

**Supplemental Figures for:**

**Ontogeny of hepatic transporters and drug metabolizing enzymes in humans and in non-clinical species**

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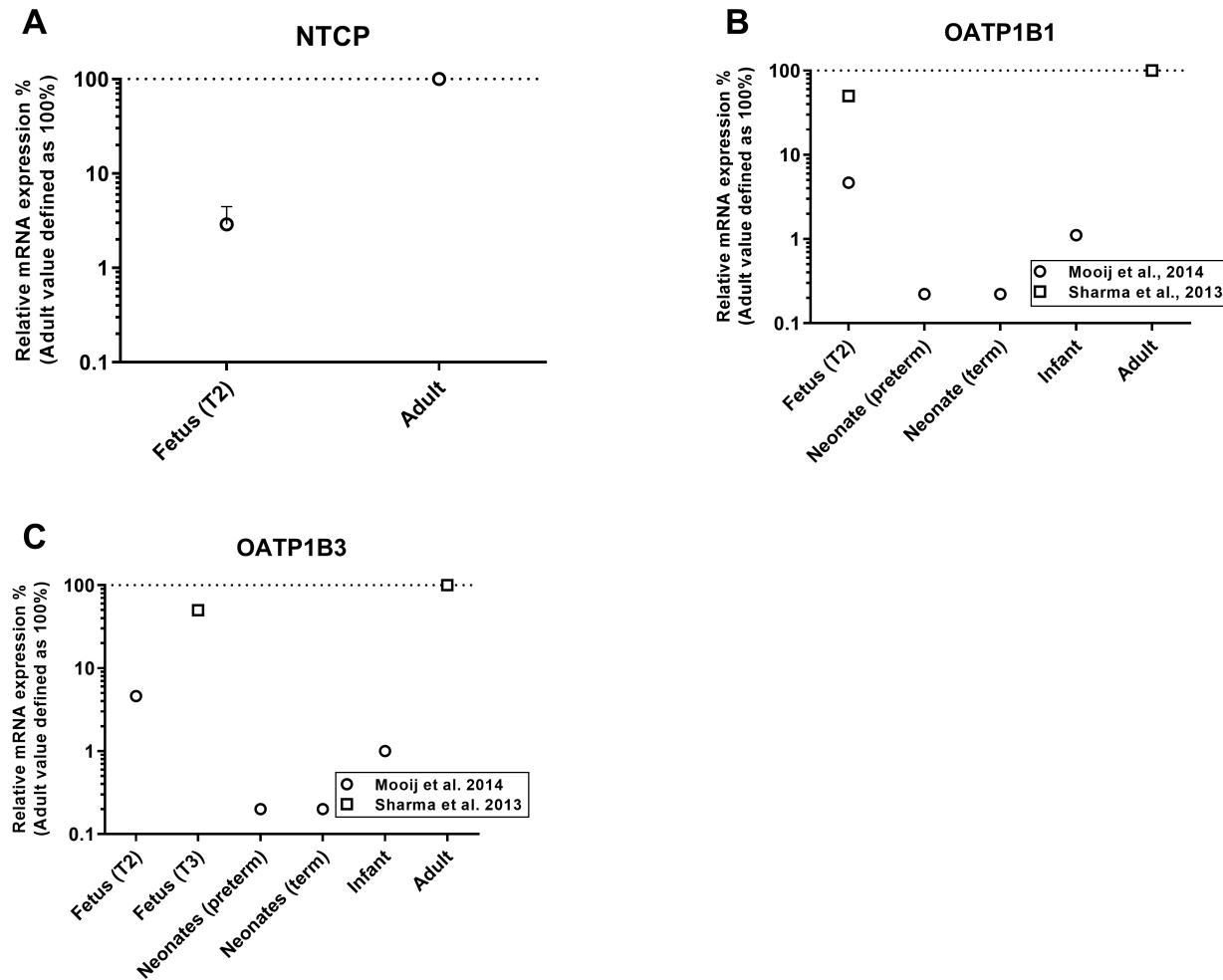
<sup>YY</sup>contributed equally to this work

# Author to whom correspondence should be sent

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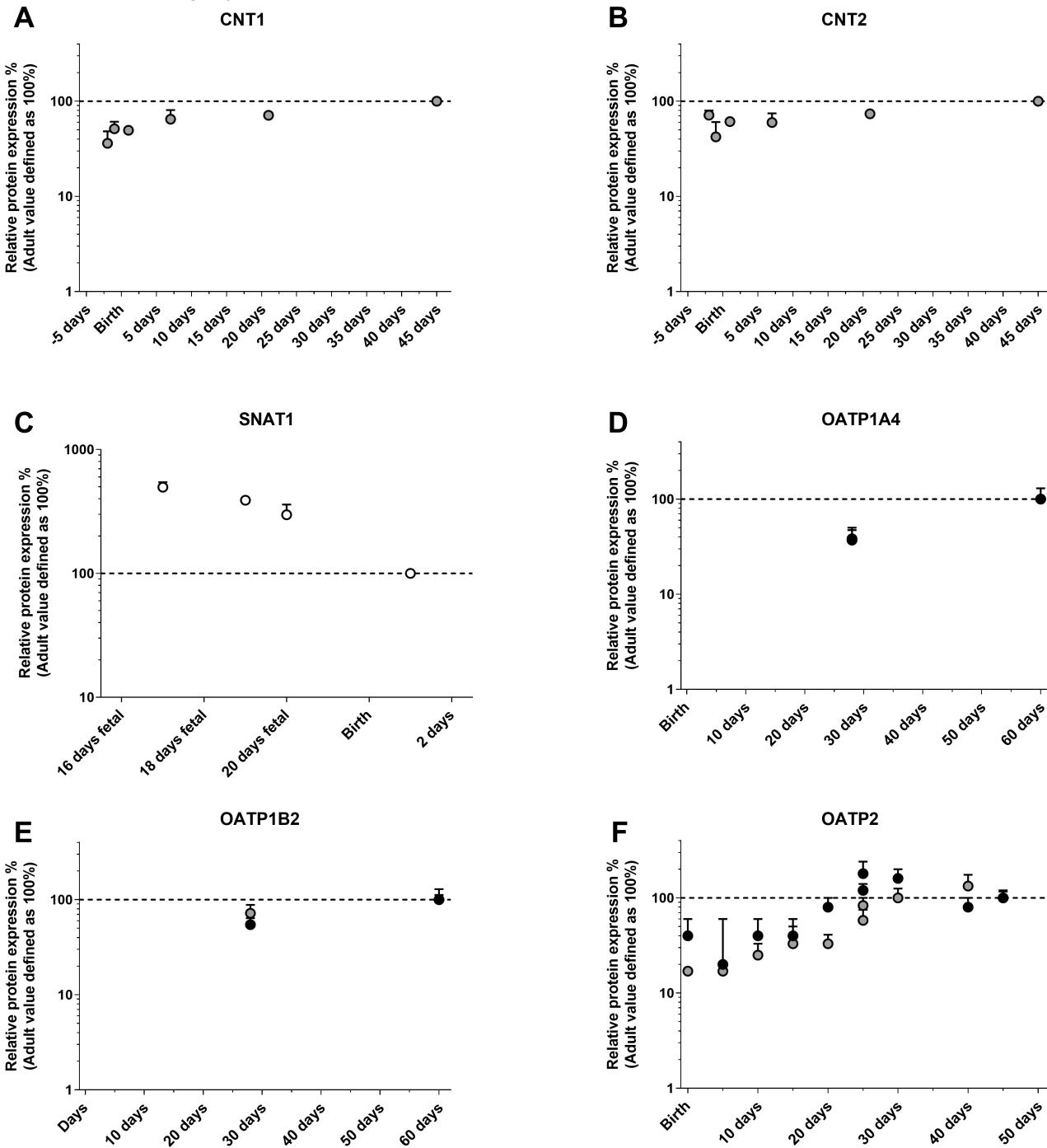
### Supplemental Figure 1.

Pooled literature data on the ontogeny of hepatic mRNA levels of uptake transporters in humans. Symbols represent relative mRNA expression in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative mRNA expression and the error bars show the standard deviation. See Table 1 for explanation on the ontogeny profiles and literature references.



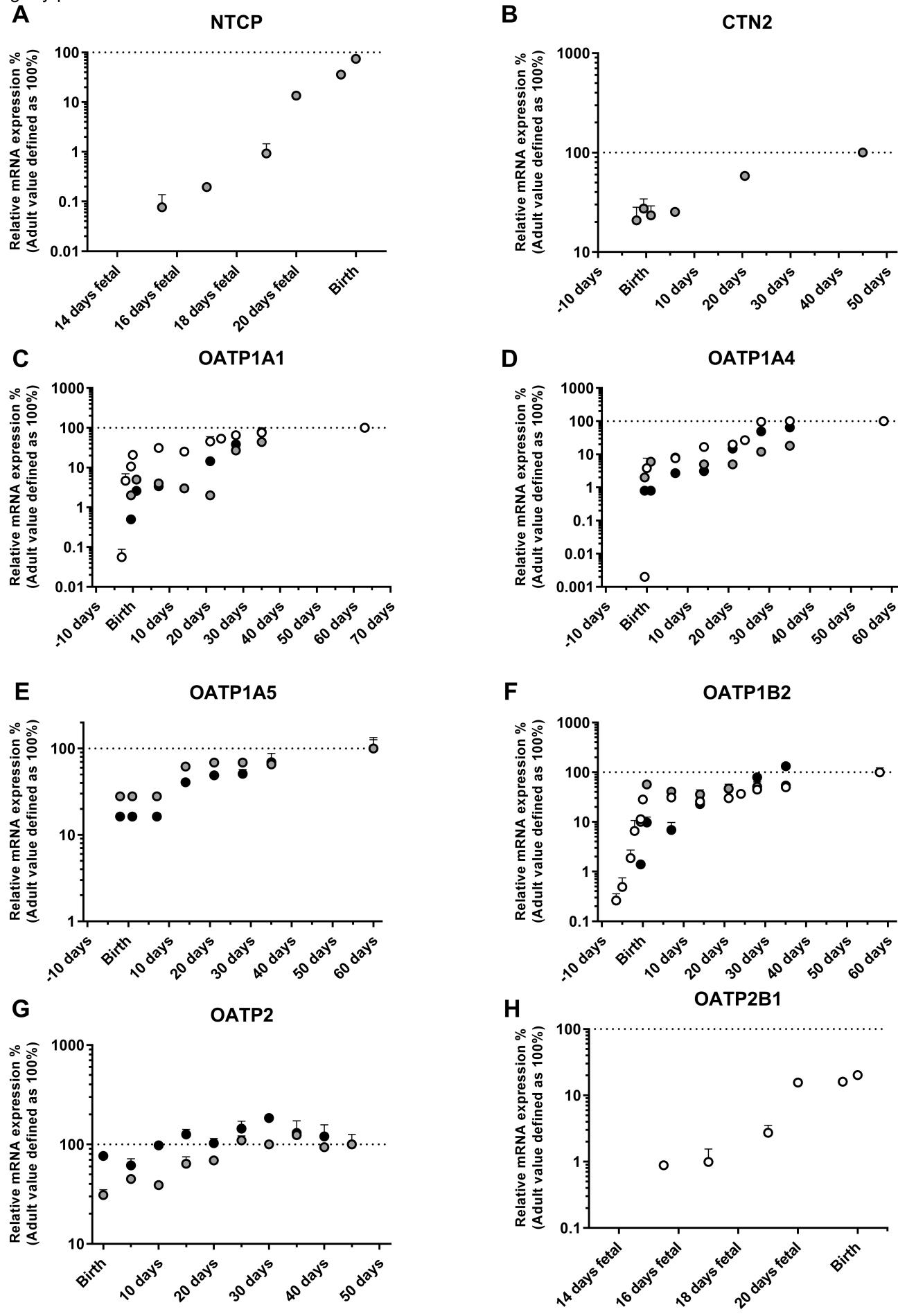
## Supplemental Figure 2.

