

# **KIR/HLA genotypes confer susceptibility and progression in patients with autoimmune hepatitis**

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**Table S1. HLA Association Studies in Type 1 AIH.**

Year	Author	Country	HLA studied	Significant HLA association	AIH	Controls	P
1980	Mackay <sup>1</sup>	Australia	A, B, DRw	DRw3	74%	32%	
1987	Krawitt <sup>2</sup>	US	A, B, DR	B8-DR3	60% (6/10)	39% (20/51)	
1990	Seki <sup>3</sup>	Japan	A, B, DR, DQ	Bw54	45.2% (14/31)	10.9% (42/386)	< 0.000005
				DR4	90.3% (28/31)	38.6% (149/386)	< 0.000001
1991	Donaldson <sup>4</sup>	UK	A, B, DR	A1-B8-DR3	38% (42/110)	11% (11/100)	<0.0005
				DR4	80% (35/44)	39% (31/79)	0.0013 (Pc)
1992	Seki <sup>5</sup>	Japan	DR, DQA1, DQB1, DPB1	DRB1*0405	67.3% (33/49)	29.6% (13/44)	< 0.005 (Pc)
				DQA1*0301	91.8% (45/49)	63.6% (28/44)	< 0.05 (Pc)
				DQB1*0401	65.3% (32/49)	27.3% (12/44)	< 0.001 (Pc)
1993	Manabe <sup>6</sup>	UK	A, B, DR, DQ, DPB1	A1-B8-DR3-DQ2-DPB1*0401	27% (27/101)	7% (7/105)	< 0.0005
1994	Doherty <sup>7</sup>	UK	DRB, DQA, DQB	DRB3*0101	58% (69/119)	25% (44/177)	
				DRB1*04:01	81%	42%	< 0.000001 (Pc)
1994	Fainboim <sup>8</sup>	Argentina	DRB1, DQB1	DRB1*1301	66.6%	10.5%	0.00001 (Pc)
				DQB1*0603			0.00001
1997	Strettell <sup>9</sup>	US	A, B, DRB1, DQA1, DQB1, DPB1	DRB1*0301	51% (44/86)	19% (19/102)	0.00003 (Pc)
				DQA1*0501	56% (48/86)	34% (35/102)	0.0341 (Pc)
				DQB1*0201	58% (50/86)	30% (31/102)	0.00143 (Pc)
				DRB1*0401	55% (23/42)	17% (14/83)	0.000132 (Pc)
				DRB1*1501	12% (10/86)	30% (31/120)	0.021 (Pc)
				DQA1*0102	17% (15/86)	38% (39/102)	0.0187 (Pc)
1997	Strettell <sup>10</sup>	UK	C	Cw*0701	54% (47/87)	34% (34/100)	0.024
1999	Bittencourt <sup>11</sup>	Brazil	DRB, DQB1	DRB1*13	70% (78/111)	26% (33/129)	< 0.00001
				DRB3	93% (103/111)	69% (89/129)	0.00007

