SUPPLEMENTARY APPENDIX

Leukemia-induced phenotypic and functional defects in natural killer cells predict failure to achieve remission in acute myeloid leukemia

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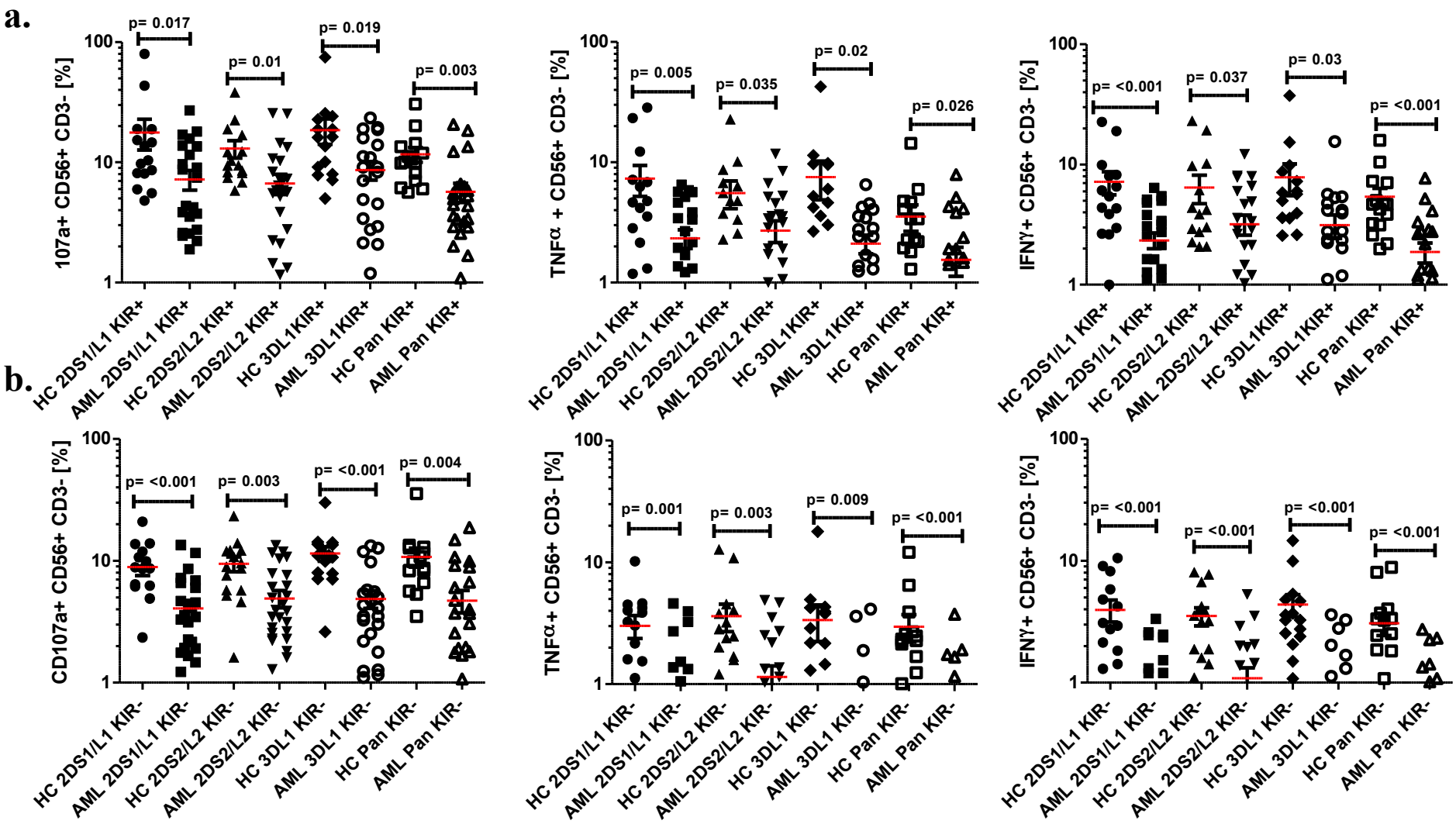
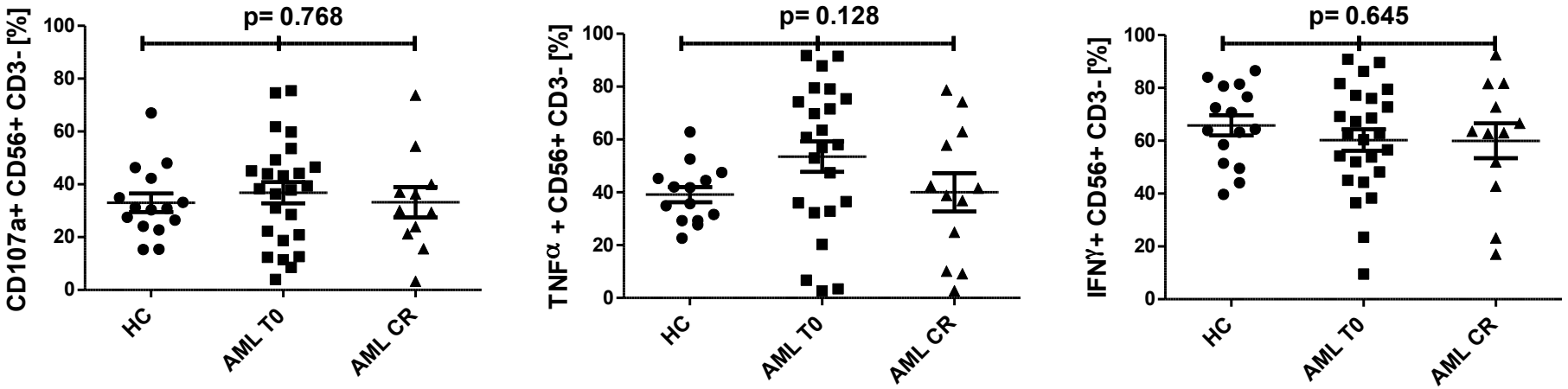
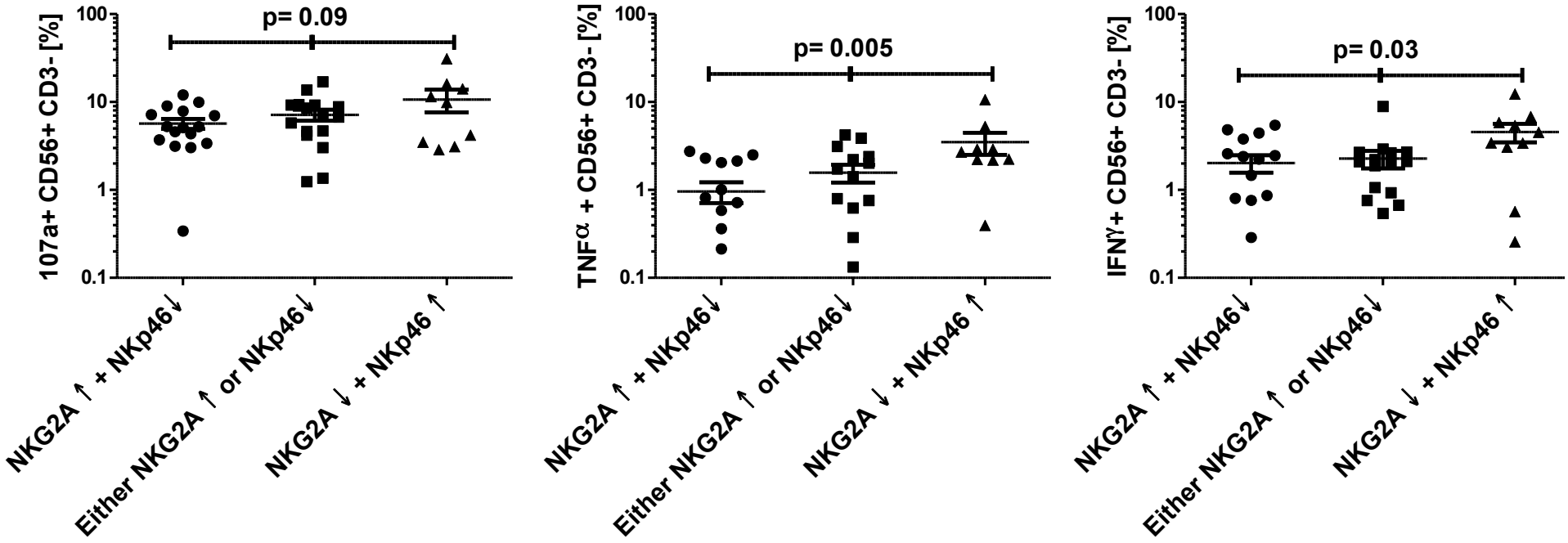
Supplementary figure 1. NK cytotoxicity and effector function in AML patients at diagnosis compared to healthy controls. (a) comparison of NK cytotoxicity and effector cytokine function in KIR+ subsets; (b) comparison of NK cytotoxicity and effector cytokine function in KIR- subsets. Horizontal bars denote mean within group. Abbreviations: HC: healthy control, AML: acute myeloid leukemia.



