

[PS1.25]

Gene Expression Profiling of the Interaction between Plasmodium falciparum and Natural Killer Cells

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Natural killer (NK) cells play a pivotal role in innate responses against *Plasmodium falciparum*. Previously we showed a direct impact of NK cells on parasitemia. However, the cause of this effect remains unclear. To elucidate the role of NK cells on *Plasmodium falciparum*, parasite RNA was isolated after 48h co-culture of FCR3-CSA with NK92. Microarray analysis revealed an impact on the expression of genes important for parasite survival, reinvasion of RBCs and protein processing. Subsequently microarrays of NK92 cells in a time-dependent manner were performed. RNA from NK92 was isolated after 0, 6, 12 and 24h of co-culture with 3D7. Additionally, we analysed the expression profile from NK cells of 3 different donors after 24h of co-cultivation with 3D7.

In NK92 comparison of expression data show almost no change on transcription level after 6 and 12h of co-cultivation compared to control. After 24h 71 genes were identified as being activated after contact with *P. falciparum*-infected erythrocytes (iRBC). Although not found up-regulated in native NK cells especially those genes are interesting, since NK92 suppress parasitemia without contact to accessory cells. Two activating NK cell receptors NKG2-C and E (KLRC2/3) were found up-regulated. KLRC2 together with CD94 is involved in NK cell-mediated cytotoxicity and ligand binding leads to granule and IFN- γ release. Microarray data were verified by RT-PCR for KLRC2/3 up-regulation. However, since KLRC2 was not found on the NK cell surface after contact to iRBC, the role of this receptor still needs to be elucidated. For the future, involvement of ligands on iRBCs will be investigated.

Overall, our results demonstrate a clear distinctive pattern of the response of freshly isolated NK cells and the cell line NK92 to *P. falciparum*. NK92 remain a useful tool since they hint to a hitherto unknown, possible engagement of typical NK cells receptors.

Keywords: Gene Expression Profiles, Plasmodium falciparum, NK cells, KLRC2/3