-	-
TNF-R5	(CD40)	-	-	-	-	-	-
TNF-R10D	(DcR2)	-	-	-	-	-	-
TNF-R13A	(BCMA)	-	-	-	-	-	-
TNF-R16	(NGFR)	-	-	-	-	-	-

Statistical significance is considered if $-\log_{10}$ P-value ≥1.30, or p ≤0.05. Please notice that HRs were higher almost for all TNF receptors measured by OLINK platform. Out of 16 TNF receptors measured by both platforms, 9 showed similar results (7 positive and 2 negative), and 7 showed discrepant results (positive on OLINK and negative on SOMAscan). HR, hazard ratio; ESKD, end stage kidney disease; TNF, tumor necrosis factor.

Supplementary Table S3. Tumor necrosis factor (TNF) receptors and ligands included in OLINK 11 panels. (A) Name of OLINK 11 panels and tumor necrosis factor (TNF) receptors and ligands included in each panel. (B) Spearman correlations coefficients (r_s) between eGFR slope and 6 TNF proteins present on INFLAMMATION Panel. Measurements were done in 38 subjects.

A.

Name of OLINK 11 Panel	**Name of TNF Receptors and/or Ligands included in each OLINK Panel**
CARDIOVASCULAR II(v.5002)	**TNF-R10A (TNFRSF10A)***, TNF-R10B (TRAIL-R2), TNF-R11A (TNFRSF11A), TNF-R13B (TNFRSF13B), TNF-L5 (CD40-L)
CARDIOVASCULAR III(v.6002)	TNF-R1A (TNF-R1), TNF-R1B (TNF-R2), TNF-R3 (LTBR), TNF-R6 (FAS), TNF-R10C (TNFRSF10C), **TNF-R11B (OPG)***, TNF-R14 (TNFRSF14), TNF-L13B (TNFSF13B)
DEVELOPMENT(v.3501)	TNF-R19L (RELT)
NEUROLOGY(v.8001)	TNF-R12A (TNFRSF12A), TNF-R21 (TNFRSF21), TNF-R27 (EDA2R)
ONCOLOGY II(v.7001)	TNF-R6B (TNFRSF6B), TNF-R7 (CD27), TNF-R19 (TNFRSF19), TNF-L6 (FASLG), TNF-L7 (CD70), **TNF-L10 (TRAIL)***, TNF-L13 (TNFSF13)
CARDIOMETABOLIC(v.3601)	-
IMMUNE RESPONSE(v.3201)	EDAR
CELL REGULATION(v.3701)	**TNF-R10A (TNFRSF10A)***
INFLAMMATION(v.3004)	TNF-R5 (CD40), TNF-R9 (TNFRSF9), **TNF-R11B (OPG)***, **TNF-L10 (TRAIL)*,** TNF-L1A (TNF), TNF-L1B (LTA), TNF-L11 (TRANCE), TNF-L12 (TWEAK), TNF-L14 (TNFSF14)
METABOLISM(v.3401)	-
ORGAN DAMAGE(v.3301)	-

*The 5 panels enclosed with box were used in our study. The TNF receptors or ligands in bold letters with asterisks are duplicated on 2 panels.

B.