Supplementary figure 2 . NK cytotoxicity (CD107a degranulation), TNFα and IFNγ production in AML patients at diagnosis (T0), remission (CR) and healthy controls (HC) following stimulation with PMA/ionomycin. Horizontal bars denote mean expression. Error bars denote standard deviation between individuals within group. P values represent significance of one way ANOVA test.

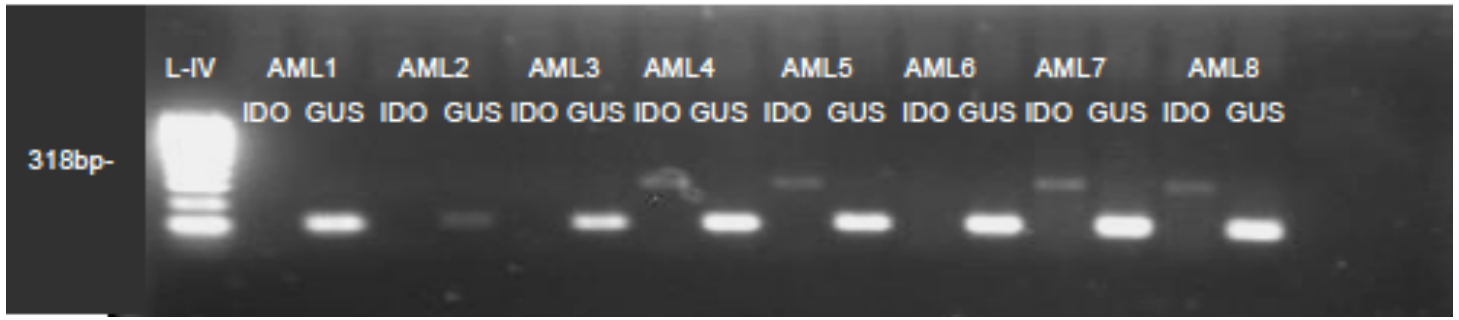


Supplementary figure 3. Relationship between NKG2A and NKp46 expression and effector function. Individuals were separated based on the expression of NK receptors (above or below the median). NKG2A^{hi} NKp46^{lo} NK cells displayed the poorest NK effector function against leukemia targets (one way ANOVA).

