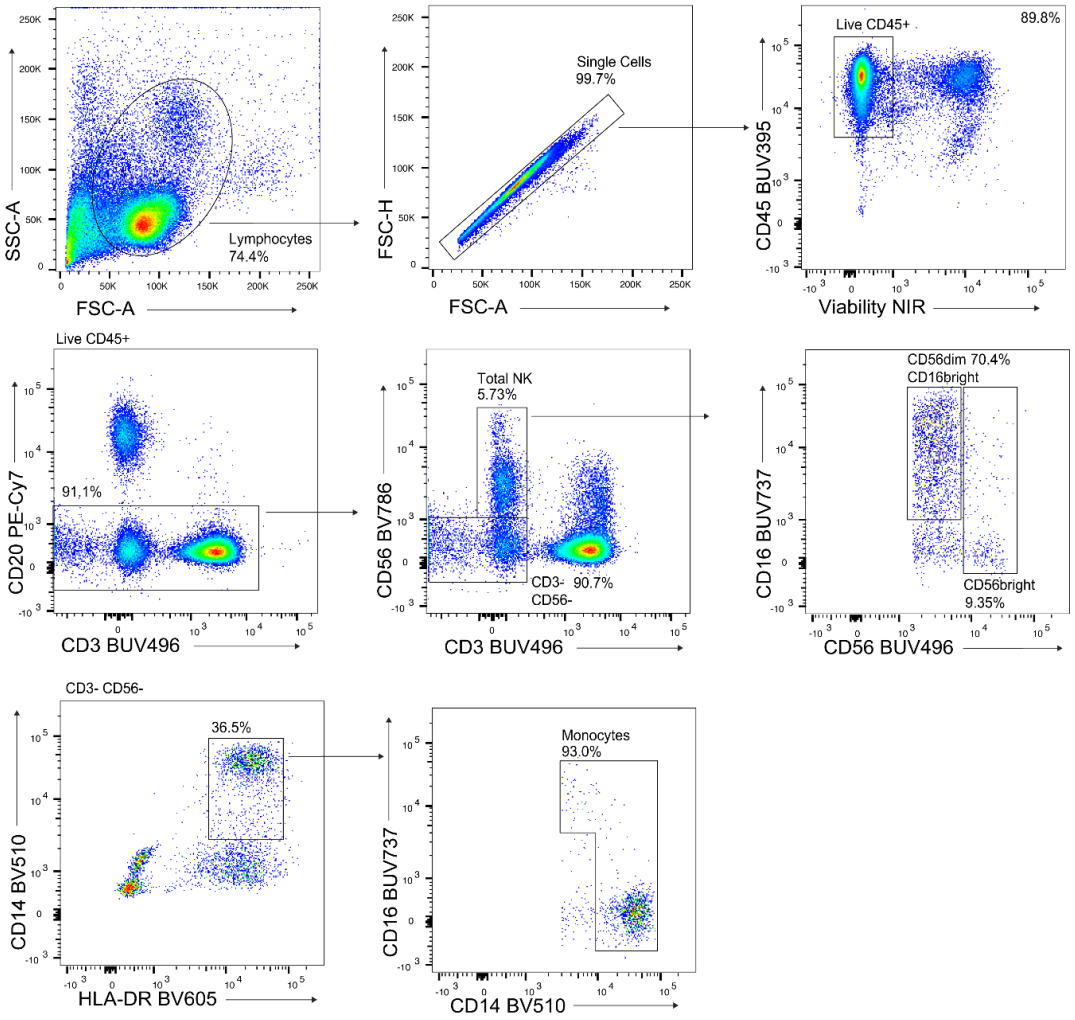
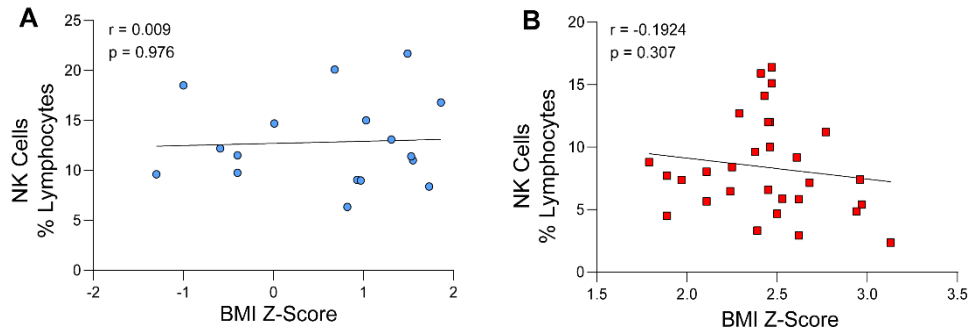