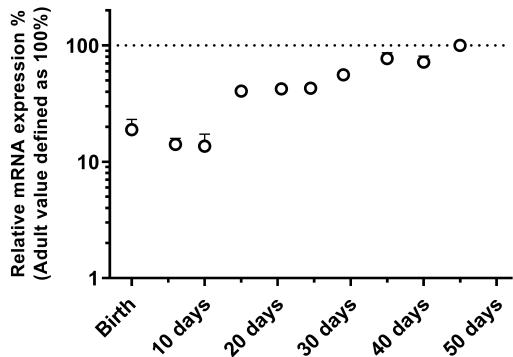
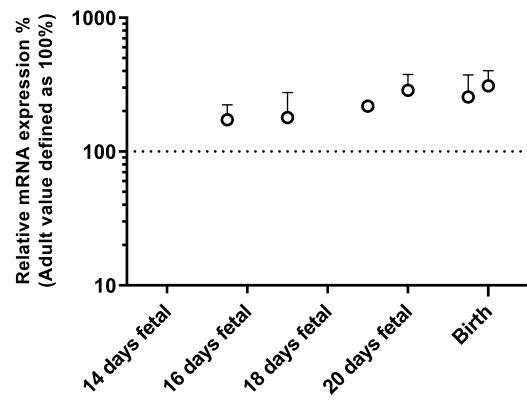
Pooled literature data on the ontogeny of hepatic protein expression levels of uptake transporters in rats. Symbols represent protein expression measurements in mixed-gender rat population (open), male rats (grey) and female rats (black) in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative mRNA expression and the error bars show the standard deviation. See Table 2 for explanation on the ontogeny profiles and literature references.



### Supplemental Figure 3.

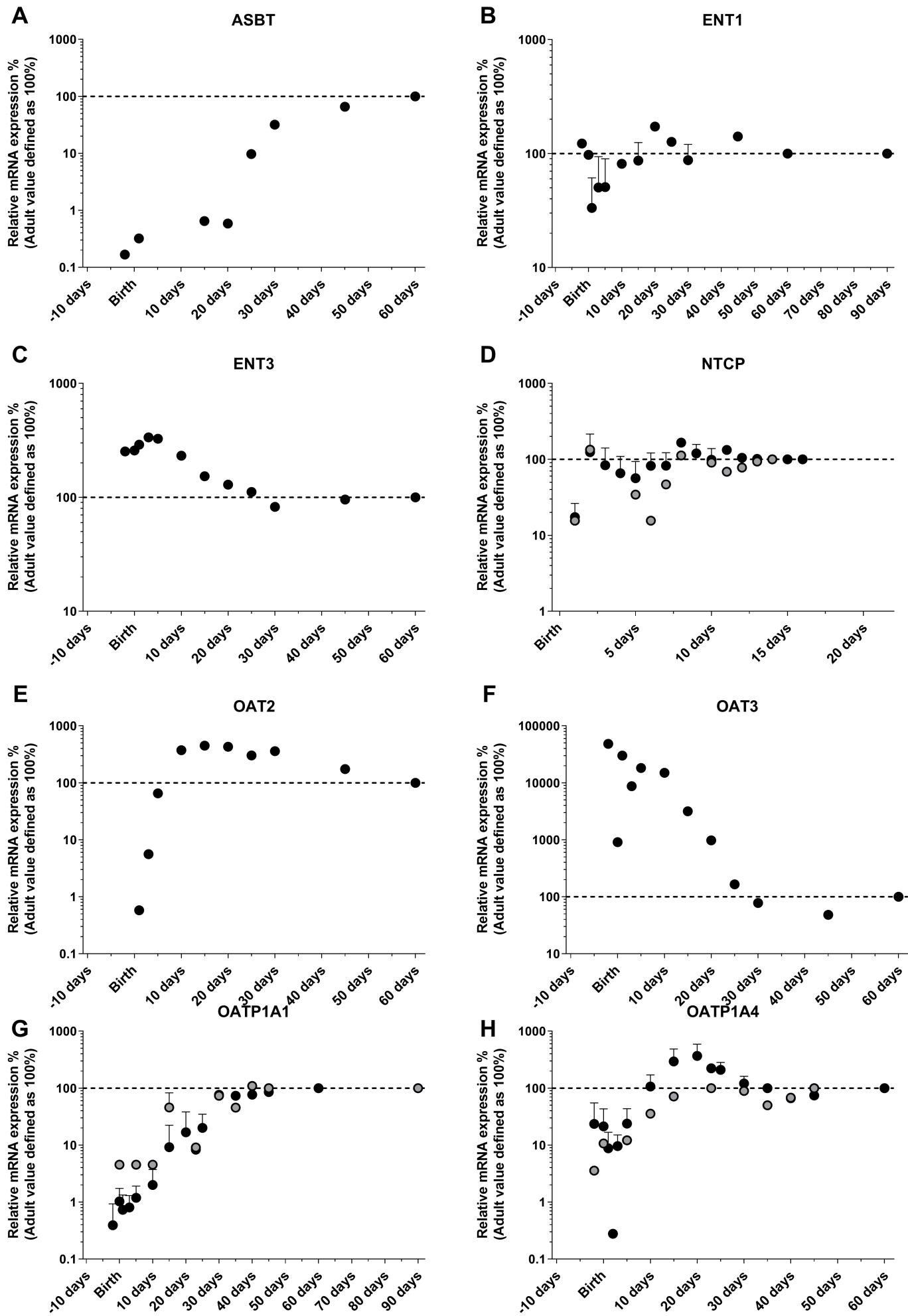
Pooled literature data on the ontogeny of hepatic mRNA levels of uptake transporters in rats. Symbols represent relative mRNA expression in mixed-gender rat population (open), male rats (grey) and female rats (black) in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative mRNA expression and the error bars show the standard deviation. See Table 2 for explanation on the ontogeny profiles and literature references.

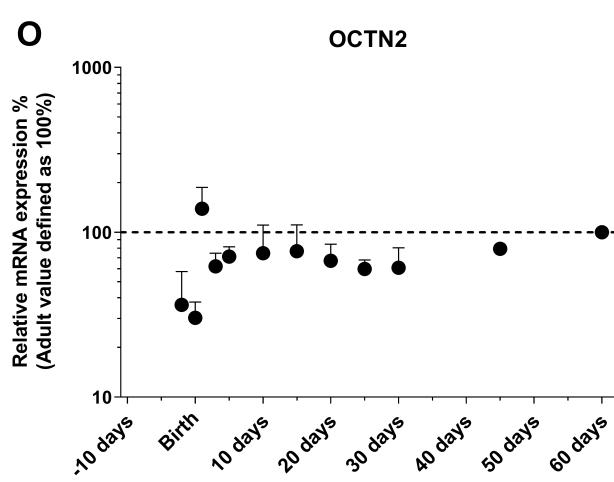
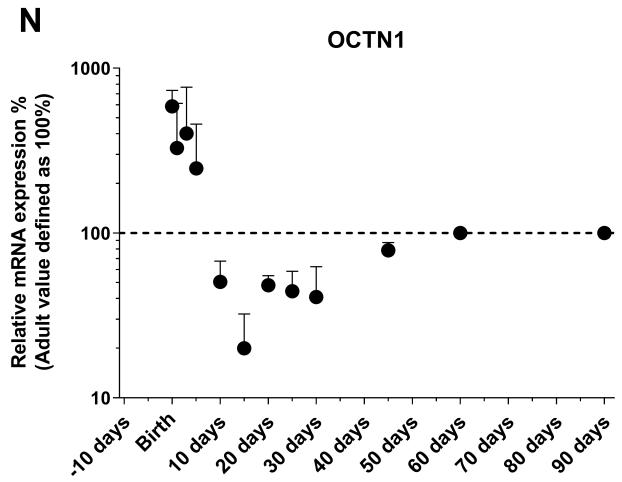
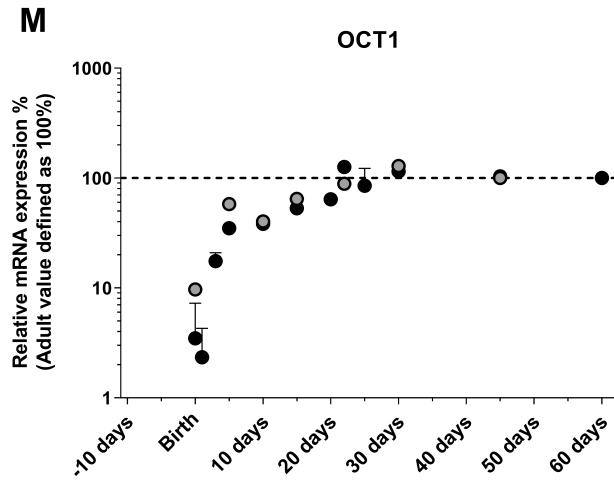
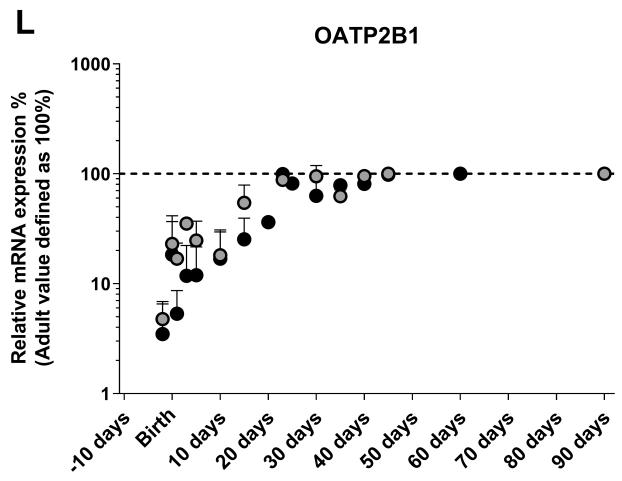
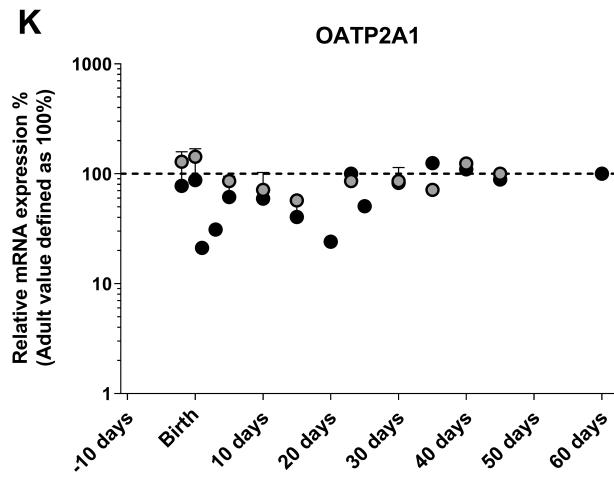
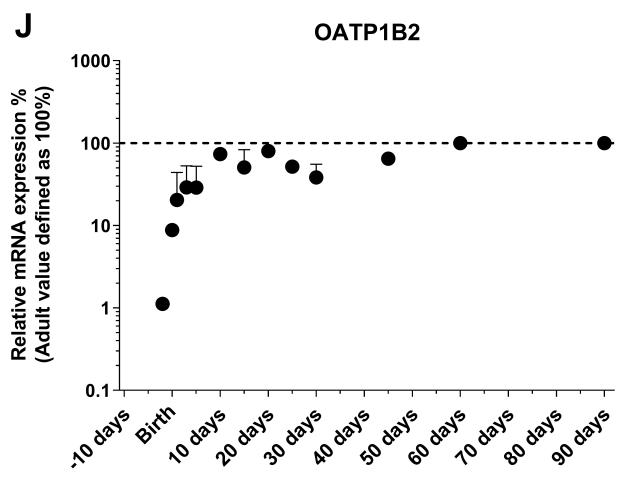
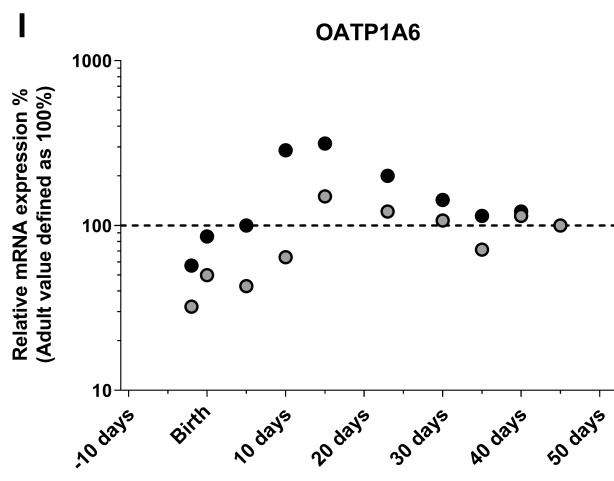


