Supplemental material

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Supplementary Files

Supplementary Table 1. Prevalence of antibodies against AGE and MAA in healthy controls (n= 80) versus RA (n=648), non-RA (n=538), AI no RA (n=234) and non-AI (n=166) patient groups.

	Anti-AGE		Anti-MAA	
	aU/mL	*n, % positive*	aU/mL	*n, % positive*
HC (n=80)	94,2 [52,7 – 160,6]	6 (7,5)	358,4 [282,4 – 480,8]	3 (3,8)
RA (n=648)	233,1 [130,4 – 367,4]	289 (44,6)*	931,8 [663,2 – 1277,4]*	299 (46,1)*
non-RA (n=538)	177,8 [93,8 – 309,4]	177 (32,9)*	728,3 [485,1 – 1111,0]*	163 (30,3)*
AI no RA (n=234)	192,6 [102,3 – 328,6]	90 (38,5)*	853,7 [592,1 – 1246,5]*	97 (41,5)*
non-AI (n=166)	171,0 [107,2 – 286,4]	46 (27,7)*	666,1 [485,5 – 922,4]*	33 (19,9)*

Results are presented as median [IQR] and n (%)

* Statistically significant difference between patient group and healthy controls (p≤0.001)

Abbreviations: AGE, advanced glycation end-product; AI, Autoimmune (including psoriatic arthritis, paraneoplastic arthritis, SLE, sarcoidosis and spondyloarthritis); HC, Healthy controls; IQR, interquartile range; MAA, malondialdehyde-acetaldehyde adduct; non-AI, non-autoimmune (including septic arthritis, gout, pseudogout); RA rheumatoid arthritis.

Supplementary Table 2. Association anti-AGE and anti-MAA responses with HLA-DRB1*03 cross stratified for anti-AGE and anti-MAA for RA in part I and non-RA arthritis in part II.

Part I		RA n=648									
		HLA-DRB1*03-	HLA-DRB1*03+	Total	OR	95%CI	p-value		OR	95%CI	p-value
Anti-AGE-	Healthy controls	941 (77.7%)	270 (22.3%)	1211	1 (ref)	-	-		-	-	-
	Anti-MAA-	203 (75.5%)	66 (24.5%)	269	1.13	(0.83, 1.54)	0.43		-	-	-
	Anti-MAA+	68 (75.6%)	22 (24.4%)	90	1.13	(0.68, 1.86)	0.64		-	-	-
		HLA-DRB1.03-	HLA-DRB1.03+	Total	OR	95%CI	p-value		OR	95%CI	p-value
Anti-AGE+	Healthy controls	941 (77.7%)	270 (22.3%)	1211	1 (ref)	-	-		-	-	-
	Anti-MAA-	63 (78.8%)	17 (21.3%)	80	0.94	(0.54, 1.63)	0.83		1 (ref)	-	-
	Anti-MAA+	148 (70.8%)	61 (29.2%)	209	**1.44**	**(1.04, 1.99)**	**0.03**		1.53	(0.83, 2.82)	0.18
		HLA-DRB1*03-	HLA-DRB1*03+	Total	OR	95%CI	p-value		OR	95%CI	p-value
Anti-MAA-	Healthy controls	941 (77.7%)	270 (22.3%)	1211	1 (ref)	-	-		-	-	-
	Anti-AGE-	203 (75.5%)	66 (24.5%)	269	1.13	(0.83, 1.54)	0.43		-	-	-
	Anti-AGE+	63 (78.8%)	17 (21.3%)	80	0.94	(0.54, 1.63)	0.83		-	-	-
		HLA-DRB1.03-	HLA-DRB1.03+	Total	OR	95%CI	p-value		OR	95%CI	p-value
Anti-MAA+	Healthy controls	941 (77.7%)	270 (22.3%)	1211	1 (ref)	-	-		-	-	-
	Anti-AGE-	68 (75.6%)	22 (24.4%)	90	1.13	(0.68, 1.86)	0.64		1 (ref)	-	-
	Anti-AGE+	148 (70.8%)	61 (29.2%)	209	**1.44**	**(1.04, 1.99)**	**0.03**		1.27	(0.72, 2.24)	0.40

