

**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  $\leq 0.05$  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 $\beta$	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- $\alpha$	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  $\leq 0.05$  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	0.04	↓fTBUT ↑IL-1RA	0.2	0.1	N/A	-0.5	<0.001	↓Schirmer ↑IL-1RA
IL-8	0.2	0.1	N/A	-0.2	0.2	N/A	0.3	0.04	↑CFS ↑IL-8	-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	0.05	↑TER ↓IL-10	0.2	0.1	N/A	-0.08	0.6	N/A	0.02	0.9	N/A
IL-1 $\beta$	-0.3	0.02	↑TER ↓IL-1 $\beta$	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	0.05	↓fTBUT ↑IL-6	0.3	0.02	↑CFS ↑IL-6	-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	↑CFS ↑MCP-1	-0.3	0.03	↓Schirmer ↑MCP-1
TNF- $\alpha$	-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  $\leq 0.05$  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 $\beta$	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- $\alpha$	<i>0.49</i>	<i>0.04</i>	$\uparrow$ DEQS $\uparrow$ TNF- $\alpha$	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  $\leq 0.05$  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 $\beta$	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- $\alpha$	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  $\leq 0.05$  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 <sub>1c</sub>			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 $\beta$	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- $\alpha$	-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<sub>1c</sub>, 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*.