

## Extended data

### Extended data, Table 1:

Core circadian clock gene set consisting of both circadian activators and repressors

#### **Activators (positive limb)**

ENSG00000133794 : BMAL1  
ENSG00000134852 : CLOCK  
ENSG00000170485 : NPAS2

#### **Repressors (negative limb)**

ENSG00000179094 : PER1  
ENSG00000132326 : PER2  
ENSG00000049246 : PER3  
ENSG00000008405 : CRY1  
ENSG00000121671 : CRY2

#### **Aucillary loop**

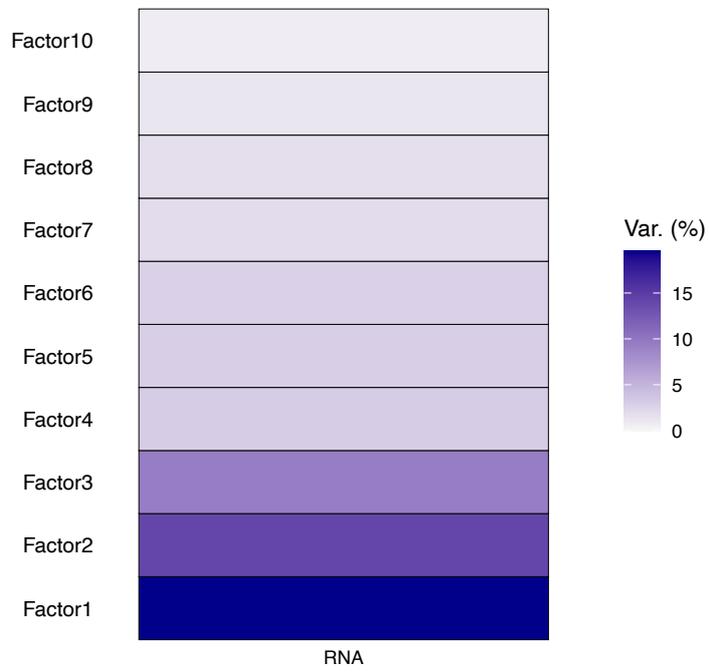
ENSG00000126368 : NR1D1  
ENSG00000174738 : NR1D2  
ENSG00000069667 : RORA

#### **Output**

ENSG00000105516 : DBP  
ENSG00000167074 : TEF  
ENSG00000108924 : HLF

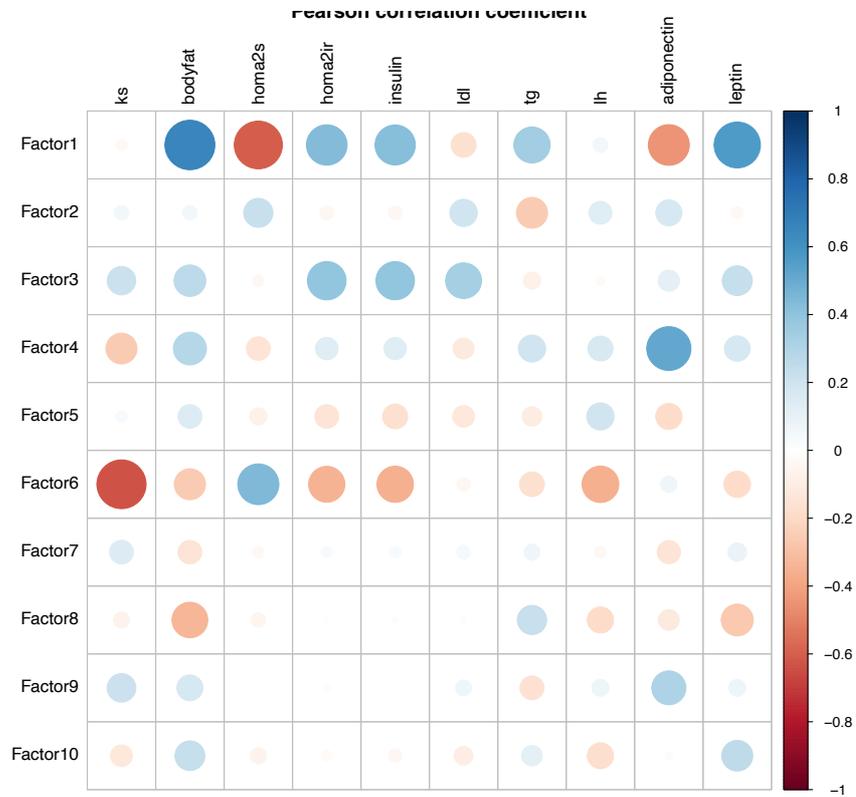
### Extended data figure 1

multi-factor analysis (MOFA) and the 10 latent gene expression factors that captured most of the variance in the dataset