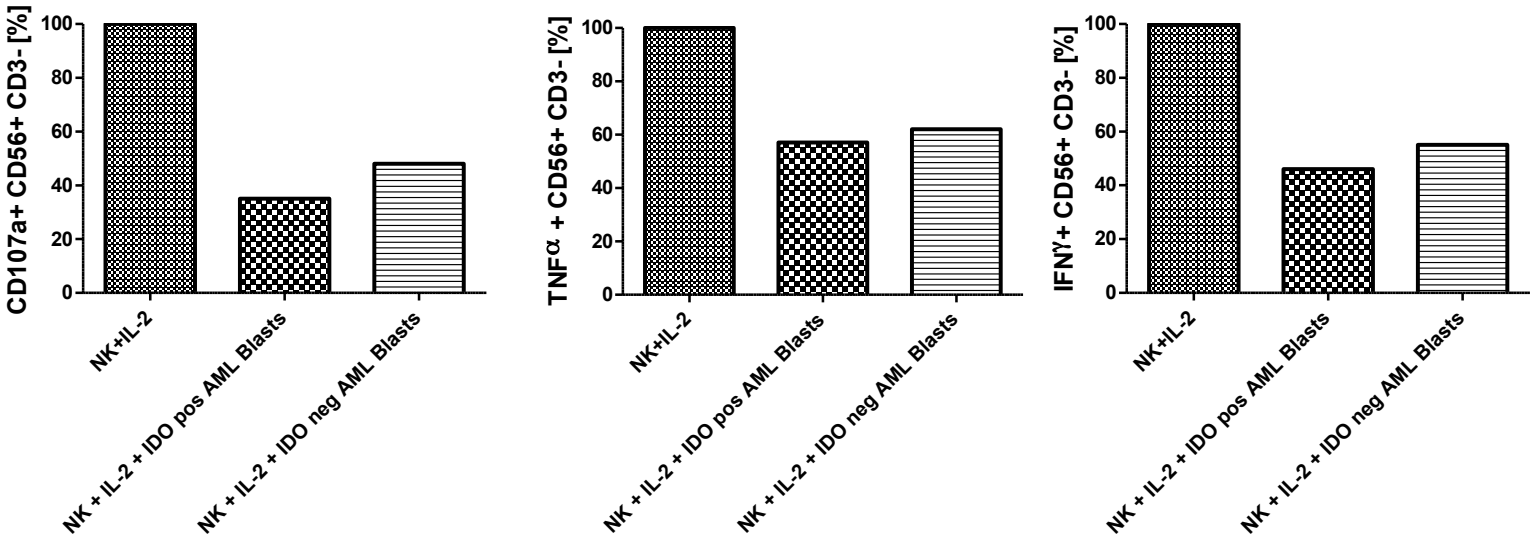


Supplementary figure 4 . IDO does not effect NK function in AML (a) Example of RT- PCR gel identifying status of IDO gene in 8 AML patients. The ladder (L-IV) is positioned far left. Primers for the positive control housekeeping gene β-glucuronidase (GUS) were run with each patient sample. Expected product size of IDO is 318bp. The gel identifies patients 4,5,7 and 8 as positive for IDO (b) Effect of IDO+ and IDO- AML blast co-culture on NK cell CD107a degranulation, TNFα and IFNγ production against K562. After 24 hours of healthy donor NK co-culture with primary AML blasts (ratio of 10:1) + IL-2 (200 iU/mL), the effector function of NK cells was assessed against K562 leukemia targets (ratio 1:1). Plots are gated on CD56+CD3- NK cells. IDO+ blasts have no greater effect on NK function than IDO- blasts.

a.



b.



Supplementary figure 5 . Secondary versus *de novo* AML: response to treatment and NK cytotoxicity. There is no significant difference between those with *de novo* AML (n=16) and secondary AML (n=16) with respect to a) response to first line treatment (Chi square test) and b) NK cytotoxicity (unpaired t tests). Grey bars represent proportion of patients achieving complete remission.