

Supplementary Table 1a. RA risk in different subgroups divided by the presence/absence of CarP-Fib and CCP antibodies, in subjects exposed to different HLA alleles compared with non-exposed subjects. EIRA

Antibody	SE Positive stratum						SE Negative stratum						Overall					
	Negative N (%)	Positive N (%)	N total	OR*	95%CI	p-value	Negative N (%)	Positive N (%)	N total	OR*	95%CI	p-value	Negative N (%)	Positive N (%)	N total	OR*	95%CI	p-value
Any DRB1*01																		
Controls	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	791(81.05)	185(18.95)	976	1.00	ref.	-
CCP-/CarP-Fib-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	363(77.56)	105(22.44)	468	1.25	0.95-1.65	0.12
CCP-/CarP-Fib+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	46(76.67)	14(23.33)	60	1.34	0.71-2.54	0.36
CCP+/CarP-Fib-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	266(75.14)	88(24.86)	354	1.50	1.12-2.02	0.0069
CCP+/CarP-Fib+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	338(72.53)	128(27.47)	466	1.67	1.28-2.18	0.0001
Any DRB1*03																		
Controls	318(83.03)	65(16.97)	383	1.0	ref.	-	338(67.20)	165(32.80)	503	1.0	ref.	-	746(76.43)	230(23.57)	976	1.0	ref.	-
CCP-/CarP-Fib-	165(77.46)	48(22.54)	213	1.48	0.96-2.29	0.077	127(59.07)	88(40.93)	215	1.37	0.97-1.93	0.074	332(70.94)	136(29.06)	468	1.30	1.01-1.68	0.042
CCP-/CarP-Fib+	19(73.08)	7(26.92)	26	1.27	0.48-3.38	0.63	16(64.00)	9(36.00)	25	1.21	0.51-2.88	0.67	44(73.33)	16(26.67)	60	1.09	0.60-1.99	0.79
CCP+/CarP-Fib-	148(75.13)	49(24.87)	197	1.65	1.07-2.55	0.024	36(55.38)	29(44.62)	65	1.74	1.01-3.01	0.046	276(77.97)	78(22.03)	354	0.91	0.67-1.22	0.51
CCP+/CarP-Fib+	205(86.13)	33(13.87)	238	0.90	0.56-1.44	0.65	47(74.60)	16(25.40)	63	0.68	0.36-1.27	0.22	417(89.48)	49(10.52)	466	0.38	0.27-0.54	<0.0001
Any DRB1*04																		
Controls	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	635(65.06)	341(34.94)	976	1.0	ref.	-
CCP-/CarP-Fib-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	300(64.10)	168(35.90)	468	1.04	0.82-1.31	0.77
CCP-/CarP-Fib+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	40(66.67)	20(33.33)	60	0.87	0.49-1.53	0.63
CCP+/CarP-Fib-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	123(34.75)	231(65.25)	354	3.59	2.76-4.66	<0.0001
CCP+/CarP-Fib+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	130(27.90)	336(72.10)	466	5.11	3.99-6.55	<0.0001
Any DRB1*07																		
Controls	337(87.99)	46(12.01)	383	1.0	ref.	-	392(77.93)	111(22.07)	503	1.0	ref.	-	819(83.91)	157(16.09)	976	1.0	ref.	-
CCP-/CarP-Fib-	196(92.02)	17(7.98)	213	0.68	0.37-1.25	0.22	183(85.12)	32(14.88)	215	0.58	0.37-0.91	<0.0001	419(89.53)	49(10.47)	468	0.60	0.43-0.85	0.0044
CCP-/CarP-Fib+	25(96.15)	1(3.85)	26	0.30	0.04-2.36	0.25	20(80.00)	5(20.00)	25	0.91	0.32-2.57	0.86	54(90.00)	6(10.00)	60	0.59	0.25-1.42	0.24
CCP+/CarP-Fib-	183(92.89)	14(7.11)	197	0.48	0.25-0.91	0.02	54(83.03)	11(16.92)	65	0.70	0.35-1.43	0.33	329(92.94)	25(7.06)	354	0.39	0.25-0.61	<0.0001
CCP+/CarP-Fib+	209(87.82)	29(12.18)	238	1.00	0.60-1.68	0.99	46(73.02)	17(26.98)	63	1.28	0.69-2.37	0.44	420(90.13)	46(9.87)	466	0.58	0.41-0.82	0.0023
Any DRB1*08																		
Controls	359(93.73)	24(6.27)	383	1.0	ref.	-	438(87.08)	65(12.92)	503	1.0	ref.	-	887(90.88)	89(9.12)	976	1.0	ref.	-
CCP-/CarP-Fib-	188(88.26)	25(11.74)	213	2.04	1.10-3.76	0.02	179(83.26)	36(16.74)	215	1.45	0.92-2.29	0.11	407(86.97)	61(13.03)	468	1.54	1.08-2.19	0.017
CCP-/CarP-Fib+	23(88.46)	3(11.54)	26	2.50	0.60-10.47	0.21	22(88.00)	3(12.00)	25	0.94	0.27-3.30	0.92	54(90.00)	6(10.00)	60	1.16	0.48-2.81	0.75
CCP+/CarP-Fib-	185(93.91)	12(6.09)	197	1.03	0.49-2.17	0.93	58(89.23)	7(10.77)	65	0.79	0.34-1.85	0.58	334(94.35)	20(5.65)	354	0.58	0.35-0.96	0.04
CCP+/CarP-Fib+	223(93.70)	15(6.30)	238	0.91	0.46-1.83	0.80	55(87.30)	8(12.70)	63	1.00	0.44-2.24	0.99	443(95.06)	23(4.94)	466	0.48	0.30-0.78	0.0028
Any DRB1*09																		
Controls	373(97.39)	10(2.61)	383	1.0	ref.	-	481(95.63)	22(4.37)	503	1.0	ref.	-	944(96.72)	32(3.28)	976	1.0	ref.	-
CCP-/CarP-Fib-	207(97.18)	6(2.82)	213	0.93	0.32-2.71	0.90	208(96.74)	7(3.26)	215	0.80	0.33-1.93	0.62	455(97.22)	13(2.78)	468	0.84	0.43-1.64	0.61
CCP-/CarP-Fib+	24(92.31)	2(7.69)	26	3.07	0.56-16.86	0.20	23(92.00)	2(8.00)	25	1.62	0.31-8.39	0.57	56(93.33)	4(6.67)	60	2.50	0.81-7.71	0.11
CCP+/CarP-Fib-	191(96.95)	6(3.05)	197	1.19	0.42-3.36	0.75	60(92.31)	5(7.69)	65	1.72	0.59-5.02	0.32	343(96.89)	11(3.11)	354	0.92	0.45-1.87	0.82
CCP+/CarP-Fib+	232(97.48)	6(2.52)	238	1.06	0.36-3.15	0.92	57(90.48)	6(9.52)	63	2.33	0.85-6.41	0.10	454(97.42)	12(2.58)	466	0.72	0.36-1.43	0.35
Any DRB1*10																		
Controls	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	956(97.95)	20(2.05)	976	1.0	ref.	-
CCP-/CarP-Fib-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	459(98.08)	9(1.92)	468	0.94	0.41-2.12	0.88
CCP-/CarP-Fib+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	58(96.67)	2(3.33)	60	1.47	0.32-6.80	0.62
CCP+/CarP-Fib-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	345(97.46)	9(2.54)	354	1.12	0.50-2.52	0.79