**OATP4****J****OATP4A1**

#### Supplemental Figure 4.

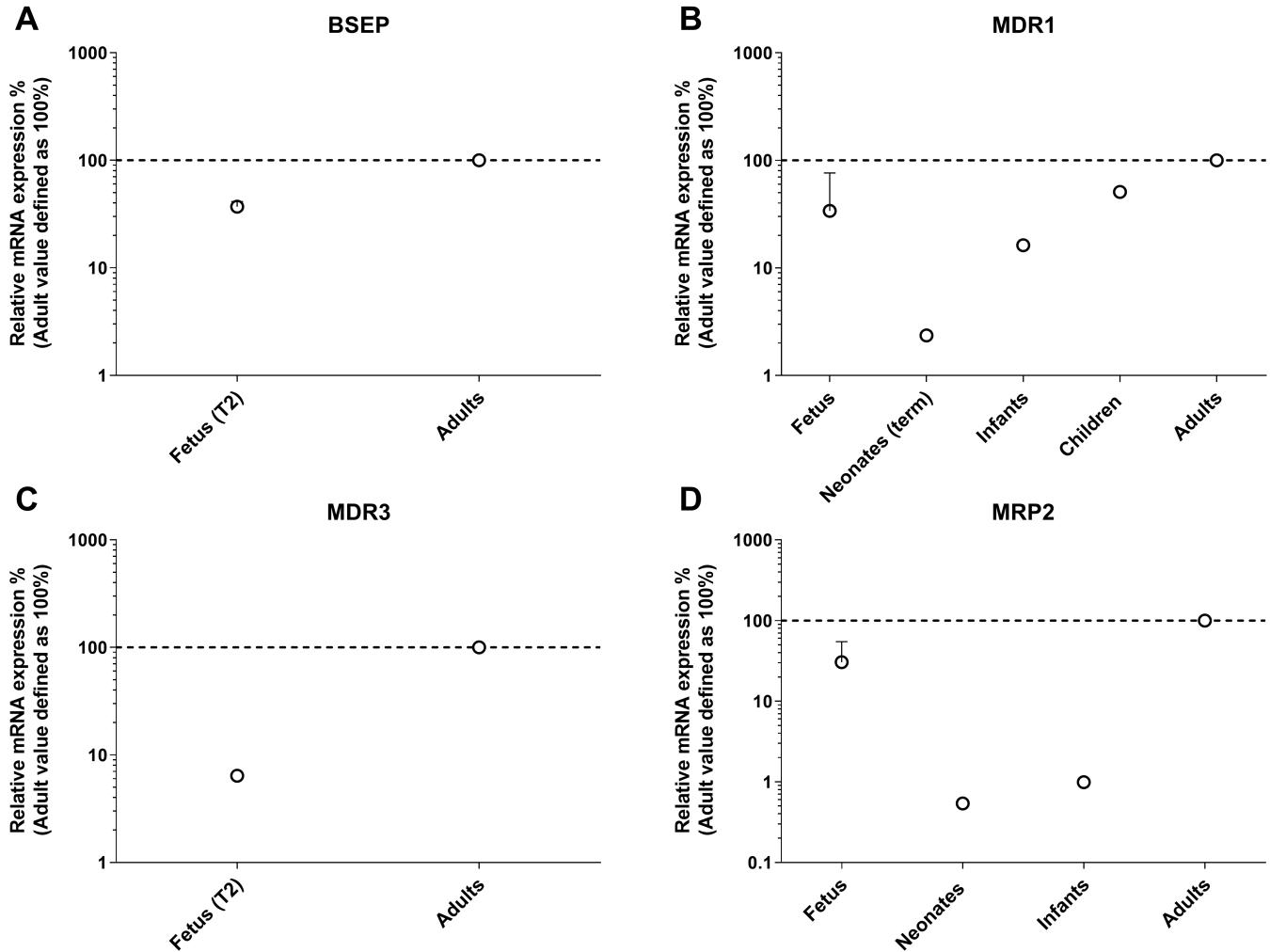
Pooled literature data on the ontogeny of hepatic mRNA expression levels of uptake transporters in mice. Symbols represent relative mRNA expression in male rats (grey) and female rats (black) in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative mRNA expression and the error bars show the standard deviation. See Table 3 for explanation on the ontogeny profiles and literature references.





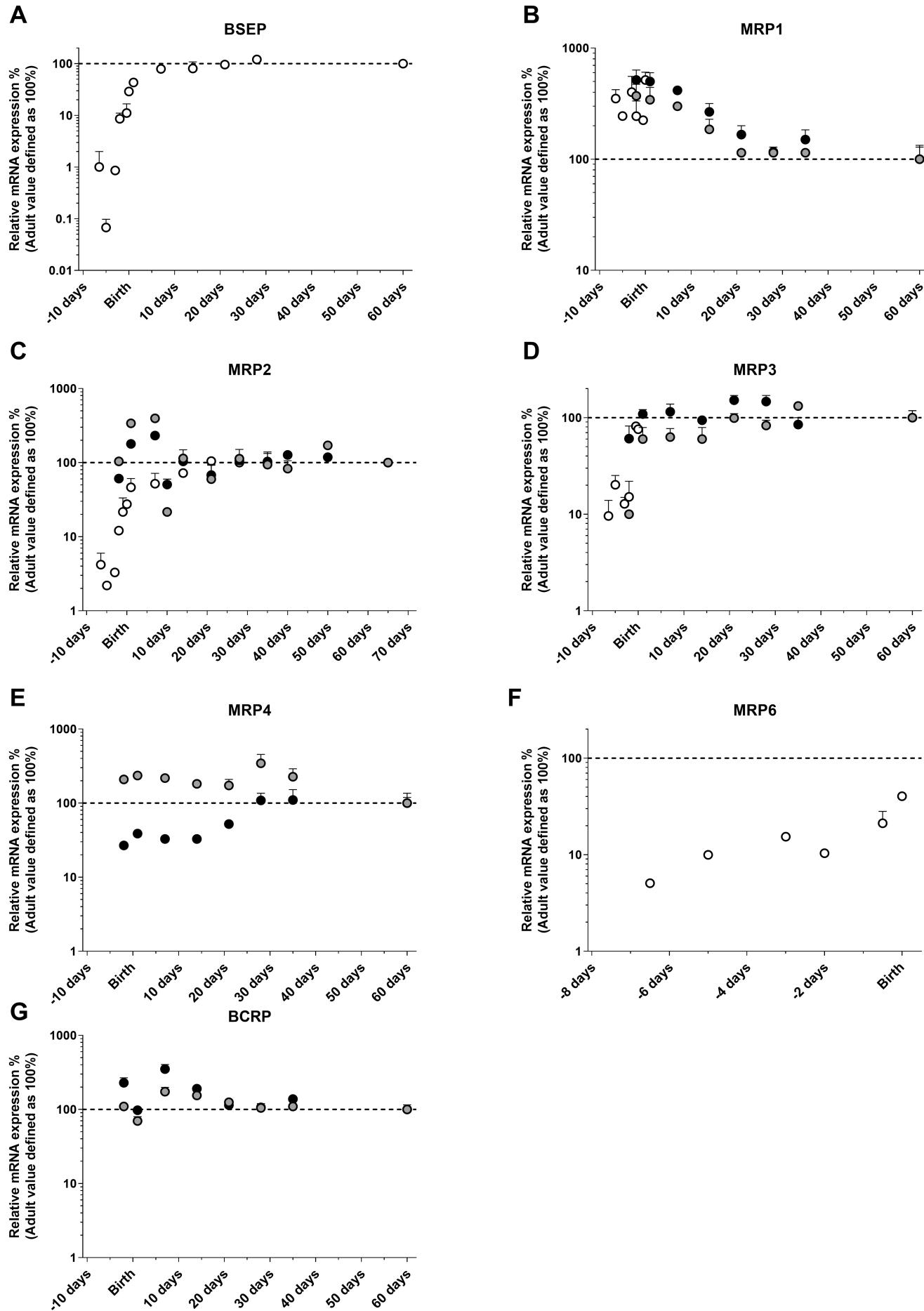
### Supplemental Figure 5.

Pooled literature data on the ontogeny of hepatic mRNA expression levels of efflux transporters in humans. Symbols represent relative mRNA expression in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative mRNA expression and the error bars show the standard deviation. See Table 4 for explanation on the ontogeny profiles and literature references.



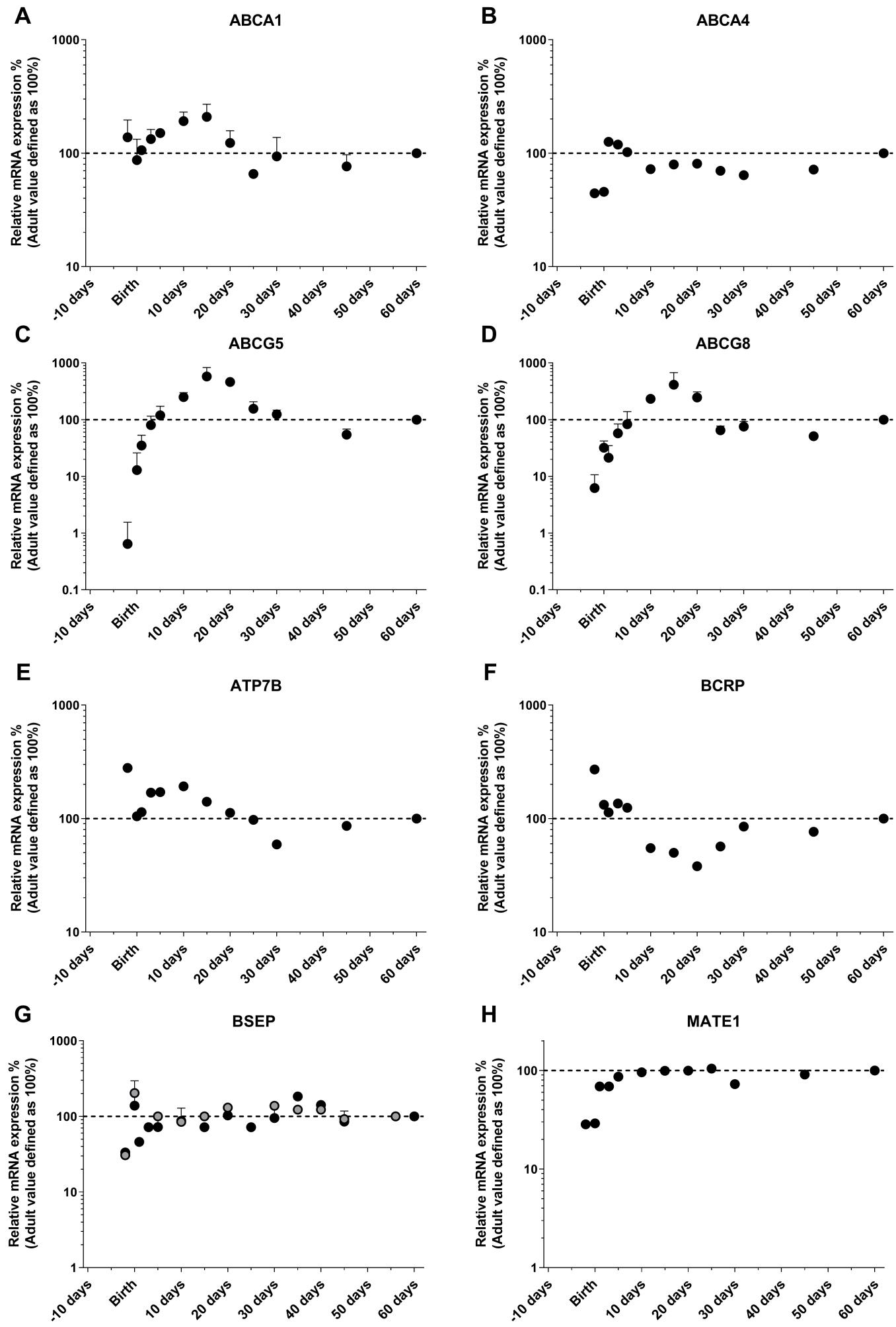
## Supplemental Figure 6.