				DQB1*06	68% (75/111)	41% (53/129)	0.00007
1999	Pando <sup>12</sup>	Argentina	DRB1, DRB3, DQA1, DQB1	DRB1*0405	11% (9/84)	1% (2/208)	< 0.005 (Pc)
2001	Goldberg <sup>13</sup>	Brazil	DRB1, DR3, DQA1, DAB1	DRB1*1301	87% (34/39)	50% (11/22)	0.00247
2003	Qiu <sup>14</sup>	China	DRB1	DRB1*04	22% (7/32)	6% (3/48)	0.08 (Pc)
2007	Fortes <sup>15</sup>	Venezuela	A, B, C, DR, DQ	DRB1*1301	34% (14/41)	7% (8/111)	0.003 (Pc)
				DQB1*04	2% (1/41)	22% (24/111)	0.016 (Pc)
2008	Lim <sup>16</sup>	Korea	A, B, C, DRB1, DQB1	DRB1*0405	37% (23/62)	14% (21/154)	0.0001
				DQB1*0401	37% (23/62)	13% (20/154)	0.00006
				DRB1*0406	2% (1/62)	12% (18/154)	0.018
				DQB1*0301	13% (8/62)	28% (43/154)	0.024
2014	Umemura <sup>17</sup>	Japan	A, B, C, DRB1, DQB1, DPB1	A*24:02	35% (108/312)	22% (90/402)	0.0053 (Pc)
				C*01:02	23% (73/312)	14% (58/402)	0.036 (Pc)
				DRB1*04:05	30% (95/312)	11% (45/402)	$4.0 \times 10^{-9}$ (Pc)
				DQB1*04:01	30% (94/312)	11% (45/402)	$3.7 \times 10^{-9}$ (Pc)
				DQB1*06:02	5% (17/312)	13% (53/402)	0.009 (Pc)
2014	de Boer <sup>18</sup>	Netherlands	Genome-wide association study	DRB1*03:01			$5.3 \times 10^{-49}$
				DQB1*04:01			$2.8 \times 10^{-18}$
2017	Oka <sup>19</sup>	Japan	DRB1, DQB1	DRB1*04:01	6.1% (22/360)	2.1% (22/1026)	0.0193 (Pc)
				DRB1*04:05	51.4% (185/360)	23.7% (243/1026)	$5.86 \times 10^{-20}$ (Pc)
				DQB1*04:01	50.6% (182/360)	20.8% (86/413)	$6.99 \times 10^{-17}$ (Pc)
				DRB1*13:02	8.3% (30/360)	15.9% (163/1026)	0.0080 (Pc)

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Abbreviations: HLA, human leukocyte antigen; AIH, autoimmune hepatitis; Pc, corrected P.

**Table S2. HLA and KIR Frequencies in Type 1 AIH and Healthy Subjects.**

	<b>AIH (n = 154)</b>	<b>Healthy subjects (n = 201)</b>	<b>P</b>	<b>OR (95% CI)</b>
HLA-A3 and -A11	38 (25%)	48 (24%)	0.862	
HLA-B Bw4	118 (77%)	154 (77%)	0.999	
HLA-B Bw4-80Ile	106 (69%)	110 (55%)	0.0070	1.83 (1.18-2.84)
HLA-B Bw4-80Thr	24 (16%)	57 (28%)	0.0045	0.47 (0.27-0.79)
HLA-B Bw6	144 (94%)	175 (87%)	0.046	2.14 (1.00-4.58)
HLA-C1	154 (100%)	199 (99%)	0.214*	
HLA-C2	18 (12%)	49 (24%)	0.0025	0.41 (0.23-0.74)
HLA-DRB1*04:05-DQB1*04:01	92 (67%)	42 (21%)	< 0.001	5.62 (3.52-8.97)
KIR2DL1	154 (100%)	201 (100%)	-	
KIR2DL2	24 (16%)	28 (14%)	0.662	
KIR2DL3	154 (100%)	201 (100%)	-	
KIR2DL4	154 (100%)	201 (100%)	-	
KIR2DL5	65 (42%)	81 (40%)	0.717	
KIR2DS1	62 (40%)	78 (39%)	0.781	
KIR2DS2	26 (17%)	32 (16%)	0.808	
KIR2DS3	20 (13%)	28 (14%)	0.797	
KIR2DS4	141 (92%)	191 (95%)	0.189	
KIR2DS5	47 (31%)	58 (29%)	0.734	
KIR3DL1	145 (94%)	191 (95%)	0.718	
KIR3DL2	152 (99%)	201(100%)	0.366*	
KIR3DL3	152 (99%)	199 (99%)	0.811*	
KIR3DS1	63 (41%)	84 (42%)	0.867	

\*Fisher's exact test.

Abbreviations: KIR, killer cell immunoglobulin-like receptor; AIH, autoimmune hepatitis.