Part II		non-RA n=246									
		HLA-DRB1*03-	HLA-DRB1*03+	Total	OR	95%CI	p-value		OR	95%CI	p-value
Anti-AGE-	Healthy controls	941 (77.7%)	270 (22.3%)	1211	1 (ref)	-	-		-	-	-
	Anti-MAA-	77 (78.6%)	21 (21.4%)	98	0.95	(0.58, 1.57)	0.84		1 (ref)	-	-
	Anti-MAA+	22 (71.0%)	9 (29.0%)	31	1.43	(0.65, 3.13)	0.38		1.50	(0.60, 3.74)	0.38
		HLA-DRB1.03-	HLA-DRB1.03+	Total	OR	95%CI	p-value		OR	95%CI	p-value
Anti-AGE+	Healthy controls	941 (77.7%)	270 (22.3%)	1211	1 (ref)	-	-		-	-	-
	Anti-MAA-	20 (55.6%)	16 (44.4%)	36	**2.79**	**(1.43, 5.46)**	**0.003**		1 (ref)	-	-
	Anti-MAA+	50 (61.7%)	31 (38.5%)	81	**2.16**	**(1.35, 3.45)**	**0.001**		0.78	(0.35, 1.72)	0.53
		HLA-DRB1*03-	HLA-DRB1*03+	Total	OR	95%CI	p-value		OR	95%CI	p-value
Anti-MAA-	Healthy controls	941 (77.7%)	270 (22.3%)	1211	1 (ref)	-	-		-	-	-
	Anti-AGE-	77 (78.6%)	21 (21.4%)	98	0.95	(0.58, 1.57)	0.84		1 (ref)	-	-
	Anti-AGE+	20 (55.6%)	16 (44.4%)	36	**2.79**	**(1.43, 5.46)**	**0.003**		**2.93**	**(1.30, 6.63)**	**0.01**
		HLA-DRB1.03-	HLA-DRB1.03+	Total	OR	95%CI	p-value		OR	95%CI	p-value
Anti-MAA+	Healthy controls	941 (77.7%)	270 (22.3%)	1211	1 (ref)	-	-		-	-	-
	Anti-AGE-	22 (71.0%)	9 (29.0%)	31	1.43	(0.65, 3.13)	0.38		1 (ref)	-	-
	Anti-AGE+	50 (61.7%)	31 (38.5%)	81	**2.16**	**(1.35, 3.45)**	**0.001**		1.52	(0.62, 3.71)	0.36

Results are presented as n (%) and OR (95% confidence interval)

Statistically significant difference between patient group and healthy controls (p≤0.05)

Abbreviations: AGE, advanced glycation end-product; MAA, malondialdehyde-acetaldehyde adduct; HC, Healthy controls; RA rheumatoid arthritis.

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Supplementary Table 3. Association anti-PTM responses with ESR and CRP cross stratified for anti-AGE and anti-MAA for RA and non-RA arthritis.

RA	Anti-AGE-			Anti-AGE+			Anti-MAA-			Anti-MAA+		
	Anti-MAA- n=267	Anti-MAA+ n=89	p-value	Anti-MAA- n=79	Anti-MAA+ n=208	p-value	Anti-AGE- n=267	Anti-AGE+ n=79	p-value	Anti-AGE- n=89	Anti-AGE+ n=208	p-value
ESR (median, IQR)	30.0 (16.0-49.0)	41.0 (22.5-57.0)	**0.009**	30.0 (18.0-47.0)	41.0 (20.0-64.8)	**0.010**	30.0 (16.0-49.0)	30.0 (18.0-47.0)	0.83	41.0 (22.5-57.0)	41.0 (20.0-64.8)	0.72
CRP (median, IQR)	15.0 (6.0-33.0)	24.0 (10.0-41.8)	**0.008**	12.0 (8.0-29.0)	22.0 (9.8-52.3)	**0.005**	15.0 (6.0-33.0)	12.0 (8.0-29.0)	0.81	24.0 (10.0-41.8)	22.0 (9.8-52.3)	0.77
non-RA	Anti-AGE-			Anti-AGE+			Anti-MAA-			Anti-MAA+		
	Anti-MAA- n= 302*	Anti-MAA+ n=54*	p-value	Anti-MAA- n=68*	Anti-MAA+ n=109*	p-value	Anti-AGE- n=302*	Anti-AGE+ n=68*	p-value	Anti-AGE- n=54*	Anti-AGE+ n=109*	p-value
ESR (median, IQR)	17.5 (8.0-36.0)	38.5 (23.0-63.5)	**<0.001**	31.0 (14.0 – 55.8)	42.00 (27.0-60.5)	**0.05**	17.5 (8.0-36.0)	31.0 (14.0 – 55.8)	**<0.001**	38.5 (23.0-63.5)	42.0 (27.0-60.5)	0.59
CRP (median, IQR)	9.0 (3.0-25.8)	21.0 (9.0-44.0)	**<0.001**	15.9 (5.0- 48.3)	21.0 (8.7-55.5)	0.09	9.0 (3.0-25.8)	15.9 (5.0- 48.3)	**0.05**	21.0 (9.0-44.0)	21.0 (8.7-55.5)	0.66

Results are presented as median (IQR)

*ESR and CRP levels were not determined for all patients and numbers might therefore slightly differ per variable

Statistically significant difference between groups (p≤0.05)

Abbreviations: AGE, Advanced Glycation End-products; *CRP,* C-reactive protein; *ESR,* erythrocyte sedimentation rate; *IQR,* interquartile range; *MAA,* Malondialdehyde Acetaldehyde Adducts*; RA,* rheumatoid arthritis.

Supplementary Figure 1. Presence of anti-MAA or anti-AGE is not associated with SDFR in RA patients (n=624). (A) Kaplan Meier curves presenting percentage remission in anti-AGE positive and -negative RA. (B) left panel: percentage remission in anti-MAA positive and -negative RA. Right panel: data stratified for CCP2 status. The number of patients entering the time interval is shown under each graph. *Abbreviations: AGE, Advanced Glycation End-product; CarP, Carbamylated Protein; CCP2, citrullinated cyclic peptide 2; MAA, Malondialdehyde-Acetaldehyde Adduct.*