Test2

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Contents

0.0.1 The expression of all TRAs associated with a tissue cannot be used to infer organ development

In this research, we attempt to draw conclusions about the developmental state of a tissue based on the expression of genes associated with it alone. Therefore, we analyzed the share of differentially expressed transcripts above a certain expression level over time, as shown in Fig. ???A. Furthermore, we observed trends within the median expression of all differentially expressed transcripts associated with a tissue (Fig. ???B). Since both metrics only showed in miniscule changes, we hypothesized that distinct, counteracting trends in expression exsisted within one tissue. Thus, k-means clustering was used to determine groups of TRAs with similar expression patterns. For each of these clusters, the median expression was plotted as shown in Fig. ???C.

Fig. 2 bla bla

Expression over time of Spleen–related differentially expressed transcripts
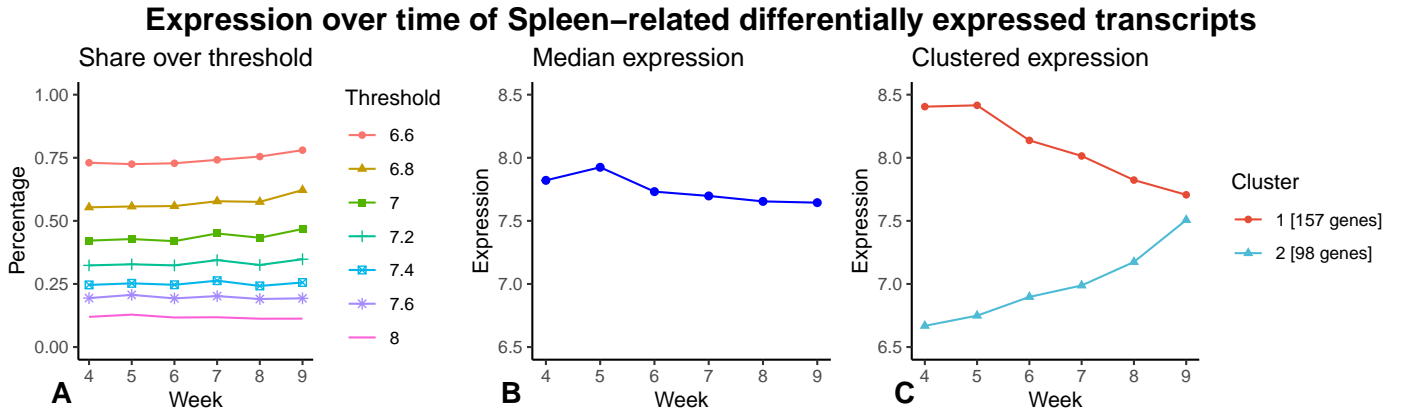
Figure 1: *A. For different expression thresholds the share of differentially expressed transcripts with higher expressions than the threshold is depicted. B. The median*

1 bla bla

For the spleen (2A), we determined a largely constant expression of immune-related genes throughout the time frame, with a slight increase in some functions from week 7-9. The brain (2B) showed an increase in neuron projection morphogenesis from a previously inactive state (expression < 6.8) in week 4 to a significant expression (>7.5) by week 8. Synaptic signaling stayed at relatively constant expression levels. Heart-associated functions (2C) can be grouped into two categories. Cardiac functions (cardiac muscle tissue development, heart contraction) are highly expressed in week 4 and fall continously until week 8. In contrast, general muscle gene sets are rising from originally lower expression levels during the observed time. The liver (@ref(fig: ORA-plot)D) shows no clear expression patterns, with some metabolic functions increasing through time (organic hydroxy compound metabolic process) while others stay mostly constant (cellular amino acid metabolic process) or fall (organic acid catabolic process). In contrast, skeletal muscle gene sets (@ref(fig: ORA-plot)E) show a very clear trend. After a mostly slight increase between week 4 and 8, a sharp rise in expression levels is visible from week 8 to 9. The testis-associated sets (@ref(fig: ORA-plot)F)

Main functions from overrepresentation analysis plotted by tissue

Spleen

FUNCTION	ADJ_P_VALUE
lymphocyte activation	1×10^{-65}
T cell activation	3×10^{-56}
adaptive immune response	4×10^{-53}
immune effector process	5×10^{-50}
positive regulation of immune response	8×10^{-50}
regulation of cell activation	3×10^{-49}
regulation of leukocyte activation	4×10^{-49}
regulation of lymphocyte activation	8×10^{-48}
leukocyte cell-cell adhesion	2×10^{-42}
immune response-regulating signaling pathway	1×10^{-41}

