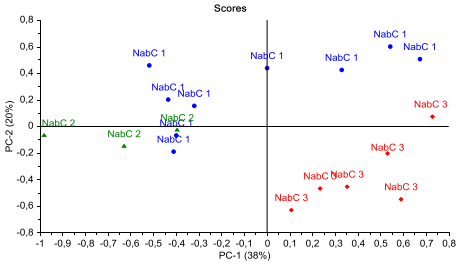
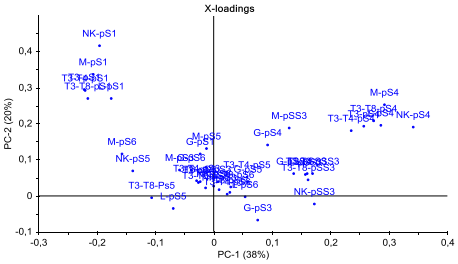
11. Appendix

Supplement Figure 1

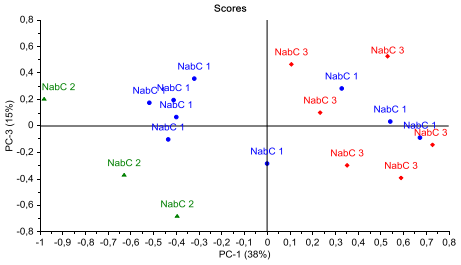
a)



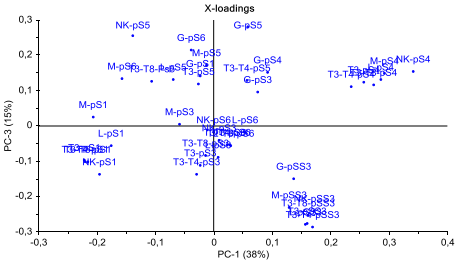
b)



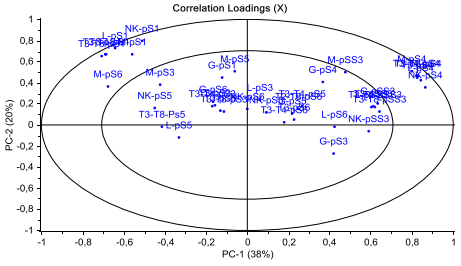
c)



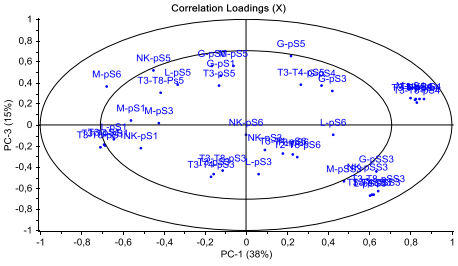
d)



e)

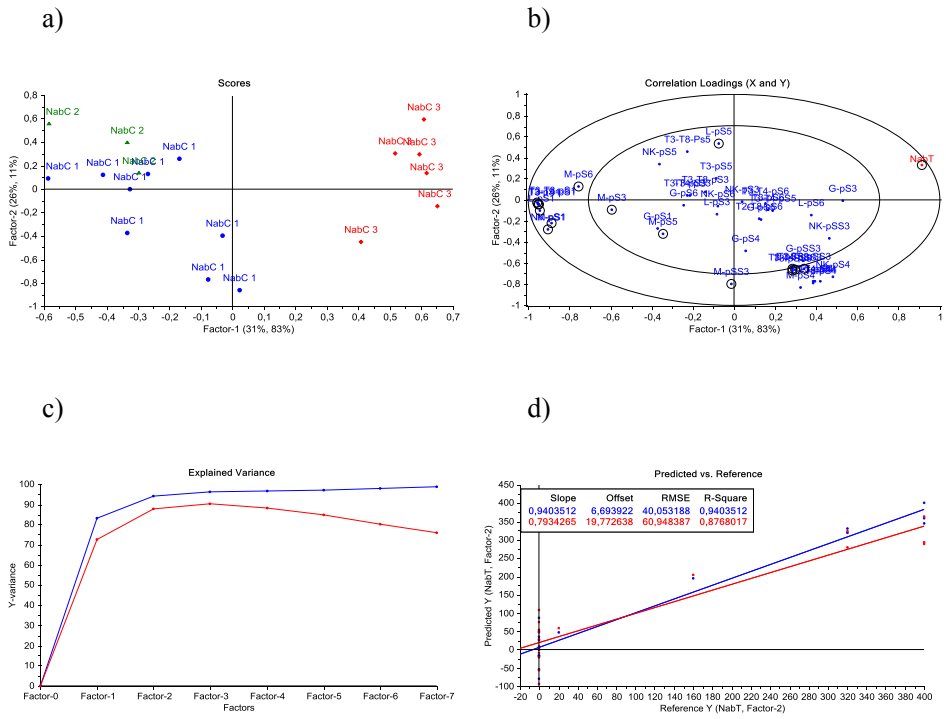


f)



S1 2D plots of PCA of the Stat protein data acquired after IFN-β stimulation *in vivo* in whole blood. a-d) Scores and loading plots are shown for the first three most important PCs. **a)** PC1 and PC2 clearly distinguish NAb high patients (NabC 3) from NAb-negative patients (NabC 2). **c)** PC3 was necessary to separate NAb C2, a patient with low NAb titer. The loading plots show the variables – the Stats in particular cell subtypes – responsible for clustering in patients. These plots have to be interpreted together with the corresponding scores plots; a) together with b), and c) together with d). Variables far away from the origin and located in the same region of the plot as the clusters in the scores plot are positively correlated with the cluster of patients and contribute most to the variation responsible for the clustering. Variables located on opposite sides are inversely correlated. Variables close to the origin contribute very little to the clustering of patients. **e and f)** The correlation loading plots show the correlation between the variables and PCs. These plots need to be interpreted with the corresponding scores plots as well, but may be easier to interpret than loading plots. The plot contains two ellipses that indicate how much variance is taken into account. The outer ellipse indicates 100% explained variance and the inner ellipse indicates 50% of explained variance. In the loading plots, pS1clustered in PC1 and PC2 for most of the cell subtypes. In the loading plots pSS3 clustered in PC1 and PC3 for most of the cell subtypes. The first letter for each variable is the first letter of the cell type and Stats is shortened to S.