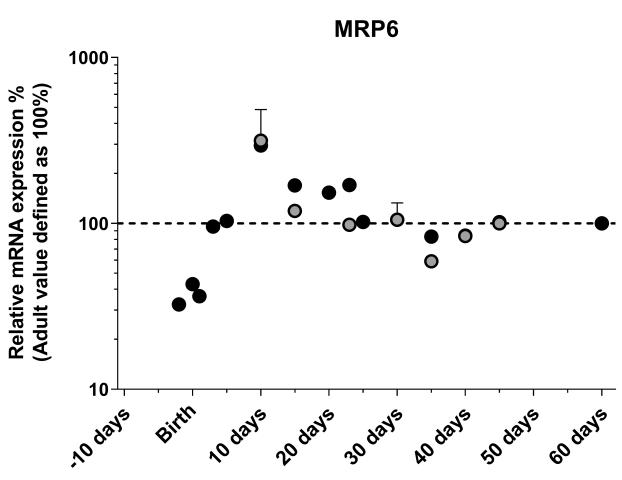
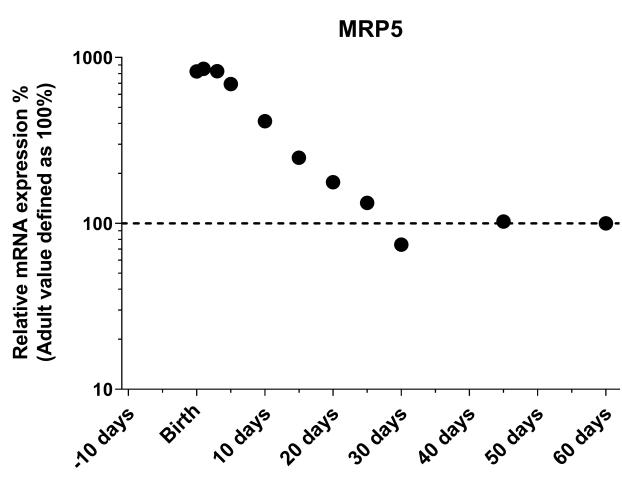
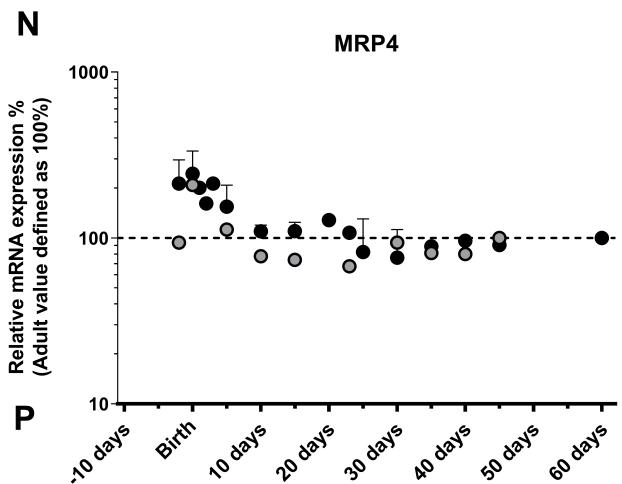
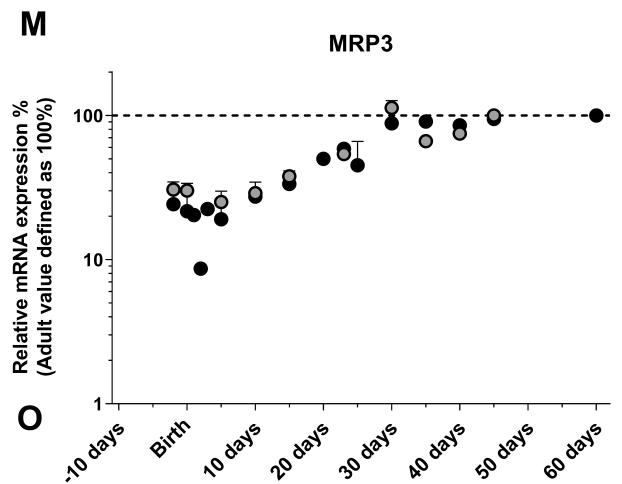
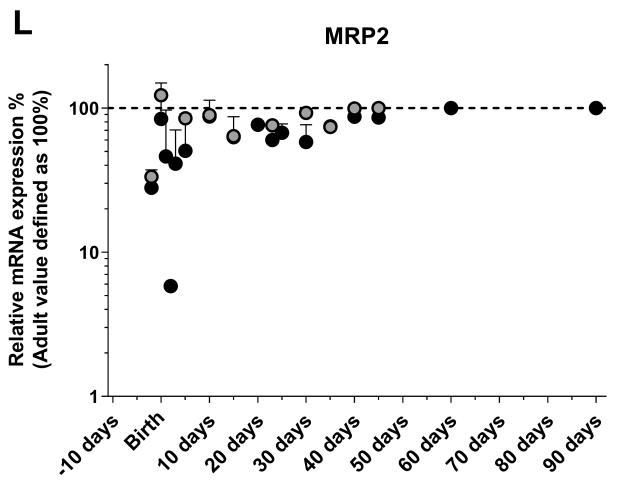
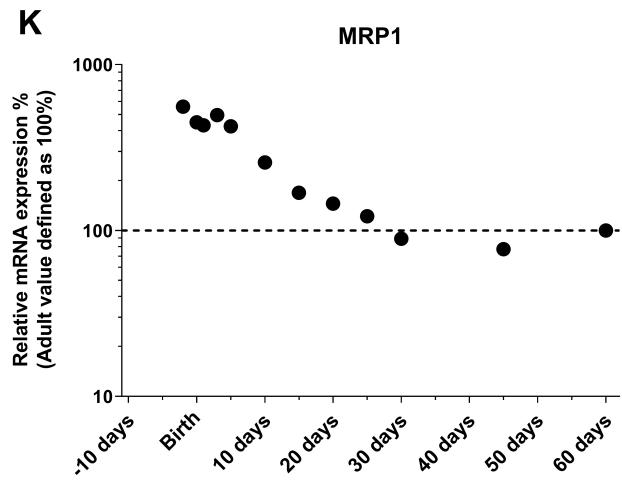
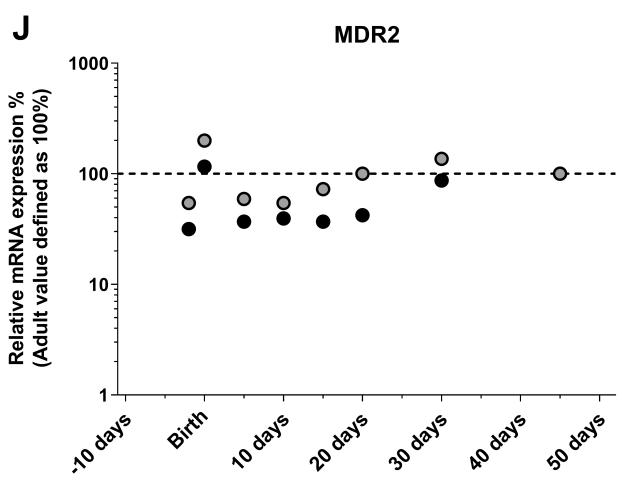
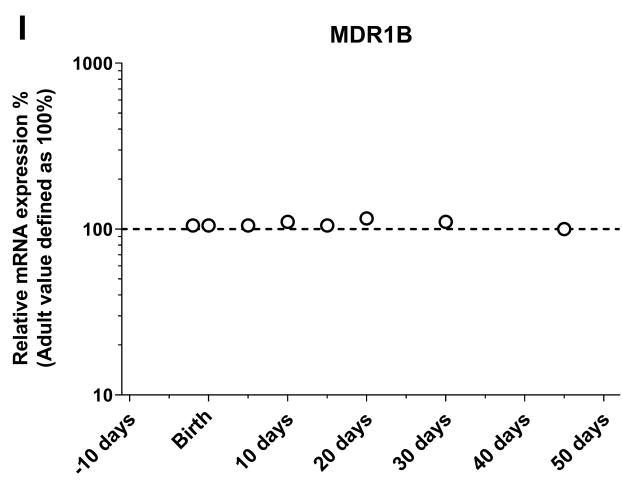
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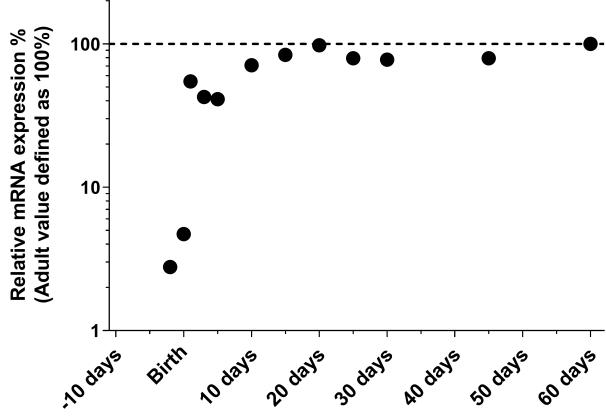


## Supplemental Figure 7.

Pooled literature data on the ontogeny of hepatic mRNA expression levels of efflux transporters in mice. The X-axes indicate either fetal levels or postnatal age in days. Symbols represent relative mRNA expression in mixed-gender rat population (open), male rats (grey) and female rats (black) in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative mRNA expression and the error bars show the standard deviation. See Table 6 for explanation on the ontogeny profiles and literature references.

