



**CMV Infection in individuals with
NK cell Licensing Genotype
predisposes to Crohn's Disease**

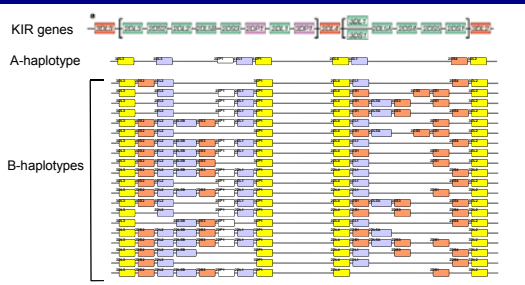
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Disclosure Statement

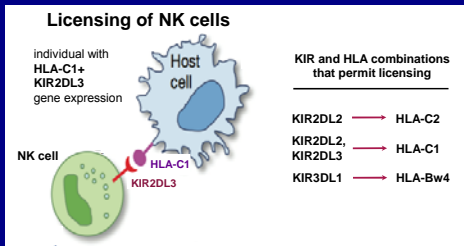
- In the past 12 months, I have had no relevant
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Two functionally distinct NK cell KIR haplotypes

Natural Killer (NK) cells belong to the innate immune system and express Killer Immunoglobulin Receptors (KIRs) on cell surface.



HLA and KIR gene driven programming of NK cells



Licensed NK cells implicated in Crohn's Disease (CD) pathogenesis by secretion of pro-inflammatory cytokines (IL-6, TNF- α , IFN- γ), promotion of T cell proliferation and Th17 differentiation (L. Lin, S Yusing, J Braun et al. *J Immunol* 2014)

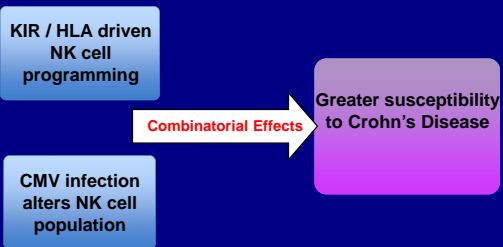
Cytomegalovirus (CMV) infection in active IBD and onset of disease.

	IBD (n = 226)	UC (n = 189)	CD (n = 37)	Healthy controls (n = 290)
CMV detection	n (%)	n (%)	n (%)	n (%)
Serum CMV IgG+	172 (76.11) ^b	139 (73.54) ^b	33 (89.19) ^b	147 (50.69)
Serum CMV IgM+	4 (1.77) ^c	3 (1.59) ^d	1 (2.70) ^e	1 (0.34)

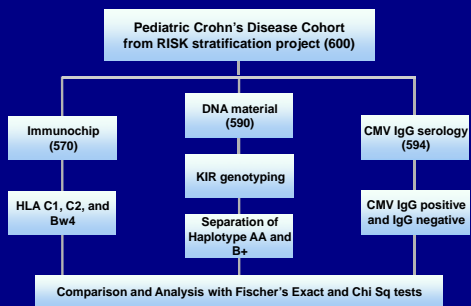
^b Compare with healthy controls, OR = 3.099, 95% CI: 2.113-4.543, P < 0.001
^c Compare with healthy controls, OR = 2.704, 95% CI: 1.119-6.022, P < 0.001
^d Compare with healthy controls, OR = 0.026, 95% CI: 0.002-0.225, P < 0.001
^e Compare with healthy controls, OR = 5.207, 95% CI: 0.578-46.914, P = 0.235
^f Compare with healthy controls, OR = 4.661, 95% CI: 0.481-45.148, P = 0.344
^g Compare with healthy controls, OR = 0.028, 95% CI: 0.001-1.112, P = 0.540

NK cells play an important role in limiting CMV infection. In turn, CMV causes expansion of licensed NK cells. The consequences of CMV induced expansion of pro-inflammatory licensed NK cells in pathogenesis of CD have not been investigated until now.