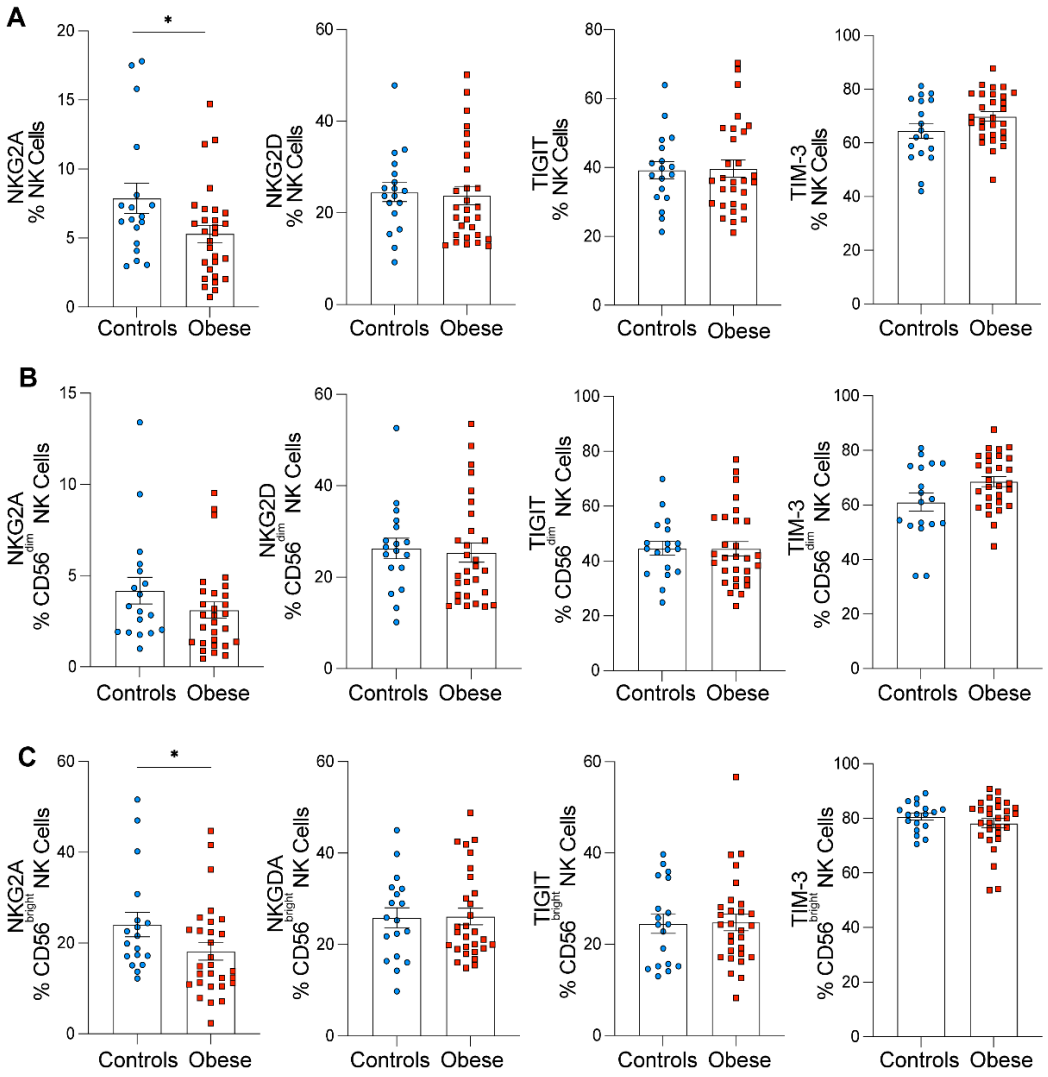
Supplemental Figure 1: Representative gating strategy for identifying NK cells, monocytes and T cells from paediatric PBMCs. NK cells were defined as $CD45^+$ $CD19/CD20^-$ $CD3^-$ $CD56^+$ leukocytes. T cells were defined as $CD45^+$ $CD19/CD20^-$ $CD3^+$ leukocytes. Monocytes were defined as $CD45^+$ $CD19/CD20^-$ $CD3^-$ $CD56^-$ $HLA\text{-}DR^+$ $CD14^+$ leukocytes.