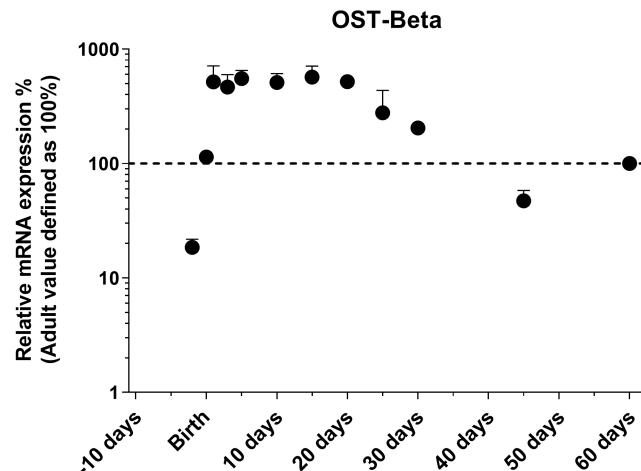




**Q****NPT1**

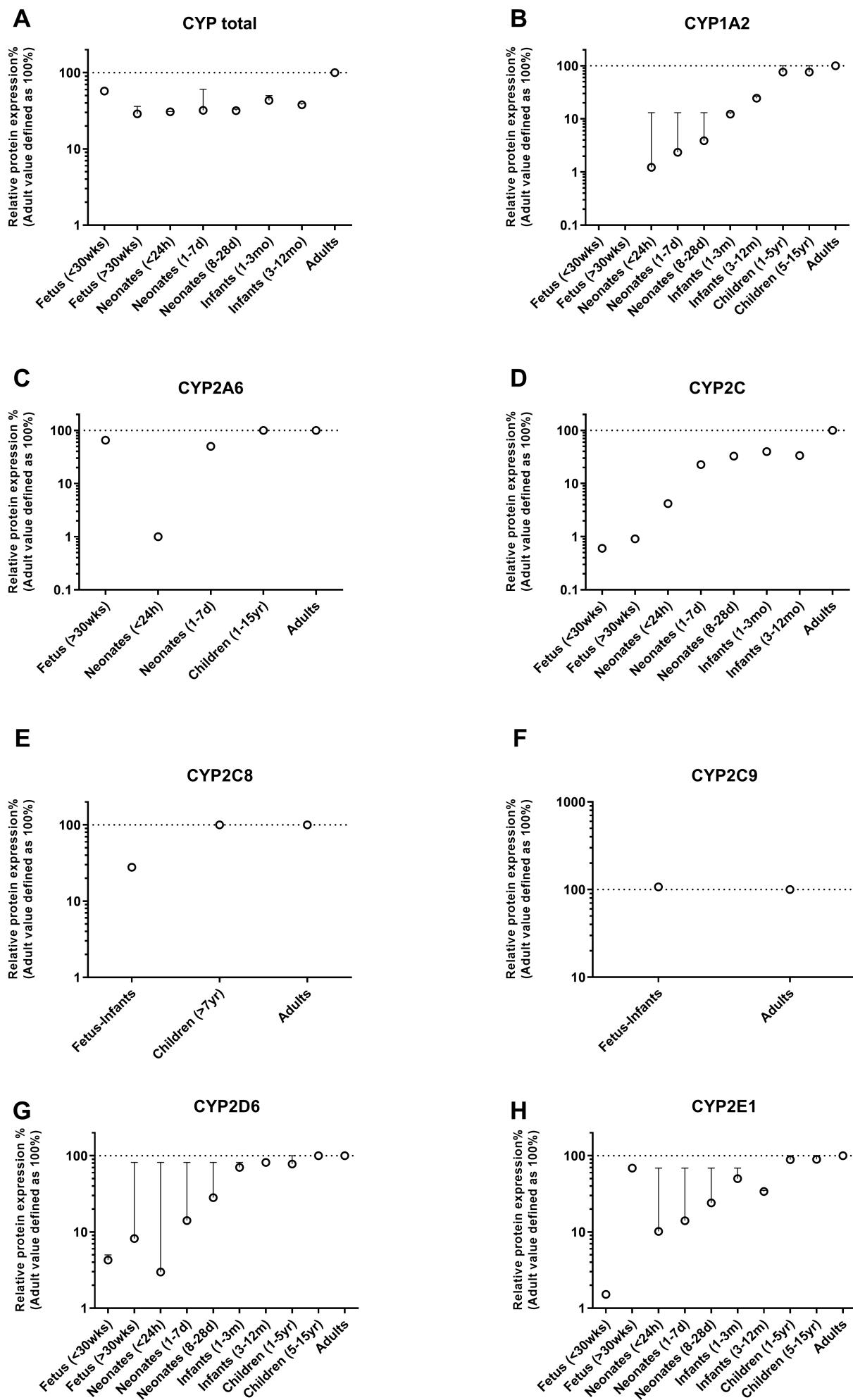
### Supplemental Figure 8.

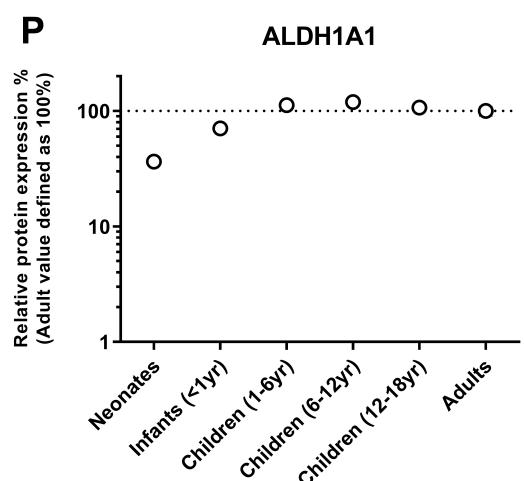
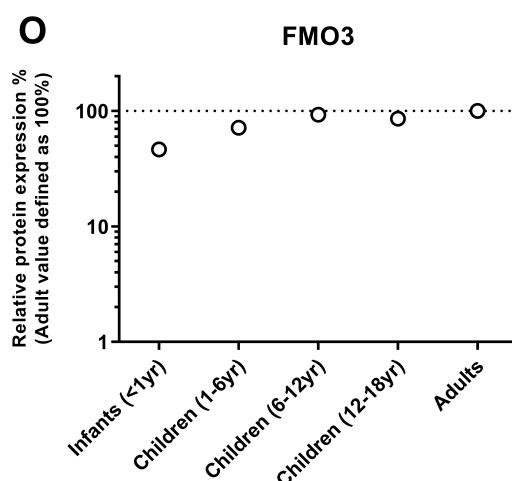
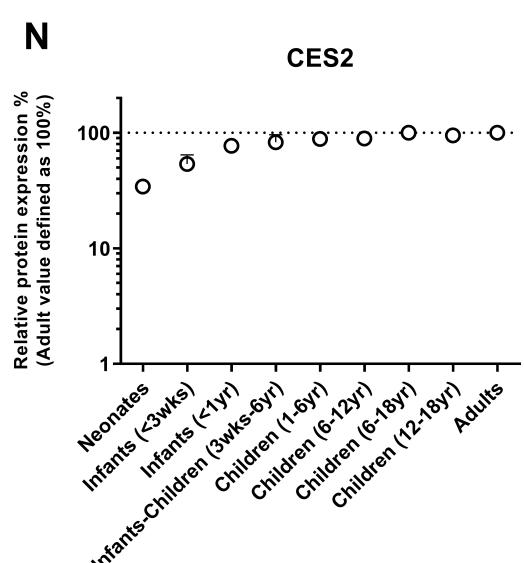
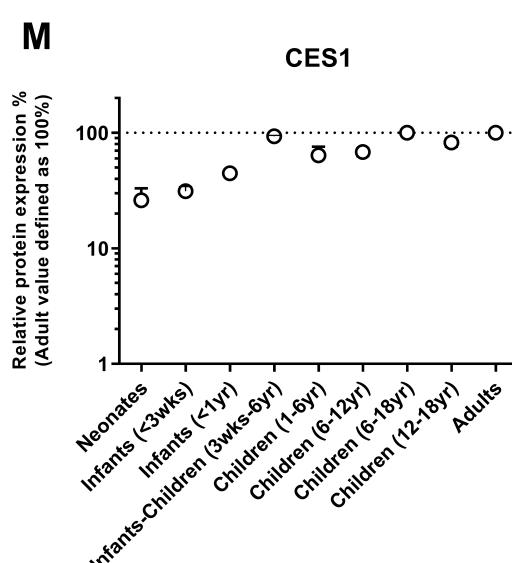
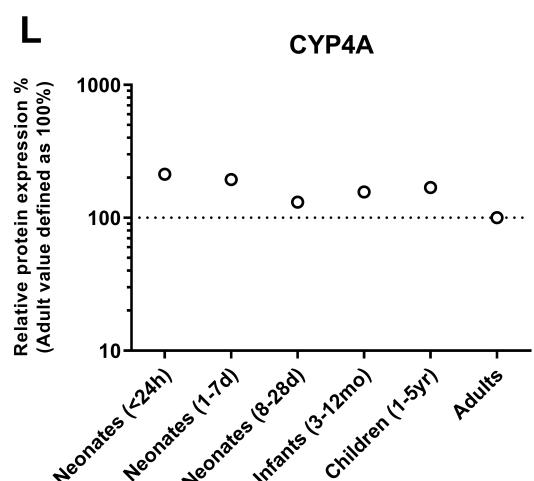
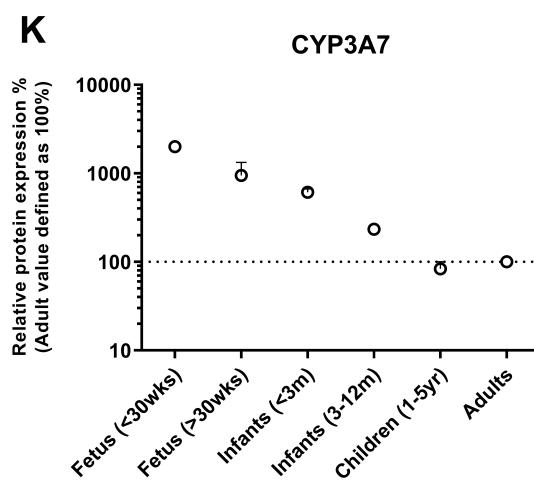
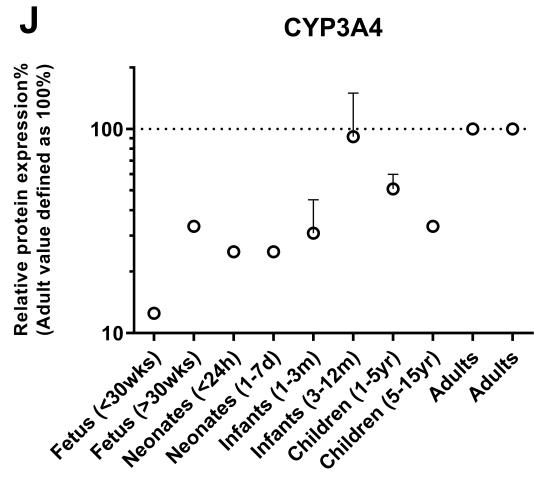
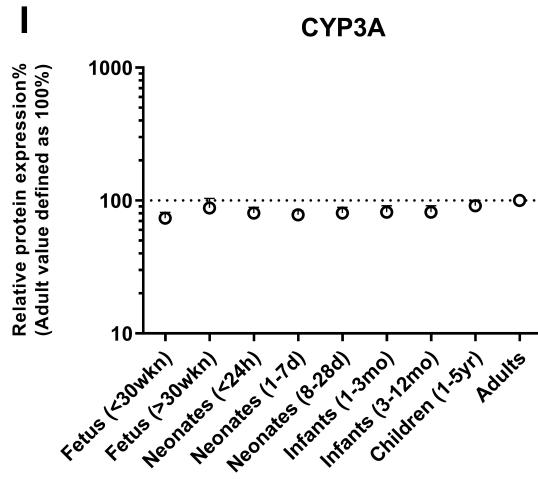
Literature data on the ontogeny of hepatic mRNA expression of the bi-directional transporter monomer Ost- $\beta$  in mice. Symbols represent relative mRNA expression in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative mRNA expression and the error bars show the standard deviation. See Table 6 for explanation on the ontogeny profiles and literature references.

