

Supplementary Figure 1: influence of G908R and R702W NOD2 polymorphisms on Aspergillus-induced IL-1 β , TNF α and IL-6 release

IL-1 β , TNF and IL-6 levels measured in culture supernatants of PBMCs stimulated with live *Aspergillus* conidia for 24 hours. The PBMCs of individuals with various genotypes of the *Nod2* receptor were compared. These genotypes included (A) the G908R mutation (wild-type; WT n=68; black circles and heterozygous; He n=5; half filled circles) and (B) the R702W mutation (wild-type; WT n=56; black circles, heterozygous; He n=5; half filled circles). Data is presented as scatterplots with a line indicating the median. The means of both groups were compared for significance using the Mann Whitney U test.







Supplementary Figure 3: gating strategy for T-cell subsets

All events were plotted based on forward scatter (FS) and side scatter (SS) characteristics. Within this plot the region of cells containing lymphocytes was gated (red gate) and examined for CD4 expression. Within the cell selection the CD4 PeCy7 signal was plotted against the side scatter (SS) and the population of CD4+ cells was gated (green gate). Within the CD4+T-cell selection IFN γ , IL-22, and IL-17A expression was examined by plotting gIFN-FITC, IL-22-PE and IL-17-Alexa647 signals respectively against the CD4 PeCy7 signal. The percentage of cells within the CD4+ population positive for the respective cytokines (top right quadrant; blue gates) were used for analysis.



Supplementary Figure 4: gating strategy for surface dectin-1 expression

Monocytes or macrophages were plotted based on their forward scatter (FSC-A) and side scatter (SSC-A) characteristics. No cells were gated in this plot this was solely performed to check whether the gated cells correspond with the expected forward scatter and side scatter characteristics of monocytes or macrophages. First CD45+ leukocytes were gated (red gate) within a plot of the CD45 KromeOrange(KO525-A) signal against the side scatter characteristics (SSC-A). On this population of cells the CD14+ cells were gated (green gate) within a plot of the CD14 FITC (CD14 FITC-A) signal against the side scatter characteristics (SSC-A). Within the CD14+ selection gate the mean fluorescence intensity (MFI) of the Dectin-1 APC signal (Dectin-1 APC-A) was measured.



Supplementary Figure 5: gating strategy for Aspergillus phagocytosis

Macrophages were plotted based on their forward scatter (FSC-A) and side scatter (SSC-A) characteristics and within this plot the macrophages were gated (red gate). The selected cells were plotted for side scatter (SSC-A) characteristics against the FITC signal of *Aspergillus*. The percentage of FITC positive macrophages was determined using a FITC+ gate (blue gate) to determine the amount of monocytes phagocytosing and the mean fluorescence intensity was determined on the FITC+ macrophages (blue gate) to determine the relative amount of phagocytosed fluorescent conidia.

RefSNP	rs2066842	rs2066844	rs2066845	rs2066847
rs2066842	D'=1	D'=1	D'=1	D'=1
	r ² =1	r ² =0.163	r ² =0.044	r ² =0.067
rs2066844	D'=1	D'=1	D'=1	D'=1
	r ² =0.163	r ² =1	r ² =0.002	r ² =0.002
rs2066845	D'=1	D'=1	D'=1	D'=1
	r ² =0.044	r ² =0.002	r ² =1	r ² =0.001
rs2066847	D'=1	D'=1	D'=1	D'=1
	r ² =0.067	r ² =0.002	r ² =0.001	r ² =1

Supplementary Table 1 – LD analysis of the NOD2 SNPs evaluated in our study.

