

## Systemic inflammation contributes to impairment of quality of life in chronic pancreatitis

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**Supplementary Table 1:** MANOVA test of the overall effect of patients characteristics and measured inflammatory mediators in serum on the EORTC QLQ-C30 scale

Variable	QLQ-C30							
	One-factor model		Adjusted Model - Smoking		Adjusted Model - Diabetes Mellitus		Adjusted Model - Current Drinker	
	Wilk's $\lambda$	P	Wilk's $\lambda$	P	Wilk's $\lambda$	P	Wilk's $\lambda$	P
Age: $\leq 53$ vs $> 53$ years	<b>0.859</b>	<b>0.02</b>	<b>0.866</b>	<b>0.04</b>	<b>0.859</b>	<b>0.02</b>	<b>0.861</b>	<b>0.03</b>
Gender: female vs. male	<b>0.779</b>	<b>&lt;0.0001</b>	<b>0.782</b>	<b>&lt;0.0001</b>	<b>0.779</b>	<b>&lt;0.0001</b>	<b>0.779</b>	<b>&lt;0.0001</b>
Pancreatitis etiology: Alcohol vs other	0.883	0.09	0.891	0.14	0.884	0.10	0.882	0.09
Current smoker: Yes vs no	<b>0.816</b>	<b>0.001</b>	-	-	<b>0.816</b>	<b>0.001</b>	<b>0.820</b>	<b>0.002</b>
Current drinker: Yes vs no	0.918	0.41	0.924	0.51	0.920	0.44	-	-
Diabetes Mellitus: Yes vs no	0.914	0.35	0.915	0.38	-	-	0.914	0.36
Eotaxin: High vs Low	0.932	0.67	0.935	0.75	0.925	0.57	0.933	0.70
Eotaxin3: High vs low	0.880	0.10	0.870	0.06	0.886	0.14	0.892	0.18
GM-CSF: High vs low	0.876	0.08	0.876	0.09	0.884	0.12	0.865	0.05
IFN $\gamma$ : High vs low	0.890	0.16	0.886	0.14	0.892	0.18	0.888	0.15
IL-2: High vs low	0.876	0.08	0.867	0.06	0.876	0.08	0.878	0.10
IL-4: High vs low	0.938	0.74	0.940	0.78	0.937	0.72	0.933	0.69
IL-5: High vs low	0.932	0.65	0.931	0.65	0.932	0.66	0.932	0.67
IL-6: High vs low	0.878	0.09	0.904	0.29	0.880	0.10	0.876	0.09
IL-7: High vs low	<b>0.855</b>	<b>0.03</b>	<b>0.855</b>	<b>0.03</b>	<b>0.853</b>	<b>0.02</b>	<b>0.845</b>	<b>0.02</b>
IL-8: High vs low	0.866	0.05	0.866	0.05	0.871	0.06	<b>0.860</b>	<b>0.04</b>
IL-10: High vs low	0.901	0.25	0.902	0.27	0.910	0.36	0.897	0.23
IL-12/IL-23p40: High vs low	<b>0.851</b>	<b>0.02</b>	<b>0.836</b>	<b>0.01</b>	<b>0.848</b>	<b>0.02</b>	<b>0.849</b>	<b>0.02</b>
IL-12p70	0.913	0.38	0.908	0.34	0.914	0.41	0.912	0.39
IL-13: High vs low	0.956	0.93	0.943	0.81	0.957	0.93	0.957	0.94
IL-15: High vs low	0.875	0.07	0.880	0.10	0.882	0.11	0.872	0.07
IL-16: High vs low	<b>0.846</b>	<b>0.02</b>	<b>0.834</b>	<b>0.01</b>	<b>0.846</b>	<b>0.02</b>	<b>0.852</b>	<b>0.03</b>
IL-17a: High vs low	0.902	0.23	0.905	0.30	0.902	0.26	0.901	0.26
IL-1 $\alpha$ : High vs low	0.947	0.84	0.955	0.92	0.946	0.84	0.950	0.88
IL-1 $\beta$ : High vs low	0.888	0.14	0.878	0.09	0.884	0.12	0.892	0.18
IP10: High vs low	<b>0.847</b>	<b>0.02</b>	<b>0.841</b>	<b>0.01</b>	<b>0.855</b>	<b>0.03</b>	<b>0.852</b>	<b>0.03</b>
MCP1: High vs low	0.916	0.42	0.919	0.48	0.916	0.43	0.918	0.47
MCP4: High vs low	0.934	0.68	0.935	0.71	0.934	0.69	0.933	0.69
MIP1a: High vs low	<b>0.825</b>	<b>0.004</b>	<b>0.791</b>	<b>&lt;0.0001</b>	<b>0.834</b>	<b>0.007</b>	<b>0.818</b>	<b>0.003</b>
MIP1b: High vs low	0.884	0.12	0.874	0.08	0.883	0.12	0.893	0.20
MDC: High vs low	<b>0.841</b>	<b>0.01</b>	<b>0.847</b>	<b>0.02</b>	<b>0.844</b>	<b>0.01</b>	<b>0.844</b>	<b>0.02</b>
TARC: High vs low	0.919	0.47	0.932	0.66	0.916	0.43	0.918	0.47
TNF $\alpha$ : High vs low	0.938	0.74	0.923	0.54	0.942	0.79	0.939	0.77
TNF $\beta$ : High vs low	<b>0.856</b>	<b>0.03</b>	<b>0.860</b>	<b>0.04</b>	<b>0.854</b>	<b>0.03</b>	<b>0.857</b>	<b>0.03</b>
VEGF: High vs low	0.905	0.29	0.918	0.46	0.906	0.30	0.908	0.34

