

Table S1. Relationships of biomarkers and ocular surface parameters in the DED-only group. R_s and p values are shown, as well as the clinical interpretation of these correlations. A p value of ≤ 0.05 was considered statistically significant. Due to there being a total of 17 subjects in the DED-only group, an r_s of > 0.46 is considered as a positive correlation and < -0.46 is considered as a negative correlation [47, 48].

Biomarkers	TER			fTBUT			CFS			Schirmer 1		
	r_s	p -value	Interpretation	r_s	p -value	Interpretation	r_s	p -value	Interpretation	r_s	p -value	Interpretation
IL-1RA	-0.1	0.7	N/A	-0.4	0.1	N/A	0.1	0.6	N/A	-0.2	0.4	N/A
IL-8	0.2	0.5	N/A	-0.02	0.9	N/A	0.1	0.6	N/A	-0.05	0.8	N/A
EGF	-0.5	0.05	\uparrow TER \downarrow EGF	0.1	0.6	N/A	-0.4	0.2	N/A	-0.03	0.9	N/A
Fractalkine	0.1	0.7	N/A	-0.2	0.4	N/A	0.2	0.5	N/A	0.02	0.9	N/A
IL-10	0.08	0.8	N/A	0.1	0.6	N/A	-0.02	0.9	N/A	0.08	0.7	N/A
IL-1 β	0.3	0.3	N/A	-0.008	0.9	N/A	0.07	0.8	N/A	0.09	0.7	N/A
IL-6	0.6	0.02	\uparrow TER \uparrow IL-6	-0.02	0.9	N/A	-0.008	0.9	N/A	-0.5	0.05	\downarrow Schirmer \uparrow IL-6
IP-10	0.09	0.7	N/A	-0.2	0.4	N/A	0.3	0.2	N/A	-0.1	0.6	N/A
MCP-1	-0.4	0.2	N/A	-0.2	0.5	N/A	0.09	0.7	N/A	0.08	0.8	N/A
TNF- α	0.02	0.9	N/A	-0.2	0.4	N/A	0.1	0.6	N/A	-0.3	0.2	N/A
VEGF	-0.4	0.09	N/A	0.3	0.3	N/A	-0.2	0.5	N/A	0.2	0.5	N/A
Leptin	0.5	0.02	\uparrow TER \uparrow Leptin	-0.1	0.7	N/A	0.2	0.3	N/A	-0.5	0.03	\downarrow Schirmer \uparrow Leptin
Insulin	-0.1	0.7	N/A	-0.3	0.3	N/A	0.04	0.9	N/A	-0.4	0.2	N/A

Key words: TER, tear evaporation rate; fTBUT, fluorescein tear break-up time; CFS, corneal fluorescein staining; r_s , Spearman correlation coefficient; N/A, not applicable.

Note: Statistically significant differences and their clinical interpretation are reported in *italics*.

Table S2. Relationships of biomarkers and ocular surface parameters in the T2D+DED group. r_s and p values are shown, as well as the clinical interpretation of these relationships. A p value of ≤ 0.05 is considered as statistically significant. Due to there being a total of 47 subjects in the T2D+DED group, an r_s of > 0.27 is considered as a positive relationship and < -0.27 is considered as a negative relationship [47, 48].