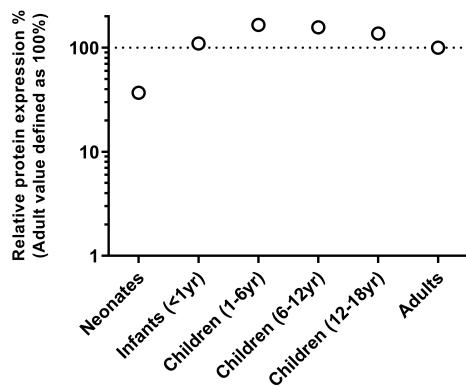
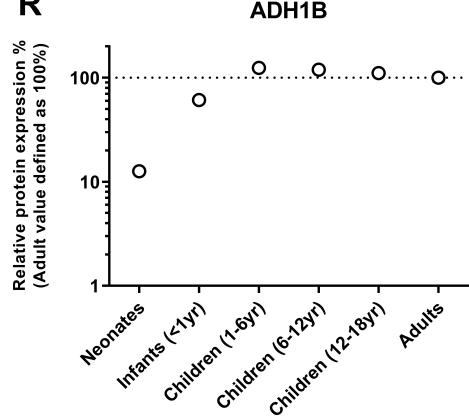
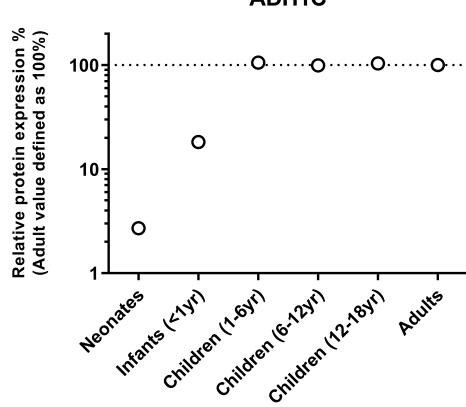


## Supplemental Figure 9.

Pooled literature data on the ontogeny of the hepatic protein expression of phase I drug metabolizing enzymes in humans. Symbols represent relative protein expression in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative protein expression and the error bars show the standard deviation. See Table 7 for explanation on the ontogeny profiles and literature references.

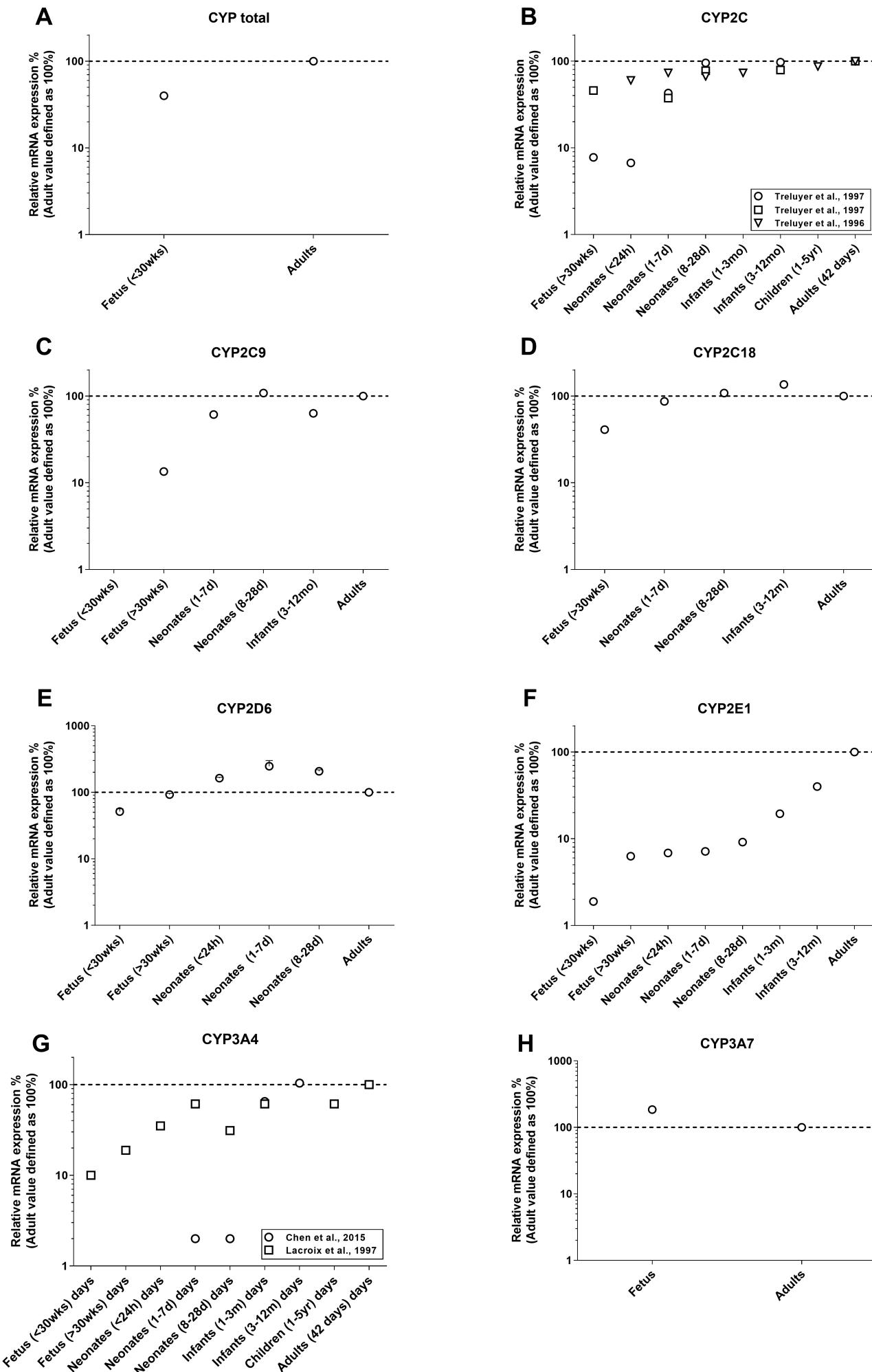




**Q****R****S**

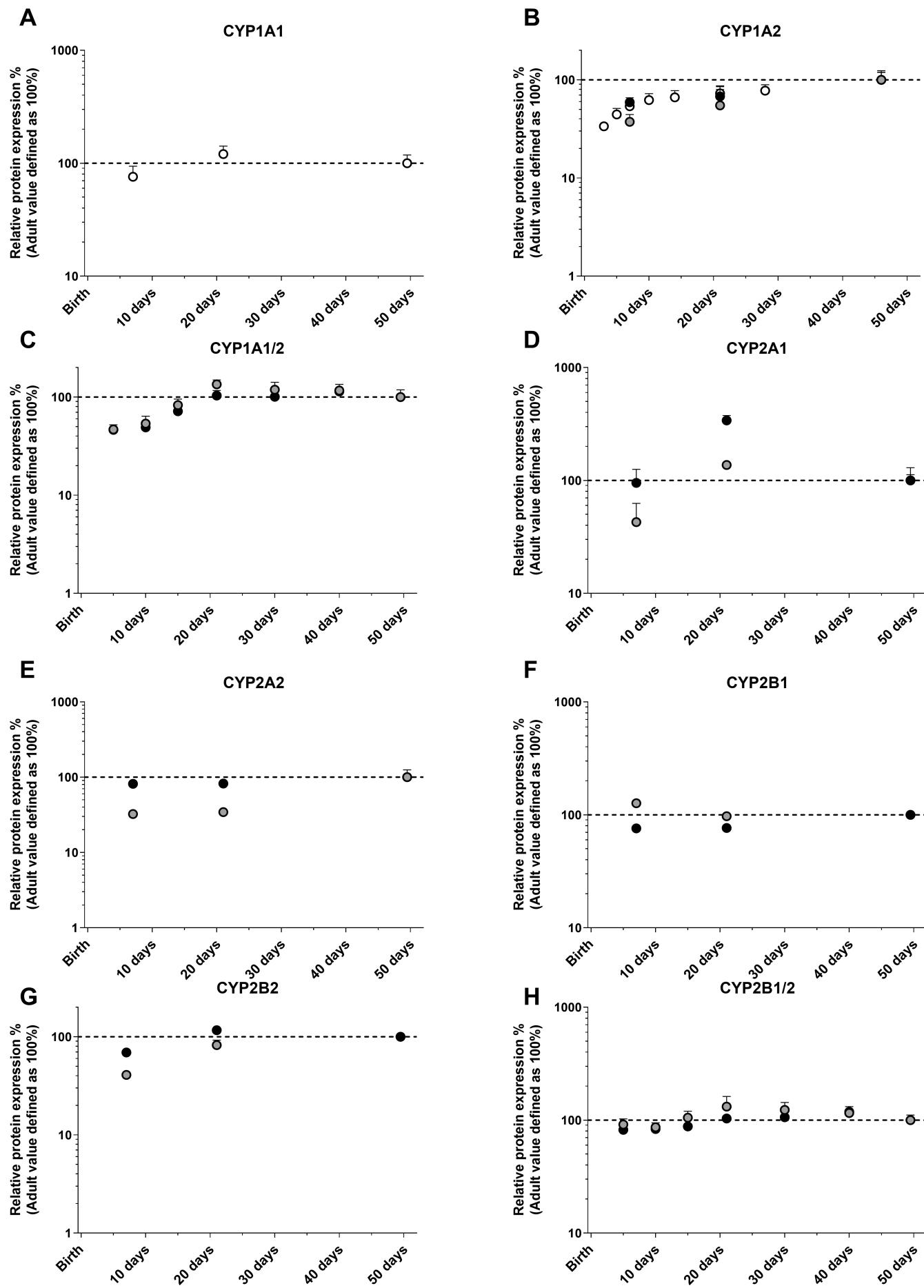
### Supplemental Figure 10.