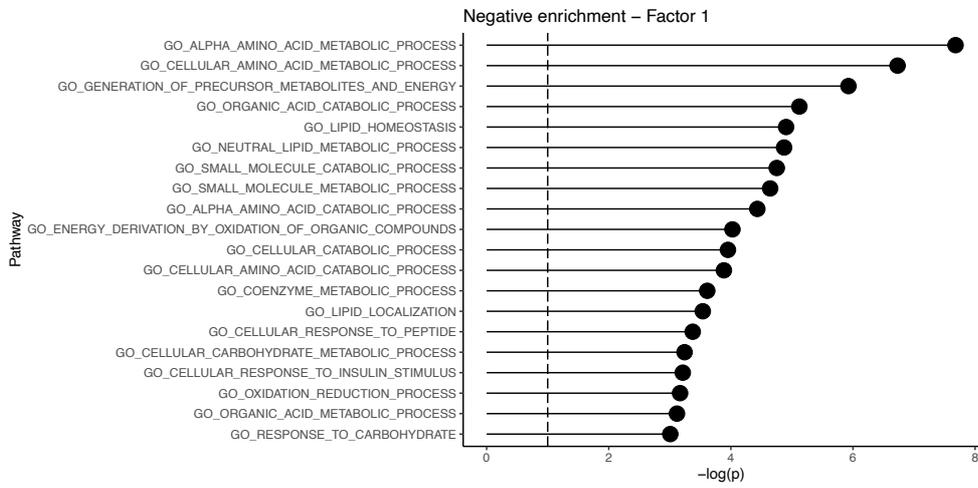
## Extended data Figure 2:

MOFA factor–trait correlation heatmap showing Pearson correlation coefficients between latent factors (Factors 1–10) and metabolic/clinical measures; color scale ranges from –1 (negative) to +1 (positive).



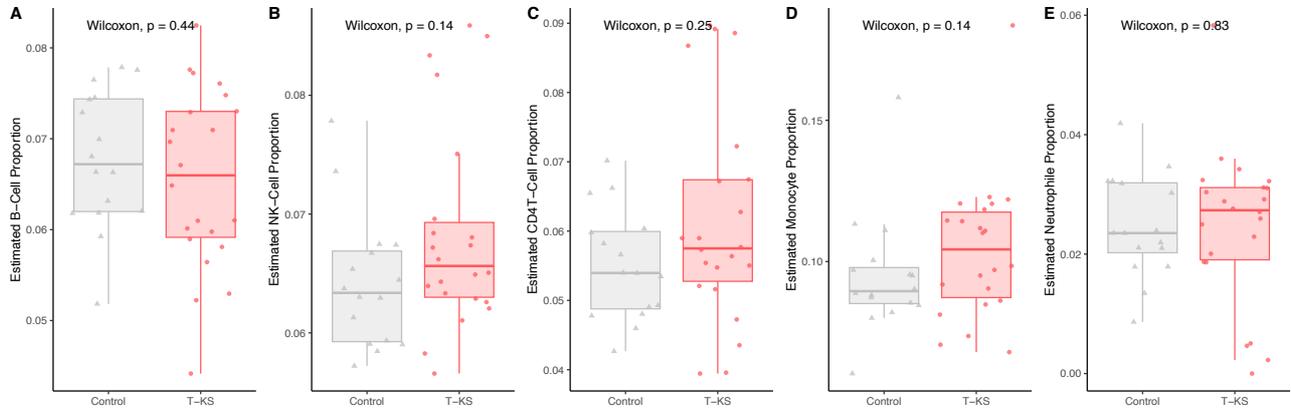
### Extended data Figure 3:

Downregulated genes in factor 1 were involved in processes such as amino acid metabolism, lipid homeostasis, and responses to glucose and insulin



## Extended data Figure 4

We observed a non-significant increase in immune cell proportions in men with KS, mainly driven by higher inferred levels of NK cells and macrophages/monocytes



## Extended data Figure 5

Upregulated Factor 6 genes were enriched in pathways related to steroid, hormone, and lipid metabolism