Results in bold:  $p < 0.05$

**Supplementary Table 2:** MANOVA test of the overall effect of patients characteristics and measured inflammatory mediators in serum on the EORTC PAN-28 scale

Variable	PAN28							
	One-factor model		Adjusted Model - Smoking		Adjusted Model - Diabetes Mellitus		Adjusted Model - Current Drinker	
	Wilk's $\lambda$	P	Wilk's $\lambda$	P	Wilk's $\lambda$	P	Wilk's $\lambda$	P
Age: $\leq 53$ vs $> 53$ years	0.895	0.70	0.893	0.69	0.897	0.72	0.892	0.68
Gender: female vs. male	<b>0.795</b>	<b>0.04</b>	0.799	0.05	<b>0.792</b>	<b>0.04</b>	<b>0.791</b>	<b>0.04</b>
Pancreatitis etiology: Alcohol vs other	0.868	0.42	0.897	0.72	0.860	0.35	0.874	0.50
Current smoker: Yes vs no	0.840	0.20			0.833	0.16	0.831	0.16
Current drinker: Yes vs no	<b>0.717</b>	<b>0.001</b>	<b>0.712</b>	<b>0.001</b>	<b>0.716</b>	<b>0.001</b>		
Diabetes Mellitus: Yes vs no	0.800	0.05	<b>0.793</b>	<b>0.04</b>			<b>0.794</b>	<b>0.04</b>
Eotaxin: High vs Low	<b>0.708</b>	<b>0.001</b>	<b>0.709</b>	<b>0.001</b>	<b>0.714</b>	<b>0.002</b>	<b>0.712</b>	<b>0.001</b>
Eotaxin3: High vs low	0.829	0.17	0.829	0.18	0.832	0.20	0.845	0.29
GM-CSF: High vs low	0.851	0.32	0.852	0.34	0.842	0.26	0.849	0.32
IFN $\gamma$ : High vs low	0.905	0.81	0.899	0.77	0.904	0.82	0.907	0.84
IL-2: High vs low	0.850	0.31	0.841	0.25	0.841	0.25	0.843	0.27
IL-4: High vs low	0.901	0.78	0.902	0.80	0.899	0.77	0.901	0.80
IL-5: High vs low	0.880	0.58	0.876	0.53	0.877	0.56	0.880	0.60
IL-6: High vs low	0.819	0.12	0.822	0.14	0.825	0.15	0.838	0.24
IL-7: High vs low	<b>0.790</b>	<b>0.04</b>	<b>0.788</b>	<b>0.04</b>	<b>0.786</b>	<b>0.04</b>	<b>0.768</b>	<b>0.02</b>
IL-8: High vs low	0.806	0.08	0.803	0.07	0.807	0.09	0.809	0.10
IL-10: High vs low	0.857	0.37	0.860	0.40	0.870	0.50	0.867	0.47
IL-12/IL-23p40: High vs low	0.854	0.34	0.863	0.44	0.853	0.34	0.856	0.38
IL-12p70	<b>0.773</b>	<b>0.02</b>	<b>0.772</b>	<b>0.02</b>	<b>0.779</b>	<b>0.03</b>	<b>0.776</b>	<b>0.03</b>
IL-13: High vs low	<b>0.777</b>	<b>0.02</b>	<b>0.782</b>	<b>0.03</b>	<b>0.777</b>	<b>0.03</b>	<b>0.780</b>	<b>0.03</b>
IL-15: High vs low	0.799	0.06	0.802	0.07	0.795	0.06	0.815	0.12
IL-16: High vs low	0.860	0.39	0.854	0.35	0.855	0.36	0.858	0.40
IL-17a: High vs low	0.930	0.96	0.929	0.96	0.929	0.96	0.924	0.94
IL-1 $\alpha$ : High vs low	0.878	0.57	0.861	0.41	0.878	0.58	0.879	0.60
IL-1 $\beta$ : High vs low	<b>0.712</b>	<b>0.001</b>	<b>0.713</b>	<b>0.001</b>	<b>0.731</b>	<b>0.003</b>	<b>0.712</b>	<b>0.001</b>
IP10: High vs low	<b>0.788</b>	<b>0.04</b>	<b>0.787</b>	<b>0.04</b>	0.798	0.06	0.792	0.05
MCP1: High vs low	<b>0.722</b>	<b>0.002</b>	<b>0.724</b>	<b>0.002</b>	<b>0.722</b>	<b>0.002</b>	<b>0.733</b>	<b>0.003</b>
MCP4: High vs low	<b>0.724</b>	<b>0.002</b>	<b>0.726</b>	<b>0.002</b>	<b>0.746</b>	<b>0.006</b>	<b>0.722</b>	<b>0.002</b>
MIP1a: High vs low	0.801	0.06	0.798	0.06	0.826	0.16	0.806	0.09
MIP1b: High vs low	0.794	0.05	0.792	0.05	0.802	0.07	0.792	0.05
MDC: High vs low	<b>0.693</b>	<b>&lt;0.0001</b>	<b>0.698</b>	<b>&lt;0.0001</b>	<b>0.690</b>	<b>&lt;0.0001</b>	<b>0.688</b>	<b>&lt;0.0001</b>
TARC: High vs low	<b>0.703</b>	<b>0.001</b>	<b>0.707</b>	<b>0.001</b>	<b>0.695</b>	<b>&lt;0.0001</b>	<b>0.698</b>	<b>&lt;0.0001</b>
TNF $\alpha$ : High vs low	0.846	0.28	0.850	0.32	0.861	0.41	0.852	0.34
TNF $\beta$ : High vs low	0.903	0.80	0.899	0.77	0.900	0.79	0.905	0.83
VEGF: High vs low	0.905	0.81	0.909	0.85	0.901	0.79	0.908	0.85