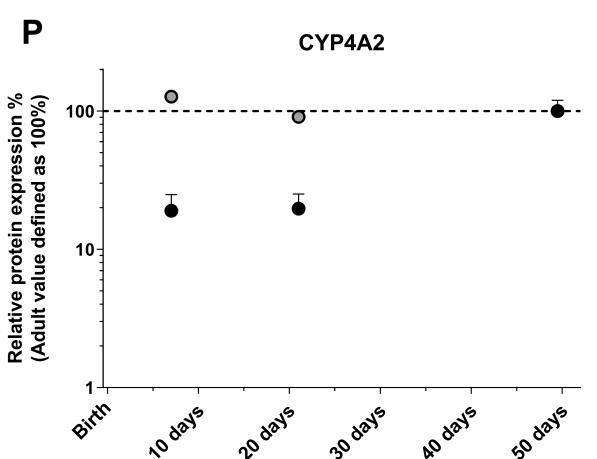
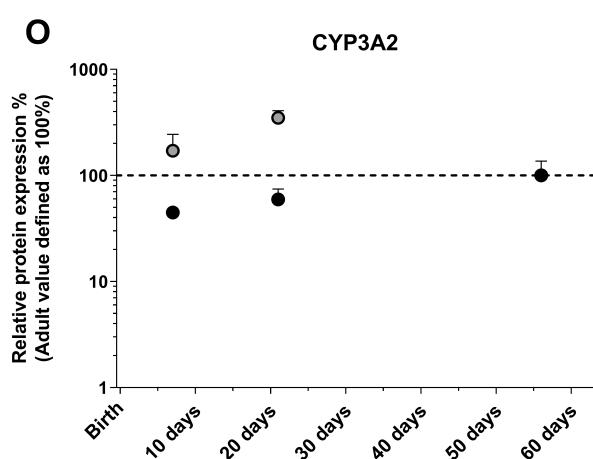
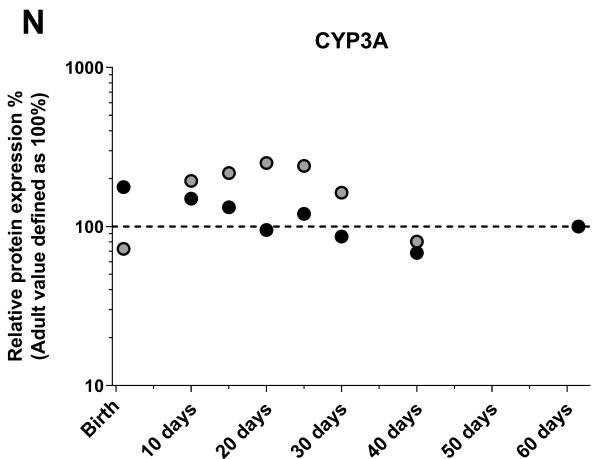
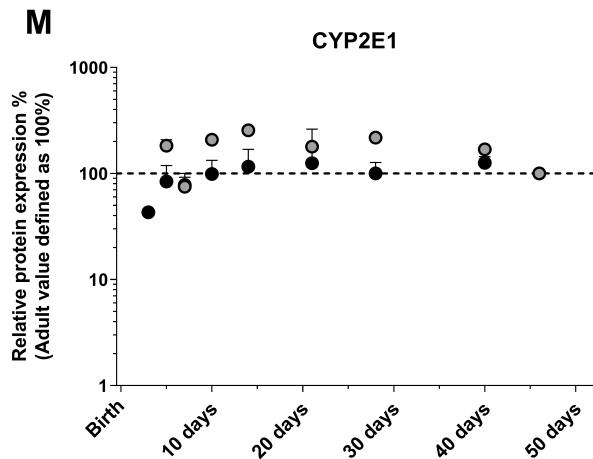
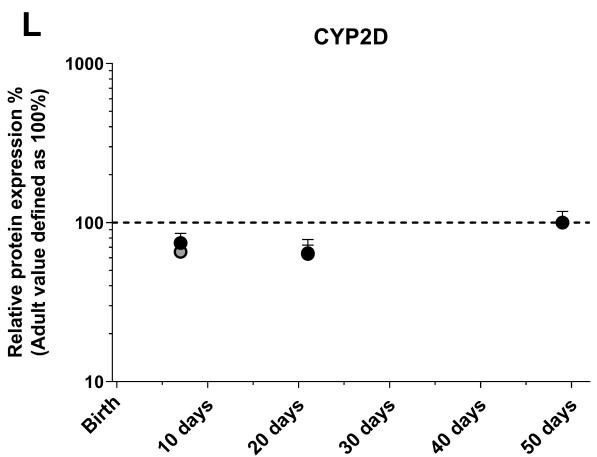
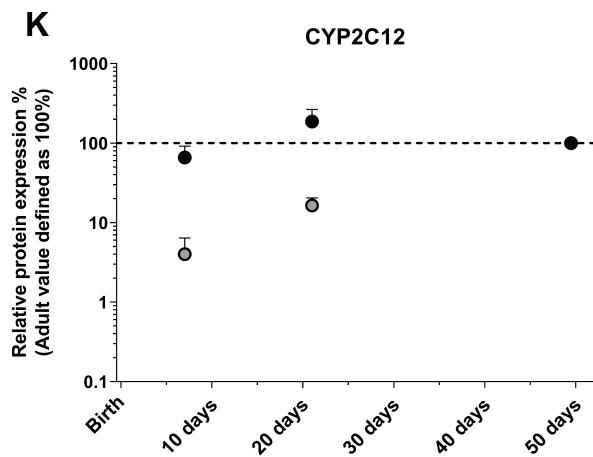
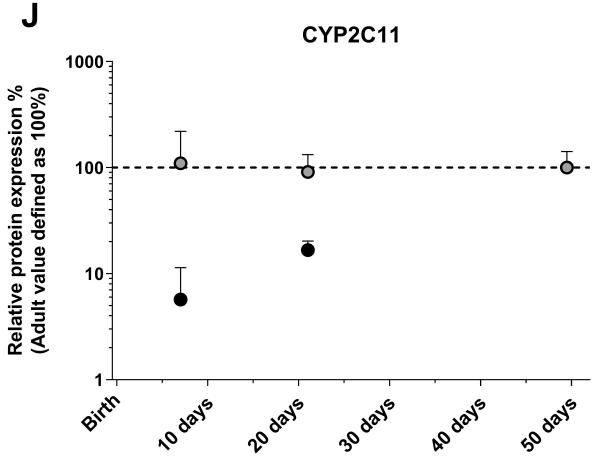
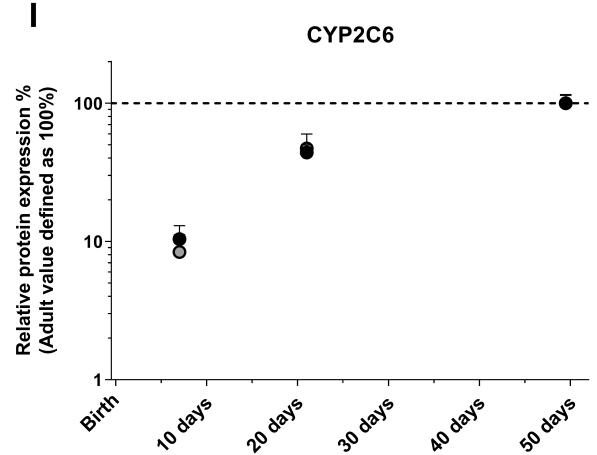
Pooled literature data on the ontogeny of hepatic mRNA expression of phase I drug metabolizing enzymes in humans. Symbols represent relative mRNA expression in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative mRNA expression and the error bars show the standard deviation. See Table 7 for explanation on the ontogeny profiles and literature references.

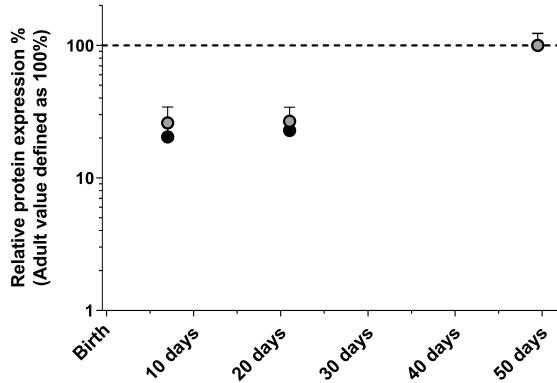


## Supplemental Figure 11.

Pooled literature data on the ontogeny of hepatic protein expression levels of phase I drug metabolizing enzymes in rats. Symbols represent relative protein expression in mixed-gender rat population (open), male rats (grey) and female rats (black) in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative protein expression and the error bars show the standard deviation. See Table 8 for explanation on the ontogeny profiles and literature references.