CCP+/CarP-Fib+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	449(96.35)	17(3.65)	466	1.69	0.87-3.28	0.12
Any DRB1*11																		
Controls	355(92.69)	28(7.31)	383	1.0	ref.	-	428(85.09)	75(14.91)	503	1.0	ref.	-	873(89.45)	103(10.55)	976	1.0	ref.	-
CCP-/CarP-Fib-	199(93.43)	14(6.57)	213	0.98	0.50-1.94	0.96	181(84.19)	34(15.81)	215	1.16	0.73-1.84	0.53	420(89.74)	48(10.26)	468	1.04	0.72-1.50	0.85
CCP-/CarP-Fib+	25(96.15)	1(3.85)	26	0.45	0.06-3.74	0.46	23(92.00)	2(8.00)	25	0.57	0.13-2.56	0.47	57(95.00)	3(5.00)	60	0.47	0.14-1.53	0.21
CCP+/CarP-Fib-	179(90.86)	18(9.14)	197	1.23	0.65-2.32	0.53	55(84.62)	10(15.38)	65	1.15	0.54-2.43	0.72	326(92.09)	28(7.91)	354	0.73	0.47-1.14	0.16
CCP+/CarP-Fib+	213(89.50)	25(10.50)	238	1.44	0.80-2.58	0.22	49(77.78)	14(22.22)	63	1.81	0.92-3.58	0.09	427(91.63)	39(8.37)	466	0.77	0.52-1.14	0.18
Any DRB1*12																		
Controls	369(96.34)	14(3.66)	383	1.0	ref.	-	473(94.04)	30(5.96)	503	1.0	ref.	-	932(95.49)	44(4.51)	976	1.0	ref.	-
CCP-/CarP-Fib-	209(98.12)	4(1.88)	213	0.45	0.14-1.41	0.17	201(93.49)	14(6.51)	215	1.03	0.52-2.04	0.93	450(96.15)	18(3.85)	468	0.79	0.45-1.40	0.42
CCP-/CarP-Fib+	23(88.46)	3(11.54)	26	4.06	0.85-19.37	0.08	22(88.00)	3(12.00)	25	2.37	0.63-8.89	0.20	54(90.00)	6(10.00)	60	2.64	1.04-6.71	0.042
CCP+/CarP-Fib-	190(96.45)	7(3.55)	197	0.89	0.34-2.31	0.81	60(92.31)	5(7.69)	65	1.18	0.42-3.33	0.75	342(96.61)	12(3.39)	354	0.72	0.37-1.40	0.33
CCP+/CarP-Fib+	226(94.96)	12(5.04)	238	1.54	0.67-3.55	0.31	62(98.41)	1(1.59)	63	0.28	0.04-2.11	0.22	453(97.21)	13(2.79)	466	0.61	0.32-1.15	0.13
Any DRB1*13																		
Controls	289(75.46)	94(24.54)	383	1.0	ref.	-	331(65.81)	172(34.19)	503	1.0	ref.	-	710(72.75)	266(27.25)	976	1.0	ref.	-
CCP-/CarP-Fib-	170(79.81)	43(20.19)	213	0.76	0.50-1.16	0.21	132(61.40)	83(38.60)	215	1.24	0.87-1.75	0.23	342(73.08)	126(26.92)	468	1.00	0.78-1.29	0.99
CCP-/CarP-Fib+	24(92.31)	2(7.69)	26	0.26	0.06-1.19	0.08	15(60.00)	10(40.00)	25	1.30	0.55-3.06	0.56	48(80.00)	12(20.00)	60	0.68	0.35-1.32	0.26
CCP+/CarP-Fib-	177(89.85)	20(10.15)	197	0.36	0.21-0.62	0.0002	47(72.31)	18(27.69)	65	0.77	0.42-1.40	0.39	316(89.27)	38(10.73)	354	0.33	0.23-0.47	<0.0001
CCP+/CarP-Fib+	206(86.55)	32(13.45)	238	0.47	0.30-0.74	0.0012	51(80.95)	12(19.05)	63	0.41	0.21-0.80	0.0095	422(90.56)	44(9.44)	466	0.27	0.19-0.38	<0.0001
Any DRB1*14																		
Controls	378(98.69)	5(1.31)	383	1.0	ref.	-	465(92.45)	38(7.55)	503	1.0	ref.	-	933(95.59)	43(4.41)	976	1.0	ref.	-
CCP-/CarP-Fib-	206(96.71)	7(3.29)	213	2.93	0.90-9.61	0.08	198(92.09)	17(7.91)	215	1.05	0.57-1.93	0.88	444(94.87)	24(5.13)	468	1.23	0.73-2.07	0.44
CCP-/CarP-Fib+	26(100)	0(0)	26	NA	NA	NA	22(88.00)	3(12.00)	25	1.87	0.50-6.91	0.35	57(95.00)	3(5.00)	60	1.13	0.33-3.83	0.85
CCP+/CarP-Fib-	189(95.94)	8(4.06)	197	3.17	1.00-10.03	0.05	62(95.38)	3(4.62)	65	0.48	0.14-1.67	0.25	343(96.89)	11(3.11)	354	0.64	0.33-1.27	0.20
CCP+/CarP-Fib+	234(98.32)	4(1.68)	238	1.36	0.35-5.20	0.66	61(96.83)	2(3.17)	63	0.43	0.10-1.88	0.26	460(98.71)	6(1.29)	466	0.27	0.12-0.65	0.0033
Any DRB1*15																		
Controls	295(77.02)	88(22.98)	383	1.0	ref.	-	312(62.03)	191(37.97)	503	1.0	ref.	-	697(71.41)	279(28.59)	976	1.0	ref.	-
CCP-/CarP-Fib-	173(81.22)	40(18.78)	213	0.74	0.48-1.14	0.17	145(67.44)	70(32.56)	215	0.76	0.54-1.08	0.12	358(76.50)	110(23.50)	468	0.75	0.58-0.97	0.03
CCP-/CarP-Fib+	20(76.92)	6(23.08)	26	1.21	0.44-3.34	0.72	19(76.00)	6(24.00)	25	0.44	0.17-1.16	0.098	48(80.00)	12(20.00)	60	0.64	0.33-1.23	0.18
CCP+/CarP-Fib-	142(72.08)	55(27.92)	197	1.32	0.89-1.98	0.17	37(56.92)	28(43.08)	65	1.22	0.71-2.09	0.48	271(76.55)	83(23.45)	354	0.78	0.59-1.04	0.09
CCP+/CarP-Fib+	172(72.27)	66(27.73)	238	1.24	0.85-1.83	0.27	34(53.97)	29(46.03)	63	1.38	0.80-2.37	0.25	371(79.61)	95(20.39)	466	0.64	0.49-0.83	0.001
Any DRB1*16																		
Controls	380(99.22)	3(0.78)	383	1.0	ref.	-	493(98.01)	10(1.99)	503	1.0	ref.	-	963(98.67)	13(1.33)	976	1.0	ref.	-
CCP-/CarP-Fib-	211(99.06)	2(0.94)	213	0.94	0.15-5.96	0.95	209(97.21)	6(2.79)	215	1.52	0.53-4.38	0.44	460(98.29)	8(1.71)	468	1.17	0.47-2.89	0.74
CCP-/CarP-Fib+	26(100)	0(0)	26	NA	NA	NA	25(100)	0(0)	25	NA	NA	NA	60(100)	0(0)	60	NA	NA	NA
CCP+/CarP-Fib-	195(98.98)	2(1.02)	197	0.90	0.14-5.68	0.91	62(95.38)	3(4.62)	65	2.47	0.58-10.47	0.22	349(98.59)	5(1.41)	354	0.93	0.32-2.70	0.89
CCP+/CarP-Fib+	233(97.90)	5(2.10)	238	2.01	0.46-8.73	0.35	57(90.48)	6(9.52)	63	5.89	1.92-18.11	0.002	455(97.64)	11(2.36)	466	1.75	0.77-3.99	0.18

*: adjusted for age, gender and residential area

Supplementary Table 1b. RA risk in different subgroups divided by the presence/absence of CarP-FCS and CCP antibodies, in subjects exposed to different HLA alleles compared with non-exposed subjects. EIRA