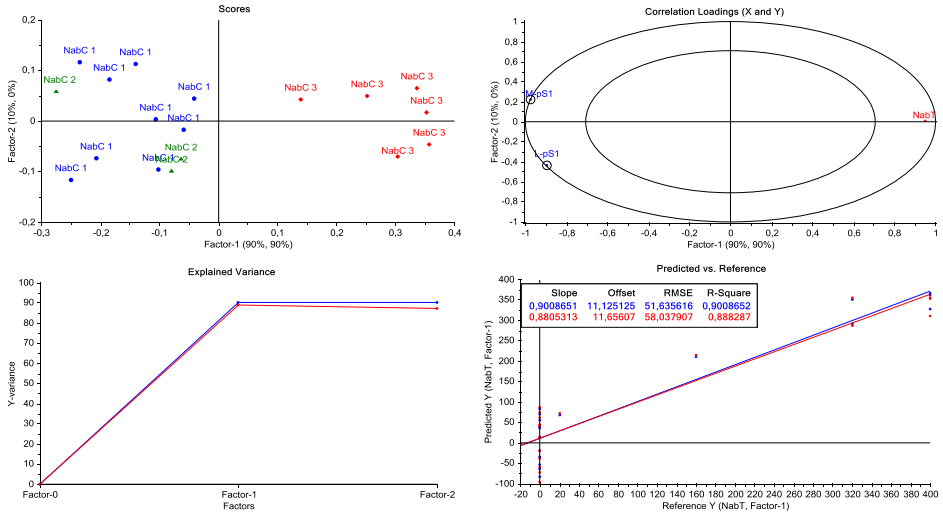
Supplement Figure 2



S2 PLSR model with all phospho-flow data included. **a)** The scores plot is similar to the scores plot in PCA and shows a distinct cluster for patients with high NAb titers (NabC 3). Factors 1 and 2 show how much of the variation in Y (NAb titers) is explained by the variation in X (pStats). Factor 1 and Factor 2 explains 94% of the variation in NAb titers based on 57% of the variation in pStat data. **b)** In the correlation loading plots, similar to PCA, highly correlated variables are shown close to the 100% explained variability circle. Significant variables based on the Jack-knife test are highlighted by circles. In this plot NabT (red) is inversely correlated with Stat1 in almost all the cell types studied and explains much of the variation along Factor 1. In the ANOVA the same variables were found to be significant. **c)** The

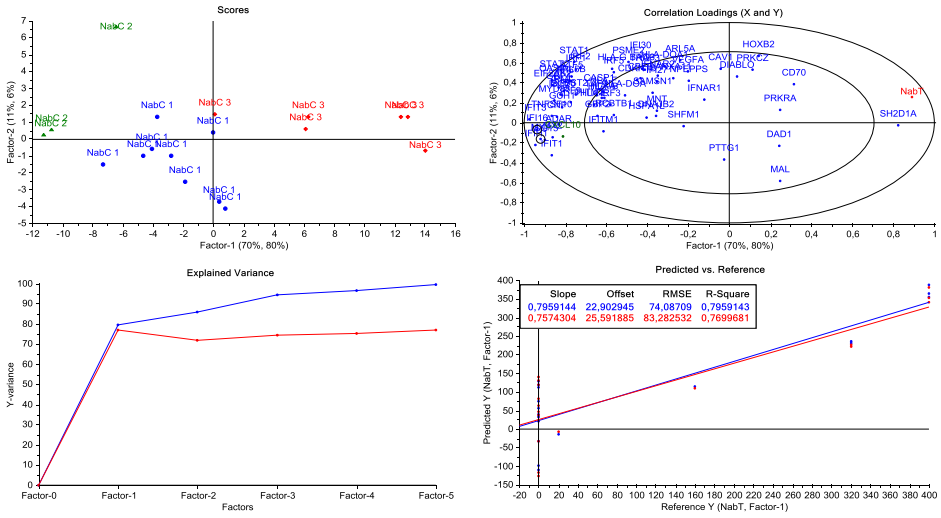
explained variance plot shows how much of the variance in NAb titers is explained by how many factors (blue line). The explained variance should increase with every factor added and the validation variance shown in the red line should follow the blue calibration variance closely. This plot allows one to choose an appropriate number of factors to include in the model. **d)** The predicted versus reference plot shows the regression lines for the chosen model. Here two factors are included and blue represents the calibration model and red the validation model.

Supplement Figure 3



S3 PLSR model for only two variables, pS1 in monocytes and in lymphocytes. Notice that pStat1 was highly correlated with NAb titers in *ex vivo* PBMC studies.

Supplement Figure 4



S4 PLSR of all gene expression data. The gene models were less predictive of NAb class than phospho-flow data.