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Active disease 20 (30.3) 74 (30.3) Conditioning regimen, no (%) 74 (30.3) RIC 45 (68.2) 150 (61.5) 0.35 Myeloablative 21 (31.8) 94 (38.5) 94 (38.5) CMV serostatus of donor and recipient, no. (%) 757 (86.4) 216 (88.5) 0.60 D-/R+ or D+/R+ 57 (86.4) 216 (88.5) 0.60 D-/R- or D+/R- 9 (13.6) 28 (11.5) Duration of neutropenia, mean days (range)† 12 (8 - 26) 13 (6 - 30) 0.31 Acute GVHD, no. (%) 70 (71.2) 209 (85.7) 0.008 Grades III - IV 19 (28.8) 35 (14.3) 35 (14.3) Antifungal prophylaxis, no. (%)‡ 71 (20.9) 73 (29.9) 73 (29.9) Other 5 (7.6) 16 (6.6) 73 (29.9) Other 5 (7.6) 16 (6.6) 73 (29.9)	Second or subsequent remission, or relapse	11 (16.7)	42 (17.2)	
Conditioning regimen, no (%)RIC $45 (68.2)$ $150 (61.5)$ 0.35 Myeloablative $21 (31.8)$ $94 (38.5)$ 0.35 CMV serostatus of donor and recipient, no. (%)D-/R+ or D+/R+ $57 (86.4)$ $216 (88.5)$ 0.60 D-/R- or D+/R- $9 (13.6)$ $28 (11.5)$ Duration of neutropenia, mean days (range)†Acute GVHD, no. (%)No GVHD or grades I – II $47 (71.2)$ $209 (85.7)$ 0.008 Grades III – IV $19 (28.8)$ $35 (14.3)$ Antifungal prophylaxis, no. (%)‡Fluconazole $36 (54.5)$ $119 (48.8)$ 0.64 Posaconazole $19 (28.8)$ $73 (29.9)$ 0 Other $5 (7.6)$ $16 (6.6)$ $10 (26.14 7)$	Active disease	20 (30.3)	74 (30.3)	
RIC 45 (68.2) 150 (61.5) 0.35 Myeloablative 21 (31.8) 94 (38.5) 94 (38.5) CMV serostatus of donor and recipient, no. (%) 7 7 86.4) 216 (88.5) 0.60 D-/R+ or D+/R+ 57 (86.4) 216 (88.5) 0.60 0.35 D-/R- or D+/R- 9 (13.6) 28 (11.5) 0.31 Duration of neutropenia, mean days (range)† 12 (8 - 26) 13 (6 - 30) 0.31 Acute GVHD, no. (%) 7 71.2) 209 (85.7) 0.008 Grades III – IV 19 (28.8) 35 (14.3) 35 Antifungal prophylaxis, no. (%)‡ 19 (28.8) 73 (29.9) 0.64 Posaconazole 19 (28.8) 73 (29.9) 0.64 None 5 (7.6) 16 (6.6) 16 (6.6)	Conditioning regimen, no (%)	, , ,	. ,	
Myeloablative 21 (31.8) 94 (38.5) CMV serostatus of donor and recipient, no. (%) 71 (31.8) 94 (38.5) D-/R+ or D+/R+ 57 (86.4) 216 (88.5) 0.60 D-/R- or D+/R- 9 (13.6) 28 (11.5) Duration of neutropenia, mean days (range)† 12 (8 - 26) 13 (6 - 30) 0.31 Acute GVHD, no. (%) 71 (71.2) 209 (85.7) 0.008 Grades III – IV 19 (28.8) 35 (14.3) Antifungal prophylaxis, no. (%)‡ 19 (28.8) 73 (29.9) Other 5 (7.6) 16 (6.6) None 6 (9.1) 26 (14.7)	RIC	45 (68.2)	150 (61.5)	0.35
CMV serostatus of donor and recipient, no. (%) $D - /R + \text{ or } D + /R +$ $57 (86.4)$ $216 (88.5)$ 0.60 $D - /R - \text{ or } D + /R 9 (13.6)$ $28 (11.5)$ Duration of neutropenia, mean days (range) ⁺ $12 (8 - 26)$ $13 (6 - 30)$ 0.31 Acute GVHD, no. (%) $47 (71.2)$ $209 (85.7)$ 0.008 Grades III - IV $19 (28.8)$ $35 (14.3)$ Antifungal prophylaxis, no. (%) [‡] $Fluconazole$ $19 (28.8)$ $73 (29.9)$ Other $5 (7.6)$ $16 (6.6)$ 0.64	Myeloablative	21 (31.8)	94 (38.5)	