Antibody	SE Positive stratum						SE Negative stratum						Overall					
	Negative N (%)	Positive N (%)	N total	OR*	95%CI	p-value	Negative N (%)	Positive N (%)	N total	OR*	95%CI	p-value	Negative N (%)	Positive N (%)	N total	OR*	95%CI	p-value
Any DRB1*01																		
Controls	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	791(81.05)	185(18.95)	976	1.0	ref.	-
CCP-/CarP-FCS-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	359(76.55)	110(23.45)	469	1.32	1.01-1.74	0.046
CCP-/CarP-FCS+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	50(84.75)	9(15.25)	59	0.80	0.38-1.67	0.55
CCP+/CarP-FCS-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	329(78.15)	92(21.85)	421	1.25	0.94-1.67	0.13
CCP+/CarP-FCS+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	275(68.92)	124(31.08)	399	2.00	1.53-2.63	<0.0001
Any DRB1*03																		
Controls	318(83.03)	65(16.97)	383	1.0	ref.	-	338(67.20)	165(32.80)	503	1.0	ref.	-	746(76.43)	230(23.57)	976	1.0	ref.	-
CCP-/CarP-FCS-	166(78.30)	46(21.70)	212	1.32	0.85-2.04	0.22	128(60.38)	84(39.62)	212	1.28	0.91-1.81	0.16	339(72.28)	130(27.72)	469	1.21	0.94-1.56	0.15
CCP-/CarP-FCS+	18(66.67)	9(33.33)	27	2.69	1.07-6.72	0.0346	15(53.57)	13(46.43)	28	1.95	0.88-4.35	0.10	37(62.71)	22(37.29)	59	1.87	1.07-3.27	0.0282
CCP+/CarP-FCS-	195(81.25)	45(18.75)	240	1.17	0.75-1.81	0.50	48(61.54)	30(38.46)	78	1.33	0.80-2.22	0.28	346(82.19)	75(17.81)	421	0.71	0.53-0.95	0.0223
CCP+/CarP-FCS+	158(81.03)	37(18.97)	195	1.31	0.82-2.09	0.26	35(70.00)	15(30.00)	50	0.84	0.43-1.63	0.60	347(86.97)	52(13.03)	399	0.48	0.35-0.67	<0.0001
Any DRB1*04																		
Controls	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	635(65.06)	341(34.94)	976	1.0	ref.	-
CCP-/CarP-FCS-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	306(65.25)	163(34.75)	469	0.99	0.78-1.25	0.93
CCP-/CarP-FCS+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	34(57.63)	25(42.37)	59	1.28	0.74-2.20	0.38
CCP+/CarP-FCS-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	141(33.49)	280(66.51)	421	3.82	2.98-4.90	<0.0001
CCP+/CarP-FCS+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	112(28.07)	287(71.93)	399	5.05	3.99-6.56	<0.0001
Any DRB1*07																		
Controls	337(87.99)	46(12.01)	383	1.0	ref.	-	392(77.93)	111(22.07)	503	1.0	ref.	-	819(83.91)	157(16.09)	976	1.0	ref.	-
CCP-/CarP-FCS-	196(92.45)	16(7.55)	212	0.66	0.36-1.23	0.19	180(84.91)	32(15.09)	212	0.58	0.37-0.92	0.02	421(89.77)	48(10.23)	469	0.58	0.41-0.83	0.0026
CCP-/CarP-FCS+	25(92.59)	2(7.41)	27	0.52	0.11-2.37	0.40	23(82.14)	5(17.86)	28	0.85	0.31-2.35	0.75	52(88.14)	7(11.86)	59	0.74	0.33-1.68	0.47
CCP+/CarP-FCS-	220(91.67)	20(8.33)	240	0.57	0.32-1.01	0.054	63(80.77)	15(19.23)	78	0.85	0.45-1.58	0.60	386(91.69)	35(8.31)	421	0.46	0.31-0.69	0.0001
CCP+/CarP-FCS+	172(88.21)	23(11.79)	195	0.96	0.56-1.67	0.90	37(74.00)	13(26.00)	50	1.17	0.58-2.34	0.66	363(90.98)	36(9.02)	399	0.52	0.35-0.77	0.0009
Any DRB1*08																		
Controls	359(93.73)	24(6.27)	383	1.0	ref.	-	438(87.08)	65(12.92)	503	1.0	ref.	-	887(90.88)	89(9.12)	976	1.0	ref.	-
CCP-/CarP-FCS-	189(89.15)	23(10.85)	212	1.85	0.99-3.47	0.054	178(83.96)	34(16.04)	212	1.38	0.87-2.21	0.17	412(87.85)	57(12.15)	469	1.41	0.99-2.03	0.060
CCP-/CarP-FCS+	22(81.48)	5(18.52)	27	4.52	1.40-14.63	0.012	23(82.14)	5(17.86)	28	1.64	0.58-4.63	0.35	49(83.05)	10(16.95)	59	2.13	1.03-4.42	0.0423
CCP+/CarP-FCS-	226(94.17)	14(5.83)	240	1.01	0.50-2.06	0.97	68(87.18)	10(12.82)	78	0.98	0.47-2.04	0.95	396(94.06)	25(5.94)	421	0.62	0.39-0.98	0.043
CCP+/CarP-FCS+	182(93.33)	13(6.67)	195	0.94	0.45-1.95	0.86	45(90.00)	5(10.00)	50	0.76	0.29-2.04	0.59	381(95.49)	18(4.51)	399	0.44	0.26-0.74	0.002
Any DRB1*09																		
Controls	373(97.36)	10(2.61)	383	1.0	ref.	-	481(95.63)	22(4.37)	503	1.0	ref.	-	944(96.72)	32(3.28)	976	1.0	ref.	-
CCP-/CarP-FCS-	204(96.23)	8(3.77)	212	1.39	0.51-3.80	0.52	205(96.70)	7(3.30)	212	0.80	0.33-1.94	0.62	454(96.80)	15(3.20)	469	0.99	0.53-1.88	0.98
CCP-/CarP-FCS+	27(100)	0(0)	27	NA	NA	NA	26(92.86)	2(7.14)	28	1.44	0.29-7.21	0.66	57(96.61)	2(3.39)	59	1.22	0.28-5.39	0.79
CCP+/CarP-FCS-	232(96.67)	8(3.33)	240	1.38	0.52-3.68	0.52	73(93.59)	5(6.41)	78	1.40	0.49-4.02	0.53	408(96.91)	13(3.09)	421	0.87	0.44-1.70	0.68
CCP+/CarP-FCS+	191(97.95)	4(2.05)	195	0.80	0.24-2.66	0.71	44(88.00)	6(12.00)	50	2.95	1.06-8.18	0.038	389(97.49)	10(2.51)	399	0.74	0.36-1.54	0.43
Any DRB1*10																		
Controls	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	956(97.95)	20(2.05)	976	1.0	ref.	-
CCP-/CarP-FCS-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	459(97.87)	10(2.13)	469	1.03	0.47-2.29	0.94
CCP-/CarP-FCS+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	58(98.31)	1(1.69)	59	0.67	0.09-5.32	0.71
CCP+/CarP-FCS-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	410(97.39)	11(2.61)	421	1.22	0.57-2.60	0.61
CCP+/CarP-FCS+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	384(96.24)	15(3.76)	399	1.78	0.90-3.54	0.10
Any DRB1*11																		
Controls	355(92.69)	28(7.31)	383	1.0	ref.	-	428(85.09)	75(14.91)	503	1.0	ref.	-	873(89.45)	103(10.55)	976	1.0	ref.	-
CCP-/CarP-FCS-	200(94.34)	12(5.66)	212	0.82	0.40-1.67	0.58	180(84.91)	32(15.09)	212	1.11	0.69-1.77	0.67	425(90.62)	44(9.38)	469	0.93	0.64-1.36	0.70