A

Spleen

Function
- adaptive immune response
- immune effector process
- lymphocyte activation
- positive regulation of immune response
- T cell activation

Brain

FUNCTION	ADJ_P_VALUE
synaptic signaling	9×10^{-43}
trans-synaptic signaling	9×10^{-43}
chemical synaptic transmission	9×10^{-43}
anterograde trans-synaptic signaling	9×10^{-43}
modulation of chemical synaptic transmission	9×10^{-25}
regulation of trans-synaptic signaling	9×10^{-25}
neuron projection morphogenesis	2×10^{-18}
cell projection morphogenesis	8×10^{-18}
plasma membrane bounded cell projection morphogenesis	2×10^{-17}
cell part morphogenesis	2×10^{-17}

B

Brain

Function
- modulation of chemical synaptic transmission
- neuron projection morphogenesis
- synaptic signaling

Heart

FUNCTION	ADJ_P_VALUE
muscle cell development	3×10^{-27}
muscle structure development	1×10^{-26}
myofibril assembly	2×10^{-24}
striated muscle cell development	2×10^{-24}
muscle tissue development	3×10^{-24}
cardiac muscle tissue development	3×10^{-24}
muscle system process	3×10^{-24}
striated muscle tissue development	2×10^{-23}
muscle cell differentiation	5×10^{-23}
heart contraction	1×10^{-22}

C

Heart

Function
- cardiac muscle tissue development
- heart contraction
- muscle cell development
- muscle structure development
- myofibril assembly

Liver

FUNCTION	ADJ_P_VALUE
monocarboxylic acid metabolic process	7×10^{-51}
small molecule catabolic process	7×10^{-39}
organic acid catabolic process	4×10^{-36}
carboxylic acid catabolic process	2×10^{-35}
steroid metabolic process	7×10^{-33}
small molecule biosynthetic process	4×10^{-31}
cellular amino acid metabolic process	1×10^{-28}
fatty acid metabolic process	6×10^{-28}
organic hydroxy compound metabolic process	9×10^{-28}
alpha-amino acid metabolic process	3×10^{-27}

D

Liver

Function
- cellular amino acid metabolic process
- monocarboxylic acid metabolic process
- organic acid catabolic process
- organic hydroxy compound metabolic process
- steroid metabolic process

Muscle - Skeletal

FUNCTION	ADJ_P_VALUE
muscle structure development	7×10^{-29}
muscle system process	8×10^{-27}
muscle organ development	5×10^{-25}
muscle cell development	1×10^{-21}
muscle contraction	1×10^{-21}
muscle cell differentiation	4×10^{-20}
striated muscle cell differentiation	4×10^{-19}
myofibril assembly	3×10^{-18}
striated muscle cell development	3×10^{-18}
striated muscle contraction	1×10^{-16}

E

Muscle – Skeletal

Function
- muscle cell development
- muscle contraction
- muscle structure development
- muscle system process
- striated muscle cell differentiation

Testis

FUNCTION	ADJ_P_VALUE
male gamete generation	1×10^{-35}
spermatogenesis	3×10^{-34}
microtubule-based movement	2×10^{-26}
cilium organization	2×10^{-26}
cilium assembly	2×10^{-23}
microtubule cytoskeleton organization	2×10^{-23}
meiotic cell cycle	2×10^{-23}
cilium movement	3×10^{-20}
nuclear division	1×10^{-18}
meiotic cell cycle process	2×10^{-18}

F

Testis

Function
- cilium organization
- male gamete generation
- meiotic cell cycle

Stomach

FUNCTION	ADJ_P_VALUE
digestion	1×10^{-4}
regulation of hormone levels	6×10^{-4}
gastric acid secretion	2×10^{-3}
peptide hormone secretion	2×10^{-3}
peptide transport	2×10^{-3}
peptide secretion	3×10^{-3}
digestive system process	6×10^{-3}
amide transport	6×10^{-3}
hormone transport	6×10^{-3}
hormone secretion	6×10^{-3}

G

Stomach

Function
- digestion
- peptide hormone secretion
- regulation of hormone levels

Skin

FUNCTION	ADJ_P_VALUE
epidermis development	2×10^{-21}
skin development	9×10^{-21}
keratinization	6×10^{-17}
keratinocyte differentiation	2×10^{-14}
epidermal cell differentiation	1×10^{-10}
intermediate filament cytoskeleton organization	9×10^{-10}
intermediate filament-based process	1×10^{-9}
intermediate filament organization	6×10^{-9}
regulation of water loss via skin	2×10^{-8}
establishment of skin barrier	1×10^{-7}