Hypothesis



Methods



• Biospecimens collected from pediatric CD patients at time of diagnosis

Results

CMV infection rates are significantly elevated in highly licensed subgroup in KIR AA haplotype

KIR haplotype AA				
HLA-B and HLA-C	CMV pos	CMV neg	Total	% positive CMV
Bw4 Bw4 C1 C1	4	2	6	66.67%
Bw4 Bw6 C1 C1	2	10	12	16.67%
Bw6 Bw6 C1 C1	8	25	33	24.24%
Bw4 Bw4 C1 C2	1	11	12	8.33%
Bw4 Bw6 C1 C2	9	37	46	19.57%
Bw6 Bw6 C1 C2	4	22	26	15.38%
Bw4 Bw4 C2 C2	6	16	22	27.27%
Bw4 Bw6 C2 C2	2	11	13	15.38%
Bw6 Bw6 C2 C2	3	4	7	42.86%

Results

Conversely, CMV infection rates are significantly lower in Bw4^{homo}C1^{homo} group with KIR Haplotype B

KIR haplotype B+				
HLA-B and HLA-C	CMV pos	CMV neg	Total	% positive CMV
Bw4 Bw4 C1 C1	1	12	13	7.69%
Bw4 Bw6 C1 C1	16	41	57	28.07%
Bw6 Bw6 C1 C1	11	64	75	14.67%
Bw4 Bw4 C1 C2	9	29	38	23.68%
Bw4 Bw6 C1 C2	16	84	100	16.00%
Bw6 Bw6 C1 C2	6	38	44	13.64%
Bw4 Bw4 C2 C2	6	15	21	28.57%
Bw4 Bw6 C2 C2	5	25	30	16.67%
Bw6 Bw6 C2 C2	4	7	11	36.36%

Correlation between CMV infection and KIR Haplotypes

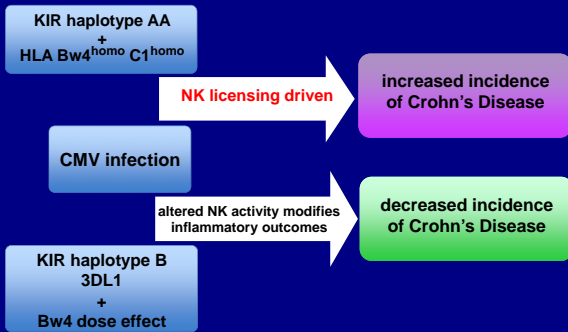
HLA-B HLA-C	KIR Haplotype	CMV IgG+	CMV IgG -	p value
Bw6 Bw6 C2 C2	AA B+	3 4	4 7	1
Bw4 Bw6 C2 C2	AA B+	2 5	11 25	1
Bw4 Bw4 C2 C2	AA B+	6 6	11 15	0.73
Bw4 Bw6 C1 C2	AA B+	9 16	37 84	0.64
Bw4 Bw4 C1 C2	AA B+	1 9	11 29	0.42
Bw6 Bw6 C1 C1	AA B+	8 11	25 64	0.28
Bw4 Bw6 C1 C1	AA B+	2 16	10 41	0.72
Bw4 Bw4 C1 C1	AA B+	4 1	2 12	0.017

Low CMV infection rate in presence of KIR 3DL1 gene in patients with Haplotype B

KIR gene	CMV IgG+	CMV IgG -	p value
2DL2 neg	19	68	0.5
2DL2 pos	58	251	
2DL5 neg	13	65	0.53
2DL5 pos	64	254	
2DL3 neg	9	39	1
2DL3 pos	68	280	
3DL1 neg	9	17	0.05
3DL1 pos	68	302	

HLA-B	KIR 3DL1	CMV IgG+	CMV IgG -	p value
Bw4+	+	47	196	0.03
	-	6	7	
Bw4 ^{homo}	+	12	54	0.008
	-	4	12	
Bw6 ^{homo}	+	20	96	0.54
	-	3	9	

Summary



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