CCP-/CarP-FCS+	24(88.89)	3(11.11)	27	1.94	0.51-7.35	0.33	24(85.71)	4(14.29)	28	0.92	0.30-2.85	0.88	52(88.14)	7(11.86)	59	1.24	0.54-2.86	0.61
CCP+/CarP-FCS-	215(89.58)	25(10.42)	240	1.47	0.82-2.64	0.19	62(79.49)	16(20.51)	78	1.72	0.91-3.25	0.09	380(90.26)	41(9.74)	421	0.93	0.63-1.37	0.71
CCP+/CarP-FCS+	177(90.77)	18(9.23)	195	1.20	0.63-2.27	0.58	42(84.00)	8(16.00)	50	1.14	0.50-2.62	0.76	373(93.48)	26(6.52)	399	0.58	0.37-0.92	0.02
Any DRB1*12																		
Controls	369(96.34)	14(3.66)	383	1.0	ref.	-	473(94.04)	30(5.96)	503	1.0	ref.	-	932(95.49)	44(4.51)	976	1.0	ref.	-
CCP-/CarP-FCS-	206(97.17)	6(2.83)	212	0.64	0.24-1.76	0.39	197(92.92)	15(7.08)	212	1.15	0.59-2.24	0.68	448(95.52)	21(4.48)	469	0.92	0.53-1.60	0.77
CCP-/CarP-FCS+	26(96.30)	1(3.70)	27	1.17	0.13-10.32	0.89	26(92.86)	2(7.14)	28	1.37	0.30-6.29	0.68	56(94.92)	3(5.08)	59	1.22	0.36-4.13	0.75
CCP+/CarP-FCS-	233(97.08)	7(2.92)	240	0.77	0.29-2.00	0.58	74(94.87)	4(5.13)	78	0.78	0.25-2.37	0.66	410(97.39)	11(2.61)	421	0.54	0.27-1.07	0.08
CCP+/CarP-FCS+	183(93.85)	12(6.15)	195	1.85	0.81-4.22	0.15	48(96.00)	2(4.00)	50	0.72	0.16-3.22	0.67	385(96.49)	14(3.51)	399	0.79	0.43-1.47	0.46
Any DRB1*13																		
Controls	289(75.46)	94(24.54)	383	1.0	ref.	-	331(65.81)	172(34.19)	503	1.0	ref.	-	710(72.75)	266(27.25)	976	1.0	ref.	-
CCP-/CarP-FCS-	168(79.25)	44(20.75)	212	0.79	0.52-1.21	0.28	129(60.85)	83(39.15)	212	1.29	0.91-1.83	0.15	342(72.92)	127(27.08)	469	1.02	0.79-1.31	0.89
CCP-/CarP-FCS+	26(96.30)	1(3.70)	27	0.12	0.02-0.89	0.04	18(64.29)	10(35.71)	28	0.96	0.42-2.19	0.91	48(81.36)	11(18.64)	59	0.59	0.30-1.16	0.12
CCP+/CarP-FCS-	208(86.67)	32(13.33)	240	0.49	0.31-0.77	0.002	60(76.92)	18(23.08)	78	0.55	0.31-0.98	0.04	371(88.12)	50(11.88)	421	0.36	0.26-0.50	<0.0001
CCP+/CarP-FCS+	175(89.74)	20(10.26)	195	0.34	0.20-0.58	<0.0001	38(76.00)	12(24.00)	50	0.59	0.29-1.19	0.14	367(91.98)	32(8.02)	399	0.23	0.16-0.34	<0.0001
Any DRB1*14																		
Controls	378(98.69)	5(1.31)	383	1.0	ref.	-	465(92.45)	38(7.55)	504	1.0	ref.	-	933(95.59)	43(4.41)	976	1.0	ref.	-
CCP-/CarP-FCS-	205(96.70)	7(3.30)	212	2.88	0.88-9.44	0.08	196(92.45)	16(7.55)	212	1.02	0.54-1.91	0.96	446(95.10)	23(4.90)	469	1.17	0.69-1.99	0.56
CCP-/CarP-FCS+	27(100)	0(0)	27	NA	NA	NA	24(85.71)	4(14.29)	28	1.85	0.58-5.89	0.30	55(93.22)	4(6.78)	59	1.52	0.51-4.47	0.45
CCP+/CarP-FCS-	231(96.25)	9(3.75)	240	3.19	1.03-9.90	0.05	74(94.87)	4(5.13)	78	0.58	0.19-1.72	0.32	408(96.91)	13(3.09)	421	0.65	0.35-1.24	0.19
CCP+/CarP-FCS+	192(98.46)	3(1.54)	195	1.35	0.31-5.85	0.69	49(98.00)	1(2.00)	50	0.26	0.03-1.96	0.19	395(99.00)	4(1.00)	399	0.21	0.08-0.60	0.0036
Any DRB1*15																		
Controls	295(77.02)	88(22.98)	383	1.0	ref.	-	312(62.03)	191(37.97)	503	1.0	ref.	-	697(71.41)	279(28.59)	976	1.0	ref.	-
CCP-/CarP-FCS-	171(80.66)	41(19.34)	212	0.80	0.52-1.23	0.31	143(67.45)	69(32.55)	212	0.74	0.52-1.06	0.10	359(76.55)	110(23.45)	469	0.75	0.58-0.97	0.031
CCP-/CarP-FCS+	22(81.48)	5(18.52)	27	0.65	0.23-1.84	0.41	21(75.00)	7(25.00)	28	0.56	0.23-1.35	0.19	47(79.66)	12(20.34)	59	0.64	0.33-1.23	0.18
CCP+/CarP-FCS-	173(72.08)	67(27.92)	240	1.28	0.87-1.88	0.21	44(56.41)	34(43.59)	78	1.25	0.76-2.06	0.38	320(76.01)	101(23.99)	421	0.80	0.61-1.04	0.10
CCP+/CarP-FCS+	141(72.31)	54(27.69)	195	1.28	0.86-1.93	0.23	27(54.00)	23(46.00)	50	1.43	0.78-2.61	0.25	322(80.70)	77(19.30)	399	0.59	0.45-0.79	0.0004
Any DRB1*16																		
Controls	380(99.22)	3(0.78)	383	1.0	ref.	-	493(98.01)	10(1.99)	503	1.0	ref.	-	963(98.67)	13(1.33)	976	1.0	ref.	-
CCP-/CarP-FCS-	210(99.06)	2(0.94)	212	0.96	0.15-6.17	0.97	206(97.17)	6(2.83)	212	1.46	0.51-4.21	0.48	461(98.29)	8(1.71)	469	1.14	0.46-2.82	0.78
CCP-/CarP-FCS+	27(100)	0(0)	27	NA	NA	NA	28(100)	0(0)	28	NA	NA	NA	59(100)	0(0)	59	NA	NA	NA
CCP+/CarP-FCS-	237(98.75)	3(1.25)	240	1.19	0.22-6.29	0.84	72(92.31)	6(7.69)	78	5.14	1.67-15.85	0.0043	412(97.86)	9(2.14)	421	1.54	0.64-3.72	0.34
CCP+/CarP-FCS+	191(97.95)	4(2.05)	195	1.87	0.40-8.84	0.43	47(94.00)	3(6.00)	50	2.74	0.67-11.24	0.16	392(98.25)	7(1.75)	399	1.27	0.50-3.26	0.62

*: adjusted for age, gender and residential area

Supplementary Table 2a. RA risk in different subgroups divided by the presence/absence of CarP-Fib and CCP antibodies, in subjects exposed to different HLA alleles compared with non-exposed subjects. Netherlands