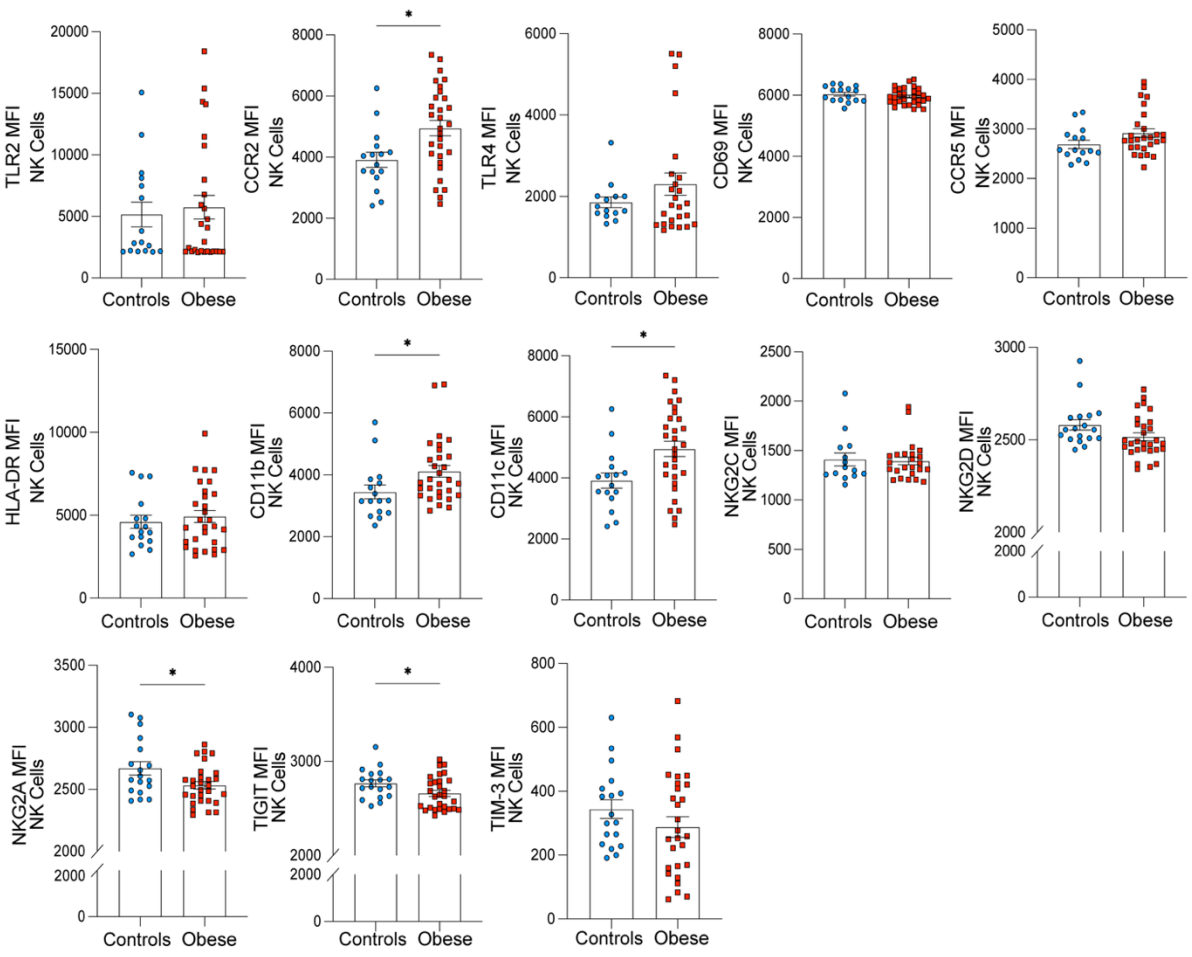
Supplemental Figure 2: BMI Z-score is not associated with NK cell frequencies in control or obese cohorts. Correlation plots showing the association between NK cell frequencies and BMI Z-score in the **A)** control cohort (Spearman's R = 0.009, p = 0.976) and **B)** obese cohort (Spearman's R = -0.1924, p = 0.307).