$\begin{array}{cccccccc} D-/R+ \ or \ D+/R+ & 57 \ (86.4) & 216 \ (88.5) & 0.60 \\ D-/R- \ or \ D+/R- & 9 \ (13.6) & 28 \ (11.5) \\ \hline \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \$	CMV serostatus of donor and recipient, no. (%)		· · · ·	
D-/R- or D+/R- $9 (13.6)$ $28 (11.5)$ Duration of neutropenia, mean days (range)† $12 (8 - 26)$ $13 (6 - 30)$ 0.31 Acute GVHD, no. (%) $47 (71.2)$ $209 (85.7)$ 0.008 No GVHD or grades I - II $47 (71.2)$ $209 (85.7)$ 0.008 Grades III - IV $19 (28.8)$ $35 (14.3)$ Antifungal prophylaxis, no. (%)‡ $19 (28.8)$ $73 (29.9)$ Other $5 (7.6)$ $16 (6.6)$ None $6 (9.1)$ $26 (14.7)$	D-/R+ or D+/R+	57 (86.4)	216 (88.5)	0.60
Duration of neutropenia, mean days (range)† 12 (8 - 26) 13 (6 - 30) 0.31 Acute GVHD, no. (%) 12 (8 - 26) 13 (6 - 30) 0.31 No GVHD or grades I - II 47 (71.2) 209 (85.7) 0.008 Grades III - IV 19 (28.8) 35 (14.3) Antifungal prophylaxis, no. (%)‡ 19 (28.8) 73 (29.9) Fluconazole 19 (28.8) 73 (29.9) Other 5 (7.6) 16 (6.6) None 6 (9.1) 26 (14.7)	D-/R- or D+/R-	9 (13.6)	28 (11.5)	
Acute GVHD, no. (%) 47 (71.2) 209 (85.7) 0.008 Grades III – IV 19 (28.8) 35 (14.3) Antifungal prophylaxis, no. (%)‡ 36 (54.5) 119 (48.8) 0.64 Posaconazole 19 (28.8) 73 (29.9) 0 Other 5 (7.6) 16 (6.6) 16 (6.6)	Duration of neutropenia, mean days (range) [†]	12 (8 – 26)	13(6-30)	0.31
No GVHD or grades I – II 47 (71.2) 209 (85.7) 0.008 Grades III – IV 19 (28.8) 35 (14.3) Antifungal prophylaxis, no. (%)‡ 5 119 (48.8) 0.64 Posaconazole 19 (28.8) 73 (29.9) 0 Other 5 (7.6) 16 (6.6) 10 (26.7) 10 (26.7)	Acute GVHD, no. (%)	(0 -0)	(* ***)	
Grades III – IV 19 (28.8) 35 (14.3) Antifungal prophylaxis, no. (%)‡ 36 (54.5) 119 (48.8) 0.64 Posaconazole 19 (28.8) 73 (29.9) Other 5 (7.6) 16 (6.6) None 6 (9.1) 26 (14.7)	No GVHD or grades I – II	47 (71 2)	209 (85 7)	0.008
Antifungal prophylaxis, no. (%)‡ 15 (25.5) 55 (24.5) Fluconazole 36 (54.5) 119 (48.8) 0.64 Posaconazole 19 (28.8) 73 (29.9) Other 5 (7.6) 16 (6.6) None 6 (9.1) 26 (14.7)	Grades III – IV	19 (28.8)	35 (14 3)	0.000
Fluconazole 36 (54.5) 119 (48.8) 0.64 Posaconazole 19 (28.8) 73 (29.9) Other 5 (7.6) 16 (6.6) None 6 (9.1) 26 (14.7)	Antifungal pronbylaxis no (%)‡	15 (20.0)	55 (14.5)	
Posaconazole 19 (28.8) 73 (29.9) Other 5 (7.6) 16 (6.6) None 6 (9.1) 26 (14.7)	Fluconazole	36 (54 5)	119 (48 8)	0.64
Other 5 (7.6) 16 (6.6) None 6 (9.1) 26 (14.7)	Posaconazole	10 (78 R)	73 (20 0)	0.04
None 6 (0.1) 26 (14.7)	Ather	5 (76)	16 (6 6)	
	None	5 (7.0) 6 (0.1)	36 (1/ 7)	

Supplementary Table 2 – Baseline characteristics of patients enrolled in the study.

RIC, reduced intensity conditioning; CMV, cytomegalovirus; D, donor; R, recipient; GVHD, graft-versus-host-disease. $^+$ Neutropenia was defined as $\leq 0.5 \times 10^9$ cells/L. $^+$ Other antifungals used in prophylaxis included voriconazole (n=10), liposomal amphotericin B (n=7), itraconazole (n=2), and caspofungin (n=2). P values were calculated by Fisher's exact probability t-test or Student's t-test for continuous variables.