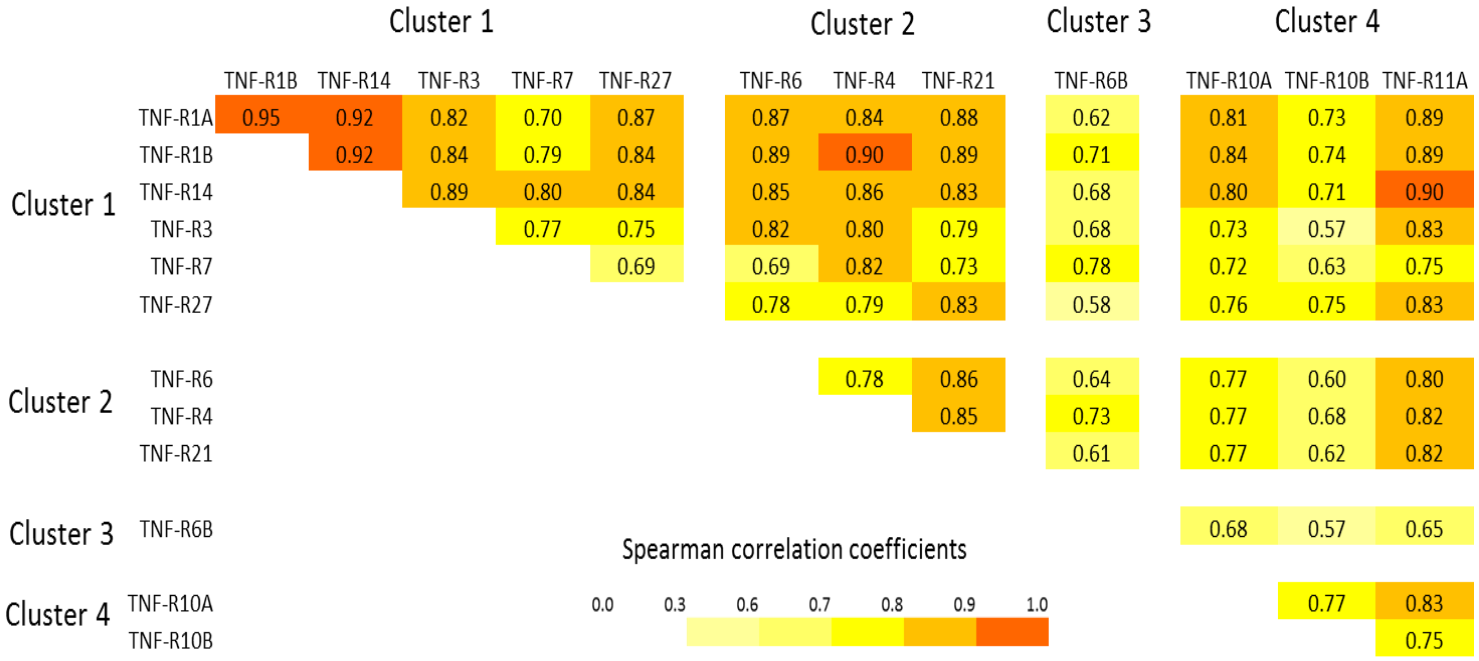
	r_s	P value	*n*
TNF-R5	-0.25	0.1325	38
TNF-R9	-0.12	0.4552	38
TNF-L1B	0.04	0.827	38
TNF-L11	-0.08	0.6275	38
TNF-L12	0.03	0.8383	38
TNF-L14	-0.08	0.6238	38

New Supplementary Table S4: Spearman rank correlation coefficients plasma concentration of 13 tumor necrosis factor (TNF) receptors and duration of plasma storage in individuals in Macro-Albuminuria (*n*= 24).