Supplemental Table 1: Cohort characteristics for phenotyping of NK cell functional markers (related to Supplemental Figure 3).

	Control cohort	**Obese cohort**	**P value**
n	20	29	-
Age (year [range])	11.15 [4 – 16]	10.9 [4 – 18]	0.79
Sex (% female)	60%	59%	0.92
Z-score (kg)	0.39 [-1.57 – 2.01]	2.46 [1.65 – 3.0]	<0.0001



Supplemental Figure 3: NK cells from children with obesity present with reduced NKG2A at rest. A) Percentages of total NK cells expressing certain functional markers as identified via flow cytometric analysis. **B)** Percentages of CD56dim NK cells expressing certain surface activation markers as identified via flow cytometric analysis. **C)** CD56bright expressing certain functional as identified via flow cytometric analysis. Each data point represents an individual donor. Statistical significance between controls and obese groups was tested using a Student's t-test or Mann-Whitney test as appropriate. Significance denoted by *; $p<0.05$.



Supplemental Figure 4: NK cells from children with obesity present with altered expression of surface markers at rest. MFI of total NK cells expressing certain functional markers as identified via flow cytometric analysis. Each data point represents an individual donor. Statistical significance between controls and obese groups was tested using a Student's t-test or Mann-Whitney test as appropriate. Significance denoted by *; $p<0.05$.

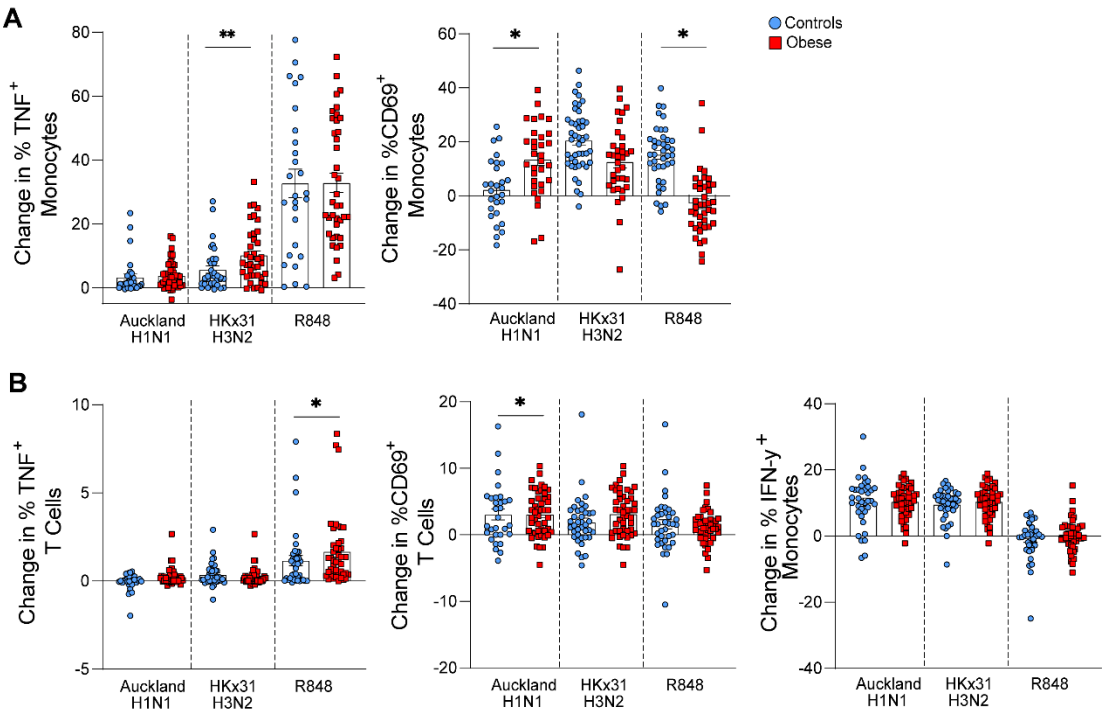
Supplemental Table 2: Multiple regression model investigating impact of sex on readouts, with two-way interactions