Antibody	SE Positive stratum						SE Negative stratum						Overall					
	Negative N (%)	Positive N (%)	N total	OR	95%CI	p-value	Negative N (%)	Positive N (%)	N total	OR	95%CI	p-value	Negative N (%)	Positive N (%)	N total	OR	95%CI	p-value
Any DRB1*01																		
Controls	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	948 (78.3)	263 (21.7)	1211	1.00	ref.	-
CCP-/CarP-Fib-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	233 (73.5)	84 (26.5)	317	1.30	0.98-1.73	0.07
CCP-/CarP-Fib+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	24 (82.8)	5 (17.2)	29	0.75	0.28-1.99	0.56
CCP+/CarP-Fib-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	104 (78.8)	28 (21.2)	132	0.97	0.63-1.51	0.89
CCP+/CarP-Fib+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	184 (71.6)	73 (28.4)	257	1.43	1.06-1.94	0.02
Any DRB1*03																		
Controls	385 (83.7)	75 (16.3)	460	1.0	ref.	-	480 (71.2)	194 (28.8)	674	1.0	ref.	-	941 (77.7)	270 (22.3)	1211	1.0	ref.	-
CCP-/CarP-Fib-	96 (77.4)	28 (22.6)	124	1.50	0.92-2.44	0.11	95 (56.5)	73 (43.5)	168	1.90	1.34-2.69	0.000	215 (67.8)	102 (32.2)	317	1.65	1.26-2.17	0.000
CCP-/CarP-Fib+	8 (50.0)	8 (50.0)	16	5.13	1.87-14.10	0.002	7 (58.3)	5 (41.7)	12	1.77	0.55-5.64	0.34	16 (55.2)	13 (44.8)	29	2.83	1.35-5.96	0.006
CCP+/CarP-Fib-	53 (76.8)	16 (23.2)	69	1.55	0.84-2.86	0.16	24 (68.6)	11 (31.4)	35	1.13	0.55-2.36	0.74	105 (79.5)	27 (20.5)	132	0.90	0.58-1.40	0.63
CCP+/CarP-Fib+	119 (81.0)	28 (19.0)	147	1.21	0.75-1.95	0.44	31 (70.5)	13 (29.5)	44	1.04	0.53-2.03	0.91	216 (84.0)	41 (16.0)	257	0.66	0.46-0.95	0.03
Any DRB1*04																		
Controls	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	875 (72.3)	336 (27.7)	1211	1.0	ref.	-
CCP-/CarP-Fib-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	232 (73.2)	85 (26.8)	317	0.95	0.72-1.26	0.74
CCP-/CarP-Fib+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	15 (51.7)	14 (48.3)	29	2.43	1.16-5.09	0.02
CCP+/CarP-Fib-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	61 (46.2)	71 (53.8)	132	3.03	2.11-4.36	0.000
CCP+/CarP-Fib+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	109 (42.4)	148 (57.6)	257	3.54	2.68-4.67	0.000
Any DRB1*07																		
Controls	395 (85.9)	65 (14.1)	460	1.0	ref.	-	502 (74.5)	172 (25.5)	674	1.0	ref.	-	973 (80.3)	238 (19.7)	1211	1.0	ref.	-
CCP-/CarP-Fib-	111 (89.5)	13 (10.5)	124	0.71	0.38-1.34	0.29	128 (76.2)	40 (23.8)	168	0.91	0.61-1.35	0.65	264 (83.3)	53 (16.7)	317	0.82	0.59-1.14	0.24
CCP-/CarP-Fib+	15 (93.8)	1 (6.2)	16	0.41	0.05-3.12	0.39	10 (83.3)	2 (16.7)	12	0.58	0.13-2.69	0.49	26 (89.7)	3 (10.3)	29	0.47	0.14-1.57	0.22
CCP+/CarP-Fib-	62 (89.9)	7 (10.1)	69	0.69	0.30-1.57	0.37	26 (74.3)	9 (25.7)	35	1.01	0.46-2.20	0.98	116 (87.9)	16 (12.1)	132	0.56	0.33-0.97	0.04
CCP+/CarP-Fib+	125 (85.0)	22 (15.0)	147	1.07	0.63-1.81	0.80	32 (72.7)	12 (27.3)	44	1.09	0.55-2.17	0.80	223 (86.8)	34 (13.2)	257	0.62	0.42-0.92	0.02
Any DRB1*08																		
Controls	435 (94.6)	25 (5.4)	460	1.0	ref.	-	611 (90.7)	63 (9.3)	674	1.0	ref.	-	1123 (92.7)	88 (7.3)	1211	1.0	ref.	-
CCP-/CarP-Fib-	122 (98.4)	2 (1.6)	124	0.29	0.07-1.22	0.09	162 (96.4)	6 (3.6)	168	0.36	0.15-0.85	0.02	309 (97.5)	8 (2.5)	317	0.33	0.16-0.69	0.003
CCP-/CarP-Fib+	15 (93.8)	1 (6.2)	16	1.16	0.15-9.14	0.89	11 (91.7)	1 (8.3)	12	0.88	0.11-6.94	0.91	27 (93.1)	2 (6.9)	29	0.95	0.22-4.04	0.94
CCP+/CarP-Fib-	65 (94.2)	4 (5.8)	69	1.07	0.36-3.18	0.90	33 (94.3)	2 (5.7)	35	0.59	0.14-2.51	0.47	126 (95.5)	6 (4.5)	132	0.61	0.26-1.42	0.25
CCP+/CarP-Fib+	144 (98.0)	3 (2.0)	147	0.36	0.11-1.22	0.10	42 (95.5)	2 (4.5)	44	0.46	0.11-1.95	0.29	252 (98.1)	5 (1.9)	257	0.25	0.10-0.63	0.003
Any DRB1*09																		
Controls	454 (98.7)	6 (1.3)	460	1.0	ref.	-	652 (96.7)	22 (3.3)	674	1.0	ref.	-	1183 (97.7)	28 (2.3)	1211	1.0	ref.	-
CCP-/CarP-Fib-	121 (97.6)	3 (2.4)	124	1.88	0.46-7.61	0.38	161 (95.8)	7 (4.2)	168	1.29	0.54-3.07	0.57	307 (96.8)	10 (3.2)	317	1.38	0.66-2.86	0.39
CCP-/CarP-Fib+	16 (100.0)	0 (0.0)	16	NA	NA	NA	12 (100.0)	0 (0.0)	12	NA	NA	NA	29 (100.0)	0 (0.0)	29	NA	NA	NA
CCP+/CarP-Fib-	68 (98.6)	1 (1.4)	69	1.11	0.13-9.39	0.92	32 (91.4)	3 (8.6)	35	2.78	0.79-9.77	0.11	128 (97.0)	4 (3.0)	132	1.32	0.46-3.82	0.61
CCP+/CarP-Fib+	139 (94.6)	8 (5.4)	147	4.36	1.49-12.77	0.007	38 (86.4)	6 (13.6)	44	4.68	1.79-12.22	0.002	242 (94.2)	15 (5.8)	257	2.62	1.38-4.98	0.003
Any DRB1*10																		
Controls	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	1180 (97.4)	31 (2.6)	1211	1.0	ref.	-
CCP-/CarP-Fib-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	313 (98.7)	4 (1.3)	317	0.49	0.17-1.39	0.18
CCP-/CarP-Fib+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	29 (100.0)	0 (0.0)	29	NA	NA	NA
CCP+/CarP-Fib-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	120 (90.9)	12 (9.1)	132	3.81	1.91-7.61	0.000
CCP+/CarP-Fib+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	230 (89.5)	27 (10.5)	257	4.47	2.62-7.63	0.000
Any DRB1*11																		