Biomarkers	TER			fTBUT			CFS			Schirmer 1 test		
	r_s	p -value	Interpretation	r_s	p -value	Interpretation	r_s	p -value	Interpretation	r_s	p -value	Interpretation
IL-1RA	-0.1	0.4	N/A	-0.3	<i>0.04</i>	<i>↓fTBUT ↑IL-1RA</i>	0.2	0.1	N/A	-0.5	<i><0.001</i>	<i>↓Schirmer ↑IL-1RA</i>
IL-8	0.2	0.1	N/A	-0.2	0.2	N/A	0.3	<i>0.04</i>	<i>↑CFS ↑IL-8</i>	-0.1	0.4	N/A
EGF	0.1	0.3	N/A	-0.05	0.7	N/A	-0.03	0.8	N/A	-0.06	0.7	N/A
Fractalkine	-0.1	0.5	N/A	-0.001	0.9	N/A	0.01	0.9	N/A	-0.1	0.4	N/A
IL-10	-0.3	<i>0.05</i>	<i>↑TER ↓IL-10</i>	0.2	0.1	N/A	-0.08	0.6	N/A	0.02	0.9	N/A
IL-1 β	-0.3	<i>0.02</i>	<i>↑TER ↓IL-1β</i>	0.1	0.3	N/A	0.1	0.5	N/A	-0.01	0.9	N/A
IL-6	0.03	0.9	N/A	-0.3	<i>0.05</i>	<i>↓fTBUT ↑IL-6</i>	0.3	<i>0.02</i>	<i>↑CFS ↑IL-6</i>	-0.3	0.08	N/A
IP-10	-0.03	0.9	N/A	-0.06	0.7	N/A	-0.2	0.1	N/A	-0.1	0.4	N/A
MCP-1	0.006	0.9	N/A	-0.2	0.3	N/A	0.3	0.03	<i>↑CFS ↑MCP-1</i>	-0.3	<i>0.03</i>	<i>↓Schirmer ↑MCP-1</i>
TNF- α	-0.2	0.3	N/A	-0.1	0.4	N/A	-0.08	0.6	N/A	-0.08	0.6	N/A
VEGF	0.09	0.5	N/A	-0.2	0.1	N/A	0.04	0.8	N/A	0.02	0.9	N/A
Leptin	-0.007	0.9	N/A	0.02	0.9	N/A	0.2	0.2	N/A	-0.04	0.8	N/A
Insulin	0.2	0.09	N/A	0.08	0.6	N/A	0.008	0.9	N/A	0.04	0.8	N/A

Key words: TER, tear evaporation rate; fTBUT, fluorescein tear break-up time; CFS, corneal fluorescein staining; r_s , Spearman correlation coefficient; N/A, not applicable.

Note: Statistically significant differences and their clinical interpretation are reported in *italics*.

Table S3. Relationships of biomarkers and symptoms of DED in the DED-only group. r_s and p values are shown, as well as the clinical interpretation of these correlations. A p value of ≤ 0.05 was considered statistically significant. Due to there being a total of 17 subjects in the DED-only group, an r_s of > 0.46 is considered as a positive correlation and < -0.46 is considered as a negative correlation [47, 48].

Biomarkers	DEQS scores (0-100)			OSDI scores (0-100)		
	r_s	p -value	Interpretation	r_s	p -value	Interpretation
IL-1RA	0.17	0.52	N/A	0.17	0.51	N/A
IL-8	0.31	0.23	N/A	0.18	0.48	N/A
EGF	0.12	0.64	N/A	0.17	0.5	N/A
Fractalkine	0.38	0.13	N/A	0.28	0.28	N/A
IL-10	0.38	0.14	N/A	0.31	0.23	N/A
IL-1 β	0.2	0.44	N/A	0.02	0.94	N/A
IL-6	-0.13	0.62	N/A	-0.42	0.09	N/A
IP-10	<i>0.57</i>	<i>0.02</i>	\uparrow DEQS \uparrow IP-10	0.24	0.36	N/A
MCP-1	-0.21	0.41	N/A	0.08	0.76	N/A
TNF- α	<i>0.49</i>	<i>0.04</i>	\uparrow DEQS \uparrow TNF- α	0.1	0.7	N/A
VEGF	<i>0.49</i>	<i>0.05</i>	\uparrow DEQS \uparrow VEGF	<i>0.47</i>	<i>0.06</i>	\uparrow OSDI \uparrow VEGF
Leptin	-0.14	0.58	N/A	-0.46	0.06	N/A
Insulin	0.21	0.41	N/A	0.09	0.74	N/A

Key words: T2D, type 2 diabetes; DED, Dry Eye Disease; r_s , Spearman correlation coefficient; N/A, not applicable.

Note: Statistically significant differences and their clinical interpretation are reported in *italics*.

Table S4. Relationships of biomarkers and symptoms of DED in the T2D+DED group. r_s and p values are shown, as well as the clinical interpretation of these relationships. A p value of ≤ 0.05 is considered as statistically significant. Due to there being a total of 47 subjects in the T2D+DED group, an r_s of > 0.27 is considered as a positive relationship and < -0.27 is considered as a negative relationship [47, 48].