Measure	Group p-value	Sex p-value	Interaction
% NKG2C NK	0.4245	0.5152	0.3186
% CD69 NK	0.8266	0.6887	0.6281
% TLR4 NK	0.2159	0.5506	0.5660
% TLR2 NK	0.5492	0.6852	0.6970
% CD11b NK	0.0200	0.1101	0.3768
% CD11c NK	0.3185	0.9218	0.9448
% CCR2 NK	0.2257	0.8487	0.7359
% CCR5 NK	0.7584	0.3186	0.6451
% HLA-DR NK	0.2520	0.6050	0.7197
% NKG2C NK^{dim}	0.6370	0.5817	0.6380
% CD69 NK^{dim}	0.2092	0.7025	0.2179
% TLR4 NK^{dim}	0.0040	0.5906	0.1736
% TLR2 NK^{dim}	0.0647	0.5450	0.4295
% CD11b NK^{dim}	0.0069	0.0953	0.1953
% CD11c NK^{dim}	0.3235	0.7010	0.9794
% CCR2 NK^{dim}	0.0420	0.9007	0.5159
% CCR5 NK^{dim}	0.9211	0.2590	0.7470
% HLA-DR NK^{dim}	0.4710	0.5226	0.9341
% NKG2C NK^{bright}	0.8056	0.4937	0.7607
% CD69 NK^{bright}	0.8473	0.7193	0.3651
% TLR4 NK^{bright}	0.6686	0.5791	0.5284
% TLR2 NK^{bright}	0.8346	0.2818	0.7268
% CD11b NK^{bright}	0.5063	0.8338	0.5085
% CD11c NK^{bright}	0.7545	0.8539	0.8724

% CCR2 NK^{bright}	0.5347	0.6981	0.6555
% CCR5 NK^{bright}	0.1193	0.3019	0.0988
MFI NKG2C NK	0.2053	0.9418	0.2940
MFI CD69 NK	0.4281	0.9872	0.7102
MFI TLR4 NK	0.3891	0.9695	0.8596
MFI TLR2 NK	0.4658	0.7197	0.9347
MFI CD11b NK	0.0847	0.1886	0.6313
MFI CD11c NK	0.3377	0.8963	0.3736
MFI CCR2 NK	0.7231	0.3330	0.3507
MFI CCR5 NK	0.4444	0.4999	0.7085
MFI HLA-DR NK	0.8989	0.4445	0.3637
MFI NKG2C NK^{dim}	0.5351	0.8324	0.3264
MFI CD69 NK^{dim}	0.9533	0.8204	0.9062
MFI TLR4 NK^{dim}	0.6033	0.9071	0.7234
MFI TLR2 NK^{dim}	0.9842	0.9422	0.6094
MFI CD11b NK^{dim}	0.0203	0.2171	0.2736
MFI CD11c NK^{dim}	0.2622	0.9952	0.6437
MFI CCR2 NK^{dim}	0.0159	0.3573	0.1360
MFI CCR5 NK^{dim}	0.7012	0.5639	0.7941
MFI HLA-DR NK^{dim}	0.7098	0.1102	0.9327
MFI NKG2C NK^{bright}	0.3691	0.6216	0.5265
MFI CD69 NK^{bright}	0.9417	0.1610	0.2470
MFI TLR4 NK^{bright}	0.3526	0.8611	0.5599
MFI TLR2 NK^{bright}	0.6201	0.1542	0.6532
MFI CD11b NK^{bright}	0.4708	0.2310	0.3165
MFI CD11c NK^{bright}	0.5220	0.3710	0.8879
MFI CCR2 NK^{bright}	0.6026	0.4285	0.1539

MFI CCR5 NK^{bright}	0.1680	0.5584	0.2569

82



Supplemental Figure 5: Monocytes and T cells from pre-pubertal or post-pubertal children with obesity have altered response to IAV stimulations. A) Monocytes and **B)** T cells from children with obesity versus controls. **A)** Monocytes defined as $CD45^+$ $CD19/CD20^-$ $CD3^-$ $CD56^-$ $HLA\text{-}DR^+$ leukocytes. **B)** T cells defined as $CD45^+$ $CD19/CD20^-$ $CD3^+$ leukocytes. **A-B)** Each data point represents an individual donor. Statistical significance between controls and obese groups was tested using a Student's t-test or Mann-Whitney test as appropriate. Significance denoted by *; $p<0.05$, **; $p<0.01$.