Controls	390 (84.8)	70 (15.2)	460	1.0	ref.	-	532 (78.9)	142 (21.1)	674	1.0	ref.	-	999 (82.5)	212 (17.5)	1211	1.0	ref.	-
CCP-/CarP-Fib-	111 (89.5)	13 (10.5)	124	0.65	0.35-1.22	0.18	126 (75.0)	42 (25.0)	168	1.25	0.84-1.85	0.27	262 (82.6)	55 (17.4)	317	0.99	0.71-1.37	0.95
CCP-/CarP-Fib+	14 (87.5)	2 (12.5)	16	0.80	0.18-3.58	0.77	10 (83.3)	2 (16.7)	12	0.75	0.16-3.46	0.71	25 (86.2)	4 (13.8)	29	0.75	0.26-2.19	0.60
CCP+/CarP-Fib-	63 (91.3)	6 (8.7)	69	0.53	0.22-1.27	0.16	24 (68.6)	11 (31.4)	35	1.72	0.82-3.59	0.15	115 (87.1)	17 (12.9)	132	0.70	0.41-1.18	0.18
CCP+/CarP-Fib+	128 (87.1)	19 (12.9)	147	0.83	0.48-1.43	0.49	36 (81.8)	8 (18.2)	44	0.83	0.38-1.83	0.65	230 (89.5)	27 (10.5)	257	0.55	0.36-0.85	0.006
Any DRB1*12																		
Controls	444 (96.5)	16 (3.5)	460	1.0	ref.	-	634 (94.1)	40 (5.9)	674	1.0	ref.	-	1154 (95.3)	57 (4.7)	1211	1.0	ref.	-
CCP-/CarP-Fib-	120 (96.8)	4 (3.2)	124	0.93	0.30-2.82	0.89	154 (91.7)	14 (8.3)	168	1.44	0.77-2.72	0.26	299 (94.3)	18 (5.7)	317	1.22	0.71-2.10	0.48
CCP-/CarP-Fib+	16 (100.0)	0 (0.0)	16	NA	NA	NA	11 (91.7)	1 (8.3)	12	1.44	0.18-11.44	0.73	28 (96.6)	1 (3.4)	29	0.72	0.10-5.41	0.75
CCP+/CarP-Fib-	68 (98.6)	1 (1.4)	69	0.41	0.05-3.13	0.39	34 (97.1)	1 (2.9)	35	0.47	0.06-3.49	0.46	130 (98.5)	2 (1.5)	132	0.31	0.08-1.29	0.11
CCP+/CarP-Fib+	143 (97.3)	4 (2.7)	147	0.78	0.26-2.36	0.66	41 (93.2)	3 (6.8)	44	1.16	0.34-3.91	0.81	250 (97.3)	7 (2.7)	257	0.57	0.26-1.26	0.16
Any DRB1*13																		
Controls	372 (80.9)	88 (19.1)	460	1.0	ref.	-	442 (65.6)	232 (34.4)	674	1.0	ref.	-	891 (73.6)	320 (26.4)	1211	1.0	ref.	-
CCP-/CarP-Fib-	100 (80.6)	24 (19.4)	124	1.02	0.61-1.68	0.96	113 (67.3)	55 (32.7)	168	0.93	0.65-1.33	0.68	237 (74.8)	80 (25.2)	317	0.94	0.71-1.25	0.67
CCP-/CarP-Fib+	14 (87.5)	2 (12.5)	16	0.60	0.14-2.71	0.51	10 (83.3)	2 (16.7)	12	0.38	0.08-1.75	0.22	25 (86.2)	4 (13.8)	29	0.45	0.15-1.29	0.14
CCP+/CarP-Fib-	63 (91.3)	6 (8.7)	69	0.40	0.17-0.96	0.04	24 (68.6)	11 (31.4)	35	0.87	0.42-1.81	0.87	115 (87.1)	17 (12.9)	132	0.41	0.24-0.70	0.001
CCP+/CarP-Fib+	132 (89.8)	15 (10.2)	147	0.48	0.27-0.86	0.014	35 (79.5)	9 (20.5)	44	0.49	0.23-1.04	0.06	232 (90.3)	25 (9.7)	257	0.30	0.20-0.46	0.000
Any DRB1*14																		
Controls	438 (95.2)	22 (4.8)	460	1.0	ref.	-	613 (90.9)	61 (9.1)	674	1.0	ref.	-	1128 (93.1)	83 (6.9)	1211	1.0	ref.	-
CCP-/CarP-Fib-	117 (94.4)	7 (5.6)	124	1.19	0.50-2.86	0.70	159 (94.6)	9 (5.4)	168	0.57	0.28-1.17	0.13	301 (95.0)	16 (5.0)	317	0.72	0.42-1.25	0.25
CCP-/CarP-Fib+	16 (100.0)	0 (0.0)	16	NA	NA	NA	10 (83.3)	2 (16.7)	12	2.01	0.43-9.38	0.38	27 (93.1)	2 (6.9)	29	1.01	0.24-4.31	0.99
CCP+/CarP-Fib-	66 (95.7)	3 (4.3)	69	0.91	0.26-3.11	0.87	32 (91.4)	3 (8.6)	35	0.94	0.28-3.17	0.92	126 (95.5)	6 (4.5)	132	0.65	0.28-1.51	0.32
CCP+/CarP-Fib+	140 (95.2)	7 (4.8)	147	1.00	0.42-2.38	0.99	43 (97.7)	1 (2.3)	44	0.23	0.03-1.73	0.15	249 (96.9)	8 (3.1)	257	0.44	0.21-0.91	0.03
Any DRB1*15																		
Controls	381 (82.8)	79 (17.2)	460	1.0	ref.	-	424 (62.9)	250 (37.1)	674	1.0	ref.	-	882 (72.8)	329 (27.2)	1211	1.0	ref.	-
CCP-/CarP-Fib-	98 (79.0)	26 (21.0)	124	1.28	0.78-2.10	0.33	119 (70.8)	49 (29.2)	168	0.70	0.48-1.01	0.06	242 (76.3)	75 (23.7)	317	0.83	0.62-1.11	0.21
CCP-/CarP-Fib+	15 (93.8)	1 (6.2)	16	0.32	0.04-2.47	0.28	5 (41.7)	7 (58.3)	12	2.37	0.75-7.56	0.14	21 (72.4)	8 (27.6)	29	1.02	0.45-2.33	0.96
CCP+/CarP-Fib-	48 (69.6)	21 (30.4)	69	2.11	1.20-3.72	0.01	25 (71.4)	10 (28.6)	35	0.68	0.32-1.44	0.31	100 (75.8)	32 (24.2)	132	0.86	0.57-1.30	0.47
CCP+/CarP-Fib+	110 (74.8)	37 (25.2)	147	1.62	1.04-2.53	0.03	23 (52.3)	21 (47.7)	44	1.55	0.84-2.86	0.16	198 (77.0)	59 (23.0)	257	0.80	0.58-1.10	0.17
Any DRB1*16																		
Controls	454 (98.7)	6 (1.3)	460	1.0	ref.	-	653 (96.9)	21 (3.1)	674	1.0	ref.	-	1184 (97.8)	27 (2.2)	1211	1.0	ref.	-
CCP-/CarP-Fib-	123 (99.2)	1 (0.8)	124	0.62	0.07-5.16	0.65	162 (96.4)	6 (3.6)	168	1.15	0.46-2.90	0.76	310 (97.8)	7 (2.2)	317	0.99	0.43-2.30	0.98
CCP-/CarP-Fib+	16 (100.0)	0 (0.0)	16	NA	NA	NA	12 (100.0)	0 (0.0)	12	NA	NA	NA	29 (100.0)	0 (0.0)	29	NA	NA	NA
CCP+/CarP-Fib-	66 (95.7)	3 (4.3)	69	3.44	0.84-14.08	0.09	35 (100.0)	0 (0.0)	35	NA	NA	NA	129 (97.7)	3 (2.3)	132	1.02	0.31-3.41	0.98
CCP+/CarP-Fib+	146 (99.3)	1 (0.7)	147	0.52	0.06-4.34	0.54	43 (97.7)	1 (2.3)	44	0.72	0.10-5.50	0.75	255 (99.2)	2 (0.8)	257	0.34	0.08-1.46	0.15

Supplementary Table2b. RA risk in different subgroups divided by the presence/absence of CarP-FCS and CCP antibodies, in subjects exposed to different HLA alleles compared with non-exposed subjects. Netherlands

