## **SUPPLEMENTARY TABLES**

Please browse the full text version of this manuscript to see the links to Supplementary Tables:

**Supplementary Table 1.** Differential expression analysis revealing increased (1), decreased (-1) or unchanged (0) gene expression at days 2,7 and 28 post-vaccination in young, older and frail adults classified as vaccine responders (R+) and non-responders (R-). Refer to methods for details of differential expression analysis.

**Supplementary Table 2.** Differential expression analysis of pre-vaccination transcriptional profiles in young vs. older adults revealing genes up-regulated  $(q<0.05 \text{ and } |Fold-Change|\geq 1.25)$  in young and older adults.

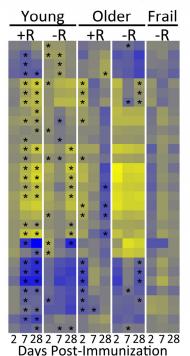
**Supplementary Table 3A.** Pathway activities obtained by QuSAGE (FDR < 0.05 for at least one of the condition) for the Blood Transcriptional Modules (BTMs) defined in [1]. QuSAGE was used to quantify the activity of each module by comparing pre- and post-vaccination transcriptional profiles. Positive activity represents up-regulation and negative activity represents down-regulation.

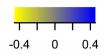
**Supplementary Table 3B.** False Discovery Rates (FDRs) associated with vaccination-induced activities (FDR < 0.05 for at least one of the condition) for the Blood Transcriptional Modules (BTMs) defined in [1]. QuSAGE was used to obtain P values for detecting the activity of each module by comparing pre- and post-vaccination transcriptional profiles. FDRs were obtained using the method of Benjamini and Hochberg [2].

**Supplementary Table 4A.** Pathway activities obtained by QuSAGE for immunological pathways from the KEGG database by comparing pre- and post-vaccination transcriptional profiles. Note that this table includes all pathways, while Figure 4 includes a subset of these pathways with FDR<0.005.

**Supplementary Table 4B.** False Discovery Rates (FDRs) associated with vaccination-induced pathway activities. QuSAGE was used to obtain P values for detecting the activity of immunological pathways from the KEGG database by comparing pre- and post-vaccination transcriptional profiles. FDRs were obtained using the method of Benjamini and Hochberg [1]. Note that this table includes all pathways, while Figure 4 includes a subset of these pathways with FDR<0.005.

## **Module Activity**





NK cell surface signature (S1) enriched in NK cells (I) (M7.2) T cell activation (II) (M7.3) enriched in T cells (I) (M7.0) platelet activation (II) (M32.1) platelet activation (I) (M32.0) CORO1A-DEF6 network (I) (M32.2) enriched in monocytes (surface) (M118.1) enriched in monocytes (IV) (M118.0) Resting dendritic cell surface signature (S10) immune activation - generic cluster (M37.0) enriched in monocytes (I) (M4.15) cell cycle and transcription (M4.0) lysosomal/endosomal proteins (M139) cell junction (GO) (M4.13) myeloid cell enriched receptors and transporters (M4.3) blood coagulation (M11.1) enriched in monocytes (II) (M11.0) Monocyte surface signature (S4) regulation of signal transduction (M3) TLR and inflammatory signaling (M16) platelet activation - actin binding (M196) enriched in myeloid cells and monocytes (M81) golgi membrane (II) (M237) mitosis (TF motif CCAATNNSNNNGCG) (M169) chaperonin mediated protein folding (II) (M204.1) nuclear pore complex (M106.0) enriched in B cells (II) (M47.1) enriched in B cells (I) (M47.0) T cell surface signature (S0) cell cycle (I) (M4.1)

**Supplementary Figure 1.** QuSAGE [1] was used to screen Blood Transcription Modules (rows) [2] to identify modules with significantly (FDR<0.0001) altered activity for at least two conditions. Coloring represents downregulated (yellow) to up-regulated (Blue) activity relative to the pre-vaccination time-point. +R indicates vaccine responder status, -R indicates non-responder status. Time points wirh FDR <0.05 are indicated with an asterisk.

- **1.** Yaari G, Bolen CR, Thakar J and Kleinstein SH. Quantitative set analysis for gene expression: a method to quantify gene set differential expression including genegene correlations. Nucleic Acids Res. 2013; 41:e170.
- **2.** Li S, Rouphael N, Duraisingham S, Romero-Steiner S, Presnell S, Davis C, Schmidt DS, Johnson SE, Milton A, Rajam G, Kasturi S, Carlone GM, Quinn C, et al. Molecular signatures of antibody responses derived from a systems biology study of five human vaccines. Nat Immunol. 2014; 15:195-204.

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