**Table S3. HLA and KIR Frequencies in Type 1 AIH Patients with or without Liver Decompensation.**

	<b>Liver decompensation (n = 19)</b>	<b>Liver compensation (n = 135)</b>	<b>P</b>	<b>OR (95% CI)</b>
HLA-A3 and -A11	7 (37%)	31 (23%)	0.189	
HLA-B Bw4	10 (53%)	108 (80%)	0.008	0.28 (0.10-0.74)
HLA-B Bw4-80Ile	8 (42%)	98 (73%)	0.007	0.25 (0.08-0.80)
HLA-B Bw4-80Thr	2 (11%)	22 (16%)	0.516*	
HLA-B Bw6	18 (95%)	126 (93%)	0.816*	
HLA-C1	19 (100%)	135 (100%)	-	
HLA-C2	3 (16%)	15 (11%)	0.831*	
KIR2DL1	19 (100%)	135 (100%)	-	
KIR2DL2	1 (8%)	23 (16%)	0.324*	
KIR2DL3	19 (100%)	135 (100%)	-	
KIR2DL4	19 (100%)	135 (100%)	-	
KIR2DL5	9 (47%)	56 (42%)	0.627	
KIR2DS1	9 (47%)	53 (39%)	0.500	
KIR2DS2	1 (8%)	25 (18%)	0.264*	
KIR2DS3	3 (16%)	17 (13%)	0.981*	
KIR2DS4	16 (84%)	125 (93%)	0.430*	
KIR2DS5	8 (42%)	39 (29%)	0.241	
KIR3DL1	16 (84%)	129 (96%)	0.147*	
KIR3DL2	19 (100%)	133 (99%)	0.584*	
KIR3DL3	19 (100%)	139 (99%)	0.584*	
KIR3DS1	9 (47%)	54 (40%)	0.541	

\*Fisher's exact test.

Abbreviations: KIR, killer cell immunoglobulin-like receptor; AIH, autoimmune hepatitis.

**Table S4. HLA and KIR Frequencies in Type 1 AIH Patients According to Survival and Liver-related Death.**

	<b>Death (n = 13)</b>	<b>Survival (n = 141)</b>	<b>P</b>	<b>OR (95% CI)</b>
HLA-A3 and -A11	4 (31%)	34 (24%)	0.844	
HLA-B Bw4	6 (46%)	112 (79%)	0.007	0.22 (0.07-0.71)
HLA-B Bw4-80Ile	5 (39%)	101 (72%)	0.031*	0.25 (0.08-0.80)
HLA-B Bw4-80Thr	1 (8%)	23 (16%)	0.674*	
HLA-B Bw6	12 (92%)	132 (94%)	0.686*	
HLA-C1	13 (100%)	141 (100%)	-	
HLA-C2	0 (0%)	18 (13%)	0.358	
KIR2DL1	13 (100%)	141 (100%)	-	
KIR2DL2	1 (8%)	23 (16%)	0.674*	
KIR2DL3	13 (100%)	141 (100%)	-	
KIR2DL4	13 (100%)	141 (100%)	-	
KIR2DL5	6 (46%)	59 (42%)	0.763	
KIR2DS1	6 (46%)	56 (40%)	0.651	
KIR2DS2	1 (8%)	25 (18%)	0.591*	
KIR2DS3	2 (15%)	18 (13%)	0.871*	
KIR2DS4	11 (85%)	130 (92%)	0.675*	
KIR2DS5	6 (46%)	41 (29%)	0.201	
KIR3DL1	11 (85%)	134 (95%)	0.360*	
KIR3DL2	13 (100%)	139 (99%)	0.397*	
KIR3DL3	13 (100%)	139 (99%)	0.397*	
KIR3DS1	6 (46%)	57 (40%)	0.688	

\*Fisher's exact test.

Abbreviations: KIR, killer cell immunoglobulin-like receptor; AIH, autoimmune hepatitis.

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