Antibody	SE Positive stratum						SE Negative stratum						Overall					
	Negative N (%)	Positive N (%)	N total	OR*	95%CI	p-value	Negative N (%)	Positive N (%)	N total	OR*	95%CI	p-value	Negative N (%)	Positive N (%)	N total	OR*	95%CI	p-value
Any DRB1*01																		
Controls	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	948 (78.3)	263 (21.7)	1211	1.0	ref.	-
CCP-/CarP-FCS-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	209 (74.1)	73 (25.9)	282	1.26	0.93-1.70	0.13
CCP-/CarP-FCS+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	42 (80.8)	10 (19.2)	52	0.86	0.43-1.73	0.67
CCP+/CarP-FCS-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	68 (69.4)	30 (30.6)	98	1.59	1.01-2.50	0.04
CCP+/CarP-FCS+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	214 (75.6)	69 (24.4)	283	1.16	0.86-1.58	0.33
Any DRB1*03																		
Controls	385 (83.7)	75 (16.3)	460	1.0	ref.	-	480 (71.2)	194 (28.8)	674	1.0	ref.	-	941 (77.7)	270 (22.3)	1211	1.0	ref.	-
CCP-/CarP-FCS-	84 (75.0)	28 (25.0)	112	1.71	1.04-2.81	0.03	87 (59.2)	60 (40.8)	147	1.71	1.18-2.47	0.005	193 (68.4)	89 (31.6)	282	1.61	1.21-2.14	0.001
CCP-/CarP-FCS+	14 (66.7)	7 (33.3)	21	2.57	1.00-6.57	0.05	13 (44.8)	16 (55.2)	29	3.04	1.44-6.45	0.004	29 (55.8)	23 (44.2)	52	2.76	1.57-4.86	0.000
CCP+/CarP-FCS-	42 (77.8)	12 (22.2)	54	1.47	0.74-2.92	0.28	15 (75.0)	5 (25.0)	20	0.83	0.30-2.30	0.83	81 (82.7)	17 (17.3)	98	0.73	0.43-1.26	0.26
CCP+/CarP-FCS+	126 (80.3)	31 (19.7)	157	1.26	0.79-2.01	0.32	38 (66.7)	19 (33.3)	57	1.24	0.70-2.20	0.47	233 (82.3)	50 (17.7)	283	0.75	0.54-1.05	0.09
Any DRB1*04																		
Controls	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	875 (72.3)	336 (27.7)	1211	1.0	ref.	-
CCP-/CarP-FCS-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	201 (71.3)	81 (28.7)	282	1.05	0.79-1.40	0.74
CCP-/CarP-FCS+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	38 (73.1)	14 (26.9)	52	0.96	0.51-1.79	0.90
CCP+/CarP-FCS-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	44 (44.9)	54 (55.1)	98	3.20	2.11-4.85	0.000
CCP+/CarP-FCS+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	121 (42.8)	162 (57.2)	283	3.49	2.67-4.55	0.000
Any DRB1*07																		
Controls	395 (85.9)	65 (14.1)	460	1.0	ref.	-	502 (74.5)	172 (25.5)	674	1.0	ref.	-	973 (80.3)	238 (19.7)	1211	1.0	ref.	-
CCP-/CarP-FCS-	99 (88.4)	13 (11.6)	112	0.80	0.42-1.51	0.49	111 (75.5)	36 (24.5)	147	0.95	0.63-1.43	0.80	233 (82.6)	49 (17.4)	282	0.86	0.61-1.21	0.38
CCP-/CarP-FCS+	20 (95.2)	1 (4.8)	21	0.30	0.04-2.30	0.25	23 (79.3)	6 (20.7)	29	0.76	0.31-1.90	0.56	45 (86.5)	7 (13.5)	52	0.64	0.28-1.43	0.27
CCP+/CarP-FCS-	46 (85.2)	8 (14.8)	54	1.06	0.48-2.34	0.89	19 (95.0)	1 (5.0)	20	0.15	0.02-1.16	0.07	89 (90.8)	9 (9.2)	98	0.41	0.21-0.83	0.013
CCP+/CarP-FCS+	136 (86.6)	21 (13.4)	157	0.94	0.55-1.59	0.81	39 (68.4)	18 (31.6)	57	1.35	0.75-2.42	0.32	244 (86.2)	39 (13.8)	283	0.65	0.45-0.94	0.02
Any DRB1*08																		
Controls	435 (94.6)	25 (5.4)	460	1.0	ref.	-	611 (90.7)	63 (9.3)	674	1.0	ref.	-	1123 (92.7)	88 (7.3)	1211	1.0	ref.	-
CCP-/CarP-FCS-	110 (98.2)	2 (1.8)	112	0.32	0.07-1.36	0.12	142 (96.6)	5 (3.4)	147	0.34	0.14-0.86	0.02	275 (97.5)	7 (2.5)	282	0.33	0.15-0.71	0.01
CCP-/CarP-FCS+	20 (95.2)	1 (4.8)	21	0.87	0.11-6.75	0.89	27 (93.1)	2 (6.9)	29	0.72	0.17-3.09	0.66	49 (94.2)	3 (5.8)	52	0.78	0.24-2.56	0.68
CCP+/CarP-FCS-	51 (94.4)	3 (5.6)	54	1.02	0.30-3.51	0.97	19 (95.0)	1 (5.0)	20	0.51	0.07-3.88	0.52	94 (95.9)	4 (4.1)	98	0.54	0.20-1.51	0.24
CCP+/CarP-FCS+	153 (97.5)	4 (2.5)	157	0.46	0.16-1.33	0.15	54 (94.7)	3 (5.3)	57	0.54	0.16-1.77	0.31	276 (97.5)	7 (2.5)	283	0.32	0.15-0.71	0.01
Any DRB1*09																		
Controls	454 (98.7)	6 (1.3)	460	1.0	ref.	-	652 (96.7)	22 (3.3)	674	1.0	ref.	-	1183 (97.7)	28 (2.3)	1211	1.0	ref.	-
CCP-/CarP-FCS-	109 (97.3)	3 (2.7)	112	2.08	0.51-8.46	0.31	141 (95.9)	6 (4.1)	147	1.26	0.50-3.17	0.62	273 (96.8)	9 (3.2)	282	1.39	0.65-2.99	0.39
CCP-/CarP-FCS+	21 (100)	0	21	NA	NA	NA	28 (96.6)	1 (3.4)	29	1.06	0.14-8.14	0.96	51 (98.1)	1 (1.9)	52	0.83	0.11-6.21	0.86
CCP+/CarP-FCS-	52 (96.3)	2 (3.7)	54	2.91	0.57-14.79	0.20	18 (90.0)	2 (10.0)	20	3.29	0.72-15.01	0.13	94 (95.9)	4 (4.1)	98	1.80	0.62-5.23	0.28
CCP+/CarP-FCS+	150 (95.5)	7 (4.5)	157	3.53	1.17-10.67	0.03	50 (87.7)	7 (12.3)	57	4.15	1.69-10.18	0.002	268 (94.7)	15 (5.3)	283	2.37	1.25-4.49	0.01
Any DRB1*10																		
Controls	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	1180 (97.4)	31 (2.6)	1211	1.0	ref.	-
CCP-/CarP-FCS-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	279 (98.9)	3 (1.1)	282	0.41	0.12-1.35	0.14
CCP-/CarP-FCS+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	51 (91.8)	1 (1.9)	52	0.75	0.10-5.58	0.78
CCP+/CarP-FCS-	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	90 (91.8)	8 (8.2)	98	3.38	1.51-7.58	0.003