Results in bold:  $p < 0.05$

**Supplementary Table 3:** Median serum levels of inflammatory mediators in pg/ml

<b>Cytokine</b>	<b>Median</b>	<b>± SD</b>
Eotaxin	130.6	100.8
Eotaxin_3	14.1	312.6
GM-CSF	0.10	0.25
IFN_g	4.78	40.72
IL_10	0.31	0.80
IL_12	86.19	67.18
IL_12p70	0.11	0.51
IL_13	0.27	2.06
IL_15	2.64	0.92
IL_16	231.32	194.22
IL_17A	3.65	6.40
IL_1a	0.00	2.01
IL_1b	0.00	1.84
IL_2	0.11	1.11
IL_4	0.02	0.10
IL_5	0.00	0.77
IL_6	0.98	15.54
IL_7	14.24	12.80
IL_8	16.83	238.5
IP_10	96.50	219.73
MCP_1	160.70	92.64
MCP_4	77.15	61.83
MDC	740.88	559.89
MIP_1a	11.75	231.67
MIP_1b	65.54	357.11
TARC	148.07	226.03
TNFa	2.96	8.72
TNFb	0.18	0.55
VEGF	142.28	151.18

**Supplementary Table 4:** All associations between inflammatory mediators and quality of life

Predictive Variable	Questionnaire	Quality of Life Domain(s)	Mean Score (Low)	Mean Score (High)	Bonferroni p-value		
Eotaxin	PAN-28	Bowel Function	24,5	34,9	0,029		
		Sexual Function	30,8	47,3	0,011		
		Abdominal Bloating	54,6	37,6	0,009		
IL-1 $\beta$	PAN-28	Sexual Function	44,5	31,8	0,048		
		Indigestion	31	48,4	0,009		
IL-7	QLQ-C30	Global Quality of Life	55,8	48,2	0,038		
		Role Functioning	65,6	54,3	0,029		
		Fatigue	43,5	53,1	0,03		
		Nausea and Vomiting	20	29,8	0,032		
		Dyspnoea	19,3	30,4	0,014		
		Insomnia	43,2	54,4	0,039		
		Diarrhoea	17,2	27,4	0,014		
	PAN-28	Healthcare satisfaction	31,1	43,1	0,044		
		Indigestion	29,9	48,3	0,005		
		Ability to plan ahead	33,8	48,8	0,017		
IL-8	QLQ-C30	Global Quality of Life	56	48,3	0,038		
		Physical Functioning	78,9	67,8	0,002		
		Cognitive Functioning	77,5	68,3	0,019		
		Social Functioning	68,1	58,2	0,045		
		Nausea and Vomiting	20	29,4	0,038		
		Dyspnoea	20,1	29,1	0,047		
		Insomnia	41,4	55,7	0,009		
		Appetite Loss	32,6	44	0,034		
IL-12/IL-23p40	QLQ-C30	Dyspnoea	29,6	29,5	0,029		
IL-12p70	PAN-28	Indigestion	32	47,4	0,02		
		Fear for future health	60,7	76,6	0,003		