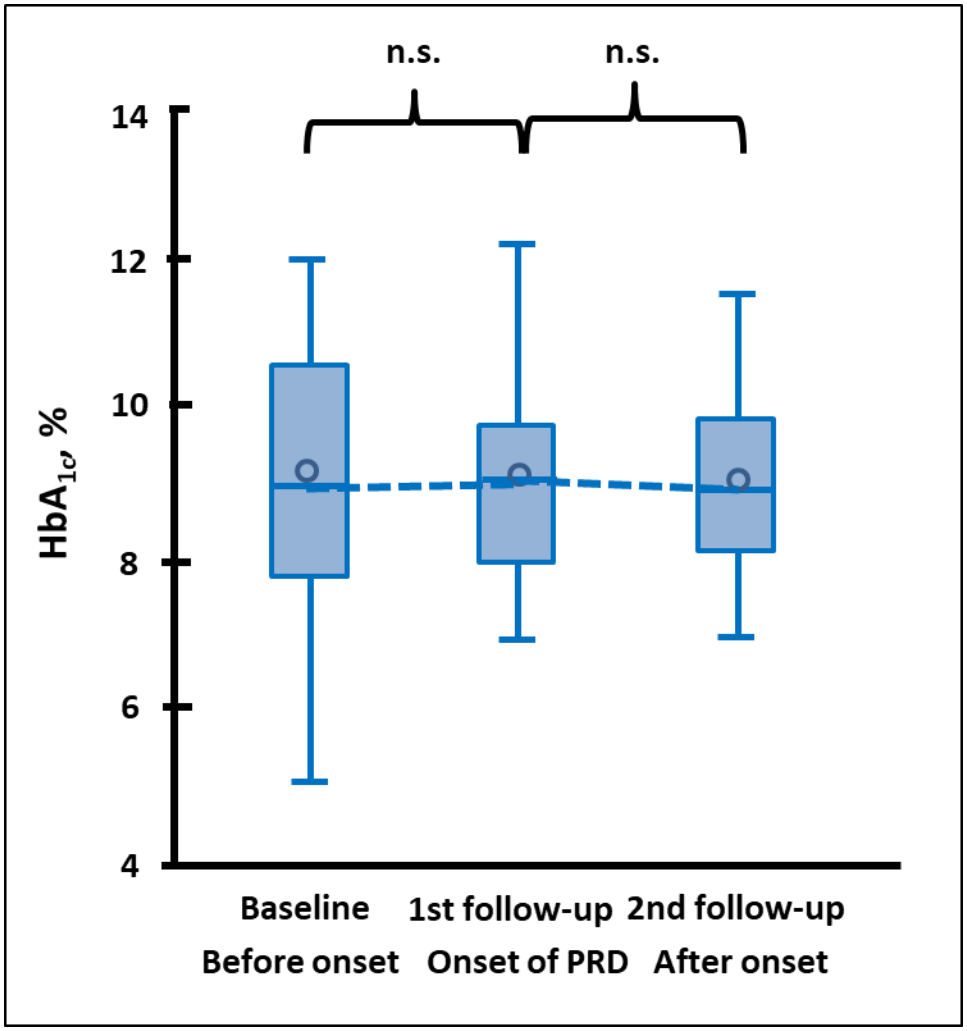
	Baseline		1st follow-up		2nd follow-up	
	r_s	P Value	r_s	P Value	r_s	P Value
TNF-R1A	0.18	0.4057	0.10	0.6360	0.09	0.6875
TNF-R1B	0.03	0.8925	0.04	0.8416	0.04	0.8432
TNF-R14	0.11	0.6188	0.00	0.9903	0.03	0.8861
TNF-R3	0.27	0.2034	0.13	0.5420	0.21	0.3172
TNF-R7	-0.06	0.7744	-0.07	0.7435	0.14	0.5244
TNF-R27	-0.25	0.2472	0.00	0.9936	0.11	0.6158
TNF-R4	0.28	0.1822	0.00	0.9952	0.06	0.7758
TNF-R21	0.29	0.1698	0.11	0.5945	0.31	0.1344
TNF-R6	0.32	0.1214	0.30	0.1523	0.46	0.0223
TNF-R6B	-0.15	0.4944	0.13	0.5474	0.02	0.9132
TNF-R10A	-0.15	0.4944	0.10	0.6360	-0.01	0.9678
TNF-R10B	-0.09	0.6728	0.00	0.9839	0.10	0.6535
TNF-R11A	-0.08	0.7238	0.03	0.9068	-0.08	0.7236

*Median duration of storage at baseline, 1st and 2nd follow-ups were 21 years (interquartile range, 17-23), 17 years (15-18), and 13 years (10-17), respectively.

Supplementary Figure S1. Matrix of Spearman correlation coefficients among baseline plasma concentrations for 13 tumor necrosis factor (TNF) receptors in the combined studies (*n*= 343).



Supplementary Figure S2. Distribution of HbA_{1c} (%) at three examinations in individuals (*n*=24) included in the Macro-Albuminuria sub-cohort.



New Supplementary Figure S3: Matrix of Spearman correlation coefficients among plasma concentrations for 6 tumor necrosis factor (TNF) receptors (TNF-R3, TNF-R6B, TNF-R7, TNF-R10A, TNF-R11A, TNF-R12A) determined in patients who had both SOMAscan and OLINK measurements (*n*= 130). (A) Correlation coefficients among TNF receptors measured using OLINK platform. (B) Correlation coefficients among TNF receptors measured using SOMAscan platform.