H

Skin

Function
- epidermis development
- keratinization
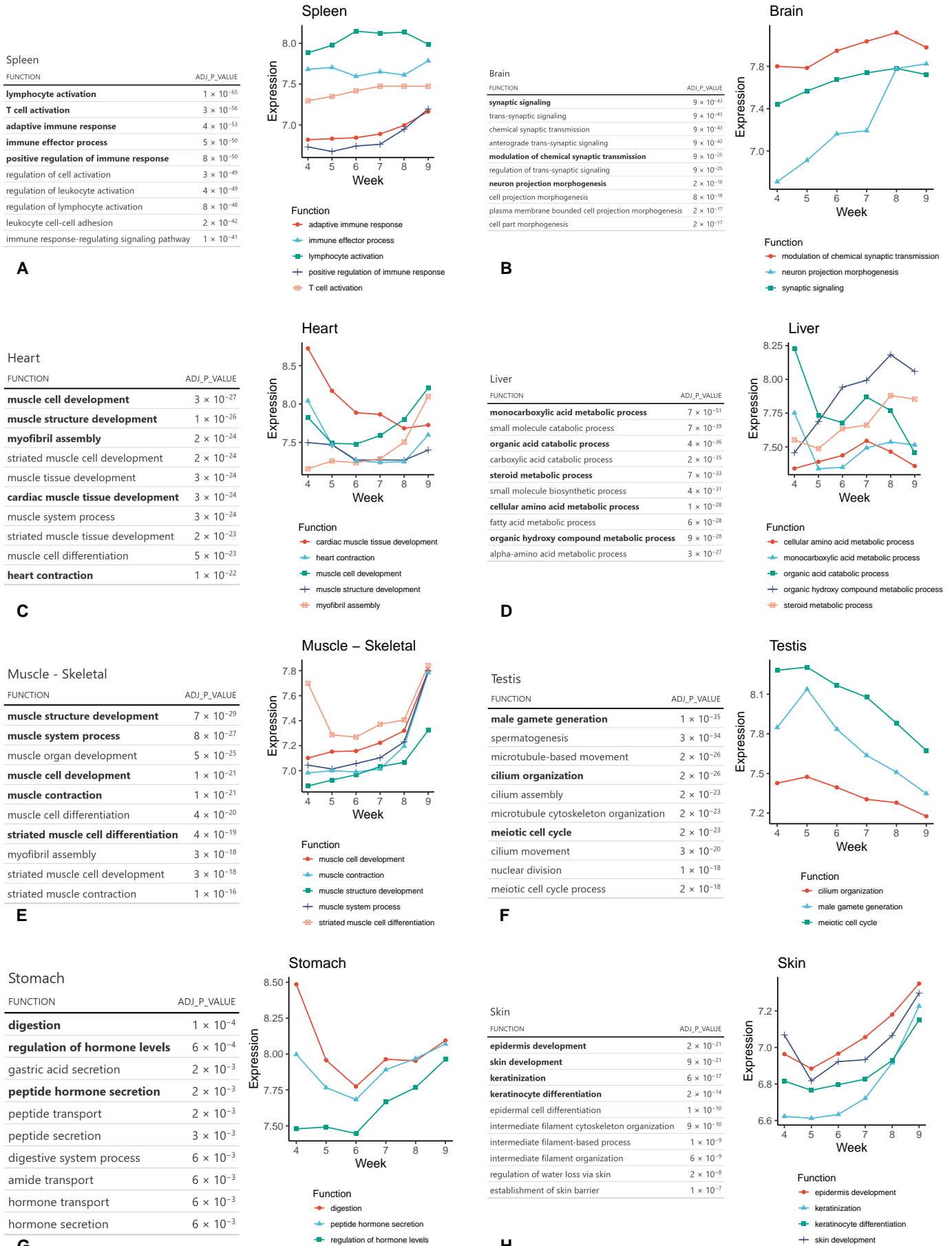- keratinocyte differentiation
- skin development

Figure 2: *For eight tissues A to H, the tables show the 10 most significant results from overrepresentation analysis. There, the functional GO annotation of all transcripts in our dataset (not only the differentially expressed ones) was compared to the functions associated with all TRAs of one tissue. The significance was determined by an adjusted p-value. Of those 10 functions, up to 5 were*