IL-13	PAN-28	Alcohol Related Guilt	26,3	13,7	0,008		
IL-16	QLQ-C30	Global Quality of Life	56,7	47,5	0,012		
		Physical Functioning	78,4	68,2	0,005		
		Role Functioning	66	54,3	0,025		
		Cognitive Functioning	77,5	68,1	0,016		
		Social Functioning	68,1	58,1	0,043		
		Fatigue	43	53,3	0,019		
		Nausea and Vomiting	17,2	32,3	0,001		
		Dyspnoea	19,2	30,1	0,015		
		Insomnia	41,3	55,9	0,007		
		Appetite Loss	29	47,7	<0,0001		
IP-10	QLQ-C30	Dyspnoea	20,2	29,3	0,043		
		Insomnia	41,1	56,4	0,005		
	PAN-28	Bowel Function	19,7	38,3	<0,0001		
		Flatulence	33,8	45,5	0,041		
MCP-1	PAN-28	Jaundice	10,7	19	0,02		
		Healthcare Satisfaction	46,9	28,7	0,002		
		Abdominal Bloating	55,7	38,8	0,009		
MCP-4	PAN-28	Bowel Function	23,8	34,8	0,019		
		Alcohol Related Guilt	26,7	13,5	0,005		
		Sexual Function	31,9	45,2	0,039		
		Ability to plan ahead	49,6	33,3	0,009		
MDC	QLQ-C30	Physical Functioning	78,7	67,8	0,003		
		Role Functioning	66,1	54	0,019		
		Social Functioning	71,7	54,4	<0,0001		
		Fatigue	43,1	53,3	0,021		
		Nausea and Vomiting	17,2	32,4	0,001		
		Dyspnoea	17,9	31,5	0,002		
		Insomnia	42,7	54,7	0,027		
	PAN-28	Financial Difficulties	30,1	42	0,026		
		Jaundice	9,6	20,2	0,003		
		Bowel Function	22	36,1	0,002		
		Sexual Function	29,3	47,2	0,005		
		Weight Loss	24,2	39,9	0,019		
		MIP-1a	QLQ-C30	Global Quality of Life	56,5	47,6	0,017
				Physical Functioning	80,2	66,2	<0,0001
Role Functioning	67			53,1	0,007		
Cognitive Functioning	78,3			67,2	0,004		
Social Functioning	72,6			53,5	<0,0001		

		Fatigue	40,9	55,6	0,001
		Nausea and Vomiting	17,6	32,1	0,001
		Dyspnoea	18,6	30,8	0,007
		Insomnia	40,5	56,9	0,003
		Appetite Loss	33	43,8	0,043
		Constipation	15,4	26,1	0,016
		Financial Difficulties	27,6	44,6	0,001
TARC	PAN-28	Jaundice	10,1	19,4	0,009
		Body Image	30,7	42,1	0,036
		Weight Loss	24,3	39,2	0,026
TNFb	QLQ-C30	Financial Difficulties	42,4	29,2	0,014