CCP+/CarP-FCS+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	253 (89.4)	30 (10.6)	283	4.51	2.68-7.59	0.000
Any DRB1*11																		
Controls	390 (84.8)	70 (15.2)	460	1.0	ref.	-	532 (78.9)	142 (21.1)	674	1.0	ref.	-	999 (82.5)	212 (17.5)	1211	1.0	ref.	-
CCP-/CarP-FCS-	103 (92.0)	9 (8.0)	112	0.49	0.24-1.01	0.05	111 (75.5)	36 (24.5)	147	1.22	0.80-1.85	0.36	237 (84.0)	45 (16.0)	282	0.90	0.63-1.27	0.54
CCP-/CarP-FCS+	17 (81.0)	4 (19.0)	21	1.31	0.43-4.01	0.64	22 (75.9)	7 (24.1)	29	1.19	0.50-2.85	0.69	41 (78.8)	11 (21.2)	52	1.26	0.64-2.50	0.50
CCP+/CarP-FCS-	48 (88.9)	6 (11.1)	54	0.70	0.29-1.69	0.42	14 (70.0)	6 (30.0)	20	1.61	0.61-4.25	0.34	86 (87.8)	12 (12.2)	98	0.66	0.35-1.23	0.19
CCP+/CarP-FCS+	138 (87.9)	19 (12.1)	157	0.77	0.45-1.32	0.34	44 (77.2)	13 (22.8)	57	1.11	0.58-2.11	0.76	251 (88.7)	32 (11.3)	283	0.60	0.40-0.89	0.012
Any DRB1*12																		
Controls	444 (96.5)	16 (3.5)	460	1.0	ref.	-	634 (94.1)	40 (5.9)	674	1.0	ref.	-	1154 (95.3)	57 (4.7)	1211	1.0	ref.	-
CCP-/CarP-FCS-	109 (97.3)	3 (2.7)	112	0.76	0.22-2.67	0.67	133 (90.5)	14 (9.5)	147	1.67	0.88-3.15	0.12	265 (94.0)	17 (6.0)	282	1.30	0.74-2.27	0.36
CCP-/CarP-FCS+	21 (100)	0	21	NA	NA	NA	28 (96.6)	1 (3.4)	29	0.57	0.08-4.27	0.58	51 (98.1)	1 (1.9)	52	0.40	0.05-2.92	0.37
CCP+/CarP-FCS-	53 (98.1)	1 (1.9)	54	0.52	0.07-4.03	0.53	18 (90.0)	2 (10.0)	20	1.76	0.40-7.86	0.46	95 (96.9)	3 (3.1)	98	0.64	0.20-2.08	0.46
CCP+/CarP-FCS+	153 (97.5)	4 (2.5)	157	0.73	0.24-2.20	0.57	55 (96.5)	2 (3.5)	57	0.58	0.14-2.45	0.46	277 (97.9)	6 (2.1)	283	0.44	0.19-1.03	0.06
Any DRB1*13																		
Controls	372 (80.9)	88 (19.1)	460	1.0	ref.	-	442 (65.6)	232 (34.4)	674	1.0	ref.	-	891 (73.6)	320 (26.4)	1211	1.0	ref.	-
CCP-/CarP-FCS-	90 (80.4)	22 (19.6)	112	1.03	0.61-1.74	0.90	101 (68.7)	46 (31.3)	147	0.87	0.59-1.27	0.47	213 (75.5)	69 (24.5)	282	0.90	0.67-1.22	0.50
CCP-/CarP-FCS+	17 (81.0)	4 (19.0)	21	1.00	0.33-3.03	0.99	20 (69.0)	9 (31.0)	29	0.86	0.38-1.91	0.71	39 (75.0)	13 (25.0)	52	0.93	0.49-1.76	0.82
CCP+/CarP-FCS-	47 (87.0)	7 (13.0)	54	0.63	0.28-1.44	0.27	14 (70.0)	6 (30.0)	20	0.82	0.31-2.15	0.68	85 (86.7)	13 (13.3)	98	0.43	0.23-0.77	0.01
CCP+/CarP-FCS+	143 (91.1)	14 (8.9)	157	0.41	0.23-0.75	0.004	44 (77.2)	13 (22.8)	57	0.56	0.30-1.07	0.08	255 (90.1)	28 (9.9)	283	0.31	0.20-0.46	0.000
Any DRB1*14																		
Controls	438 (95.2)	22 (4.8)	460	1.0	ref.	-	613 (90.9)	61 (9.1)	674	1.0	ref.	-	1128 (93.1)	83 (6.9)	1211	1.0	ref.	-
CCP-/CarP-FCS-	107 (95.5)	5 (4.5)	112	0.93	0.34-2.51	0.89	140 (95.2)	7 (4.8)	147	0.50	0.23-1.12	0.09	270 (95.7)	12 (4.3)	282	0.60	0.33-1.12	0.11
CCP-/CarP-FCS+	19 (90.5)	2 (9.5)	21	2.10	0.46-9.57	0.34	26 (89.7)	3 (9.3)	29	1.16	0.34-3.94	0.81	47 (90.4)	5 (9.6)	52	1.45	0.56-3.73	0.45
CCP+/CarP-FCS-	53 (98.1)	1 (1.9)	54	0.38	0.05-2.84	0.34	17 (85.0)	3 (15.0)	20	1.77	0.51-6.22	0.37	94 (95.9)	4 (4.1)	98	0.58	0.21-1.61	0.30
CCP+/CarP-FCS+	148 (94.3)	9 (5.7)	157	1.21	0.55-2.69	0.64	56 (98.2)	1 (1.8)	57	0.18	0.02-1.32	0.09	273 (96.5)	10 (3.5)	283	0.50	0.26-0.97	0.04
Any DRB1*15																		
Controls	381 (82.8)	79 (17.2)	460	1.0	ref.	-	424 (62.9)	250 (37.1)	674	1.0	ref.	-	882 (72.8)	329 (27.2)	1211	1.0	ref.	-
CCP-/CarP-FCS-	88 (78.6)	24 (21.4)	112	1.32	0.79-2.20	0.29	97 (66.0)	50 (34.0)	147	0.87	0.60-1.27	0.48	208 (73.8)	74 (26.2)	282	0.95	0.71-1.28	0.75
CCP-/CarP-FCS+	20 (95.2)	1 (4.8)	21	0.24	0.03-1.82	0.17	23 (79.3)	6 (20.7)	29	0.44	0.18-1.10	0.08	45 (86.5)	7 (13.5)	52	0.42	0.19-0.93	0.03
CCP+/CarP-FCS-	44 (81.5)	10 (18.5)	54	1.10	0.53-2.27	0.81	10 (50.0)	10 (50.0)	20	1.70	0.70-4.13	0.25	78 (79.6)	20 (20.4)	98	0.69	0.41-1.14	0.15
CCP+/CarP-FCS+	112 (71.3)	45 (28.7)	157	1.94	1.27-2.96	0.002	37 (65.0)	20 (35.0)	57	0.92	0.52-1.62	0.76	216 (76.3)	67 (23.7)	283	0.83	0.62-1.13	0.23
Any DRB1*16																		
Controls	454 (98.7)	6 (1.3)	460	1.0	ref.	-	653 (96.9)	21 (3.1)	674	1.0	ref.	-	1184 (97.8)	27 (2.2)	1211	1.0	ref.	-
CCP-/CarP-FCS-	111 (99.1)	1 (0.9)	112	0.68	0.08-5.72	0.72	142 (96.6)	5 (3.4)	147	1.19	0.41-2.95	0.86	276 (97.9)	6 (2.1)	282	0.95	0.39-2.33	0.92
CCP-/CarP-FCS+	21 (100)	0	21	NA	NA	NA	28 (96.6)	1 (3.4)	29	1.18	0.14-8.55	0.92	51 (98.1)	1 (1.9)	52	0.86	0.12-6.45	0.88
CCP+/CarP-FCS-	51 (94.4)	3 (5.6)	54	4.45	1.08-18.34	0.04	20 (100)	0	20	NA	NA	NA	95 (96.9)	3 (3.1)	98	1.39	0.41-4.65	0.60
CCP+/CarP-FCS+	156 (99.4)	1 (0.6)	157	0.49	0.06-4.06	0.51	56 (98.2)	1 (1.8)	57	0.71	0.07-4.21	0.57	281 (99.3)	2 (0.7)	283	0.31	0.07-1.32	0.11

Supplementary Table3. Association analysis for disease risk in different RA subgroups divided by the presence/absence of anti-CarP-FCS and anti-CCP antibodies, in subjects exposed to any *HLA-DRB1-03* alleles compared with non-exposed subjects, stratified by shared epitope status.

Group	Shared epitope positive stratum						Shared epitope negative stratum					
	Any DRB1*03		OR*	95%CI	p-value	p-value for comparing two ORs**	Any DRB1*03		OR*	95%CI	p-value	p-value for comparing two ORs**
	None N (%)	Any N (%)					None N (%)	Any N (%)				
Leiden EAC cohort												
Controls	385 (83.7)	75 (16.3)	1.0	ref.	-		480 (71.2)	194 (28.8)	1.0	ref.	-	
CCP-/CarP-FCS-	84 (75.0)	28 (25.0)	1.71	1.04-2.81	0.030	1.71 vs. 2.57,	87 (59.2)	60 (40.8)	1.71	1.18-2.47	0.005	1.71 vs. 3.04,
CCP-/CarP-FCS+	14 (66.7)	7 (33.3)	2.57	1.00-6.57	0.050	p=0.43	13 (44.8)	16 (55.2)	3.04	1.44-6.45	0.004	p=0.15
CCP+/CarP-FCS-	42 (77.8)	12 (22.2)	1.47	0.74-2.92	0.28	1.47 vs. 1.26,	15 (75.0)	5 (25.0)	0.83	0.30-2.30	0.83	0.83 vs. 1.24,
CCP+/CarP-FCS+	126 (80.3)	31 (19.7)	1.26	0.79-2.01	0.32	p=0.70	38 (66.7)	19 (33.3)	1.24	0.70-2.20	0.47	p=0.49
Swedish EIRA cohort												
Controls	318 (83.0)	65(17.0)	1.0	ref.	-		338 (67.2)	165 (32.8)	1.0	ref.	-	
CCP-/CarP-FCS-	166 (78.3)	46 (21.7)	1.32	0.85-2.04	0.22	1.32 vs. 2.69,	128 (60.4)	84 (39.6)	1.28	0.91-1.81	0.16	1.28 vs. 1.95,
CCP-/CarP-FCS+	18 (66.7)	9 (33.3)	2.69	1.07-6.72	0.035	p=0.17	15 (53.6)	13 (46.4)	1.95	0.88-4.35	0.10	p=0.35
CCP+/CarP-FCS-	195 (81.3)	45 (18.7)	1.17	0.75-1.81	0.50	1.17 vs. 1.31,	48 (61.5)	30 (38.5)	1.33	0.80-2.22	0.28	1.33 vs. 0.84,
CCP+/CarP-FCS+	158 (81.0)	37 (19.0)	1.31	0.82-2.09	0.26	p=0.88	35 (70.0)	15 (30.0)	0.84	0.43-1.63	0.60	p=0.23
Meta-analysis												
Controls	703	140	1.0	ref.	-		818	359	1.0	ref.	-	
CCP-/CarP-FCS-	250	74	1.48	1.06-2.05	0.020	1.48 vs. 2.63,	215	144	1.47	1.11-1.95	0.008	1.47 vs. 2.47,
CCP-/CarP-FCS+	32	16	2.63	1.36-5.08	0.004	p=0.11	28	29	2.47	1.43-4.27	0.001	p=0.13
CCP+/CarP-FCS-	237	57	1.25	0.86-1.81	0.24	1.25 vs. 1.29,	63	35	1.21	0.77-1.90	0.41	1.21 vs. 1.05,
CCP+/CarP-FCS+	284	68	1.29	0.92-1.79	0.14	p=0.98	73	34	1.05	0.68-1.62	0.82	p=0.55

*: Odds ratios in Sweden cohort adjusted for age, gender and residential areas. **: Odds ratios of CCP-/CarP-FCS+ RA subsets were compared with odds ratios of CCP-/CarP-FCS- RA subsets; Odds ratios of CCP+/CarP-FCS+ RA subsets were compared with odds ratios of CCP+/CarP-FCS- RA subsets.