Biomarkers	DEQS scores (0-100)			OSDI scores (0-100)		
	r_s	p -value	Interpretation	r_s	p -value	Interpretation
IL-1RA	0.08	0.6	N/A	0.02	0.88	N/A
IL-8	0.11	0.47	N/A	0.07	0.66	N/A
EGF	-0.14	0.35	N/A	-0.001	0.99	N/A
Fractalkine	-0.15	0.31	N/A	-0.03	0.84	N/A
IL-10	0.09	0.56	N/A	0.14	0.34	N/A
IL-1 β	0.2	0.17	N/A	0.14	0.34	N/A
IL-6	0.07	0.64	N/A	0.17	0.25	N/A
IP-10	0.13	0.4	N/A	0.09	0.54	N/A
MCP-1	-0.13	0.4	N/A	0.10	0.52	N/A
TNF- α	0.23	0.11	N/A	0.13	0.4	N/A
VEGF	-0.03	0.86	N/A	0.05	0.72	N/A
Leptin	0.22	0.14	N/A	0.21	0.15	N/A
Insulin	0.07	0.62	N/A	0.03	0.86	N/A

Key words: T2D, type 2 diabetes; DED, Dry Eye Disease; r_s , Spearman correlation coefficient; N/A, not applicable.

Table S5. Relationships of biomarkers and clinical data of T2D in the T2D+DED group. r_s and p values are shown, as well as the clinical interpretation of these relationships. A p value of ≤ 0.05 is considered as statistically significant. Due to there being a total of 47 subjects in the T2D+DED group, an r_s of > 0.27 is considered as a positive relationship and < -0.27 is considered as a negative relationship [47, 48].

Biomarkers	Duration of T2D			HbA _{1c}			Total Cholesterol			HDL		
	r_s	p -value	Interpretation	r_s	p -value	Interpretation	r_s	p -value	Interpretation	r_s	p -value	Interpretation
IL-1RA	-0.16	0.3	N/A	-0.21	0.16	N/A	0.18	0.23	N/A	-0.07	0.64	N/A
IL-8	-0.22	0.13	N/A	0.06	0.68	N/A	-0.03	0.86	N/A	-0.23	0.12	N/A
EGF	-0.19	0.19	N/A	-0.13	0.37	N/A	0.06	0.7	N/A	-0.005	0.97	N/A
Fractalkine	-0.12	0.44	N/A	-0.08	0.6	N/A	0.24	0.1	N/A	0.03	0.86	N/A
IL-10	0.17	0.27	N/A	0.02	0.89	N/A	-0.09	0.54	N/A	-0.17	0.27	N/A
IL-1 β	0.06	0.68	N/A	0.11	0.45	N/A	-0.24	0.11	N/A	-0.07	0.63	N/A
IL-6	-0.05	0.75	N/A	0.04	0.81	N/A	0.06	0.71	N/A	-0.04	0.8	N/A
IP-10	-0.08	0.62	N/A	0.005	0.97	N/A	0.12	0.44	N/A	-0.18	0.23	N/A
MCP-1	-0.03	0.86	N/A	-0.02	0.92	N/A	-0.26	0.08	N/A	-0.21	0.15	N/A
TNF- α	-0.11	0.46	N/A	0.21	0.15	N/A	-0.002	0.99	N/A	-0.17	0.26	N/A
VEGF	-0.3	0.04	\uparrow Duration of T2D \downarrow VEGF	0.1	0.5	N/A	0.19	0.19	N/A	0.009	0.95	N/A
Leptin	0.12	0.41	N/A	0.01	0.95	N/A	-0.14	0.34	N/A	-0.23	0.11	N/A
Insulin	-0.31	0.03	\uparrow Duration of T2D \downarrow Insulin	-0.19	0.21	N/A	-0.03	0.87	N/A	-0.39	0.007	\uparrow HDL \downarrow Insulin

Key words: T2D, type 2 diabetes; HbA_{1c}, glycated haemoglobin; HDL, high density lipoprotein; r_s , Spearman correlation coefficient; N/A, not applicable.

Note: Statistically significant differences and their clinical interpretation are reported in *italics*.