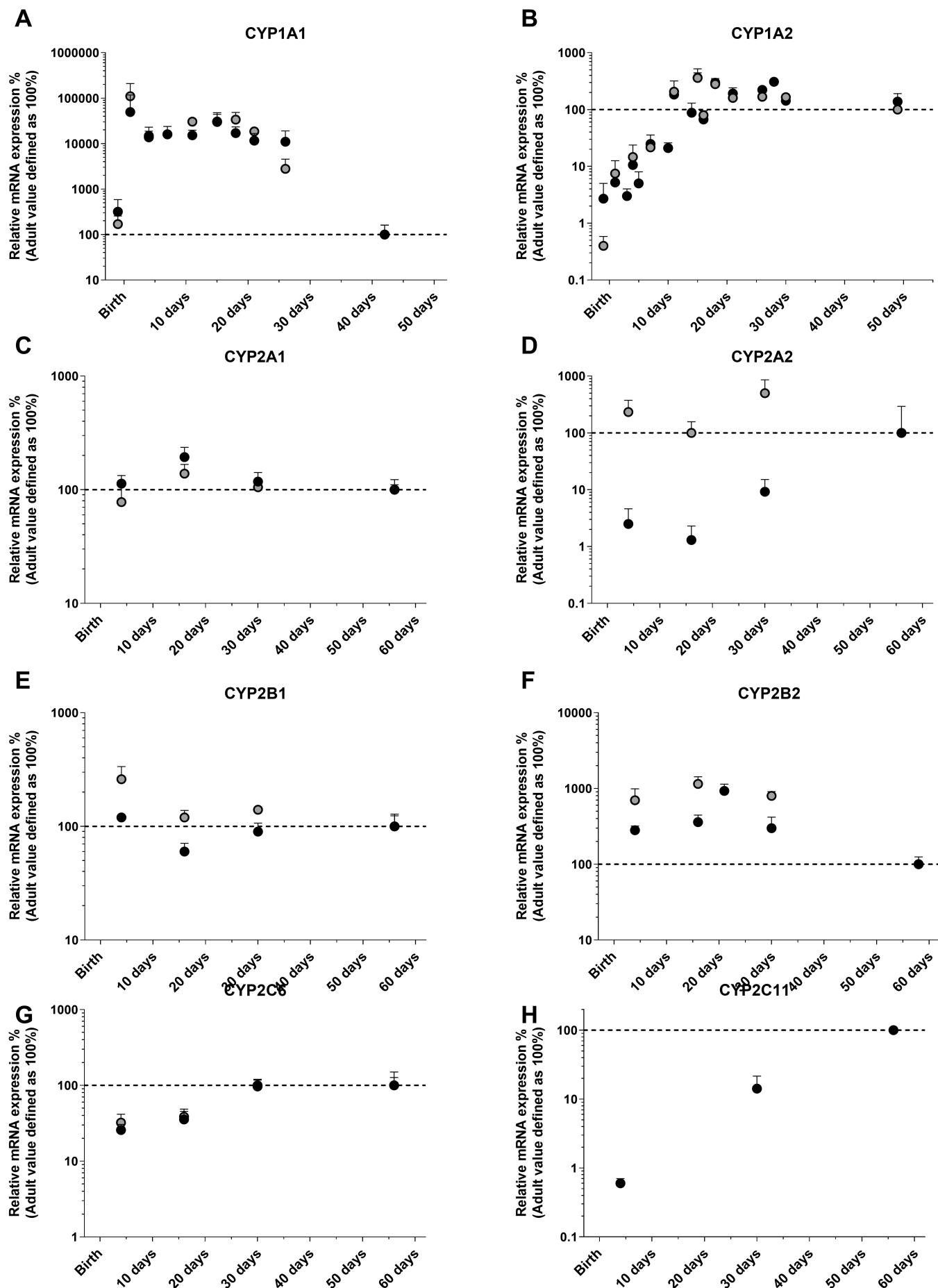


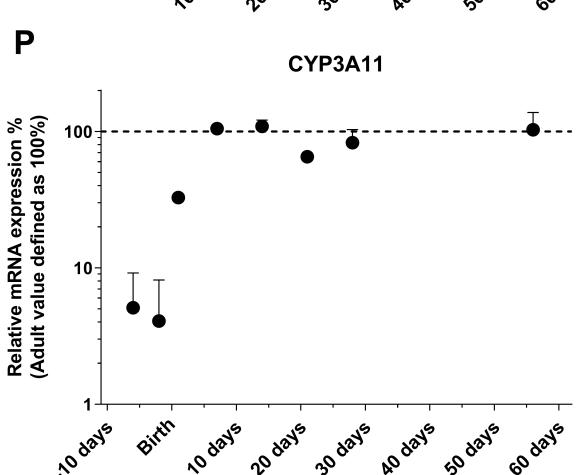
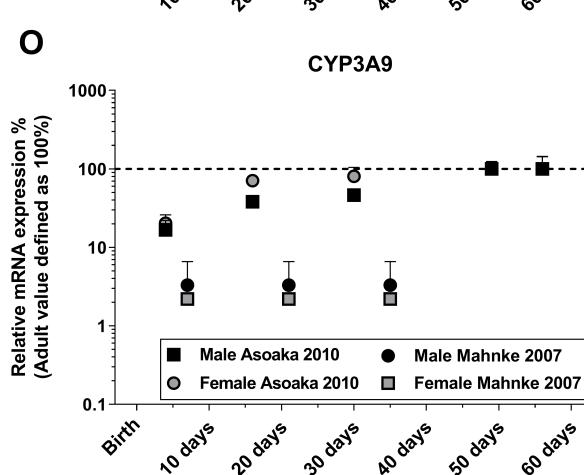
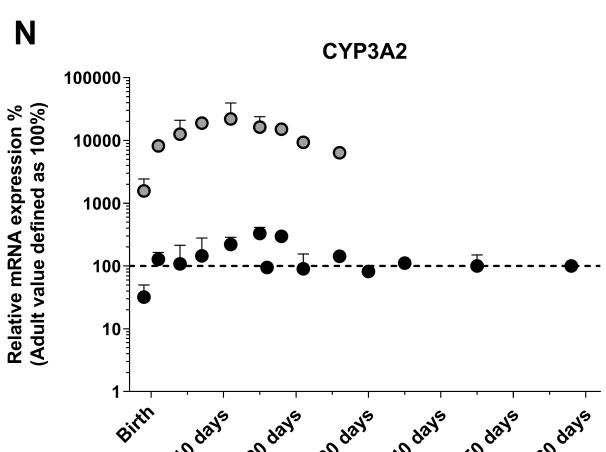
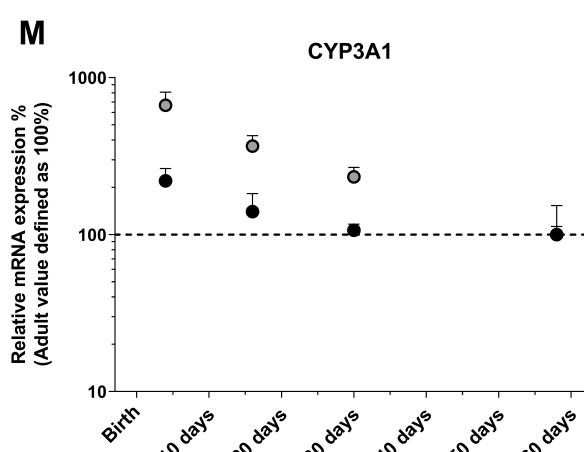
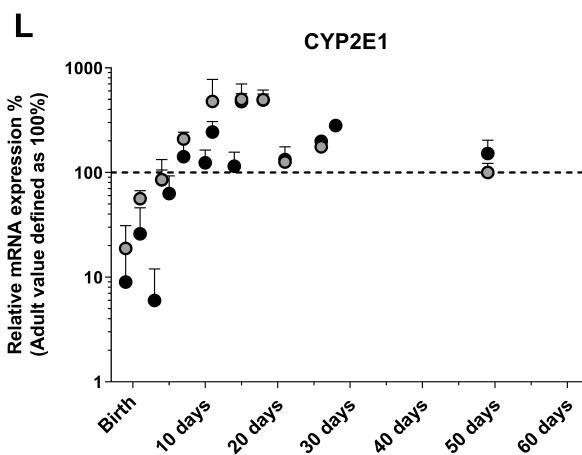
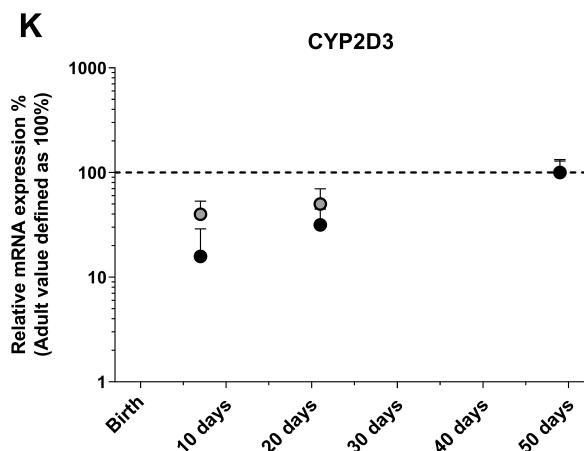
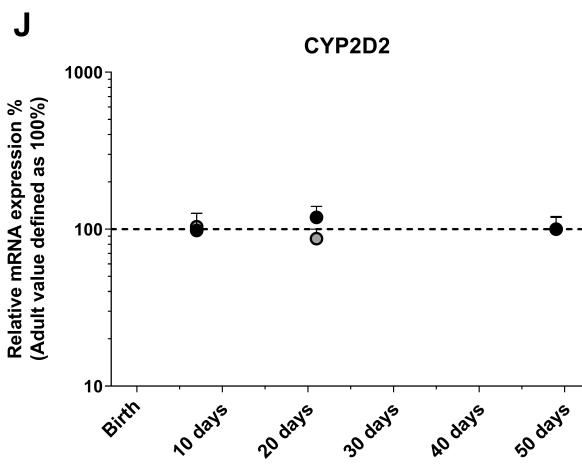
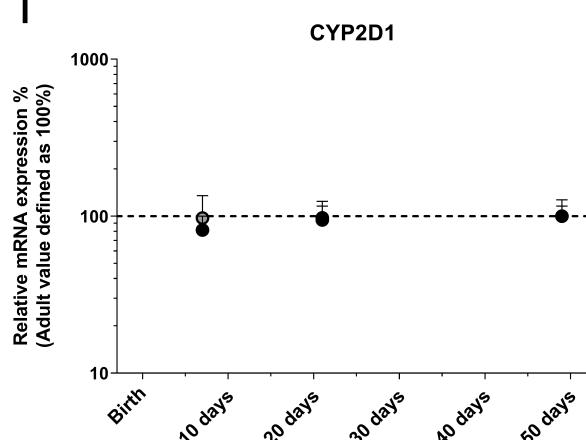


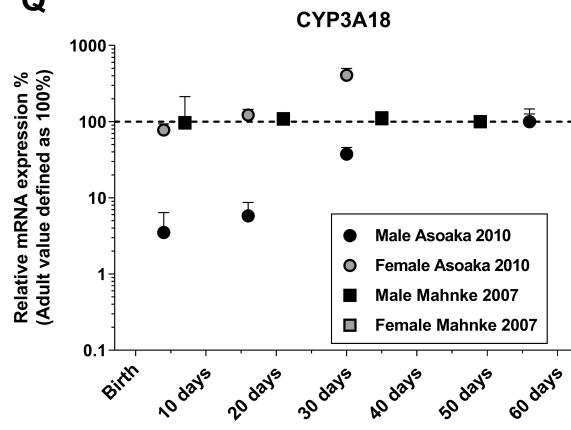
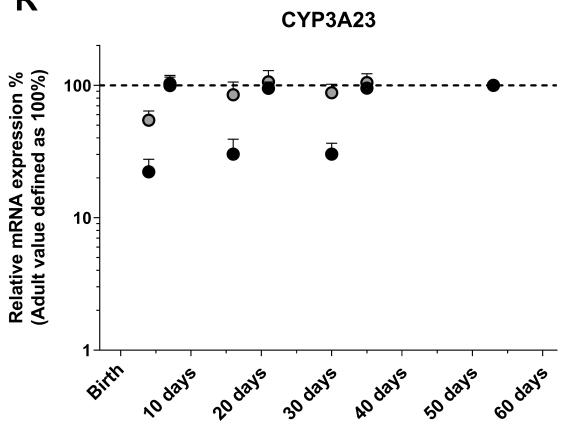
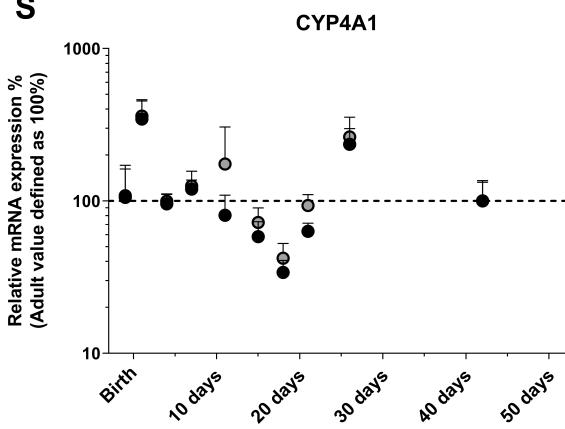
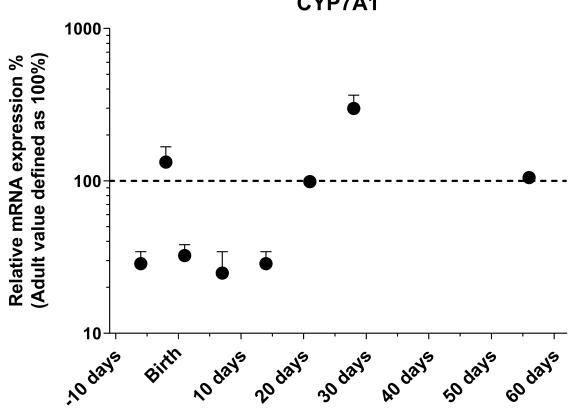
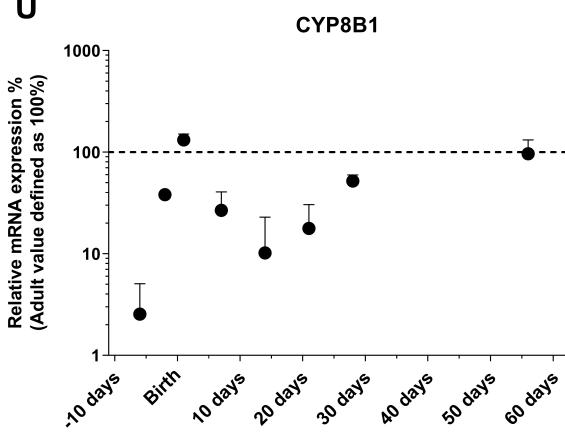
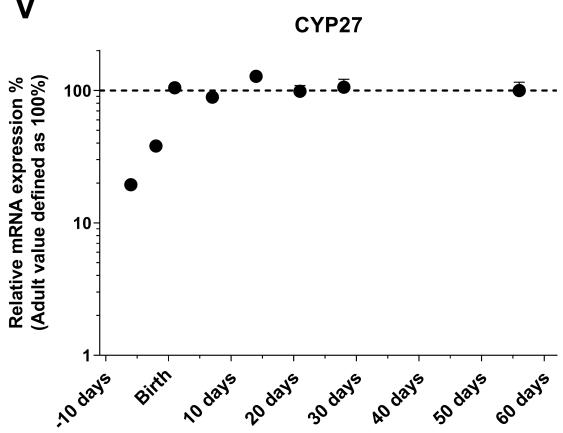
**Q****CYP4A3**

### Supplemental Figure 12.

Pooled literature data on the ontogeny of hepatic mRNA expression of phase I drug metabolizing enzymes in rats. Symbols represent relative mRNA expression in mixed-gender rat population (open), male rats (grey) and female rats (black) in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative mRNA expression and the error bars show the standard deviation. See Table 8 for explanation on the ontogeny profiles and literature references.

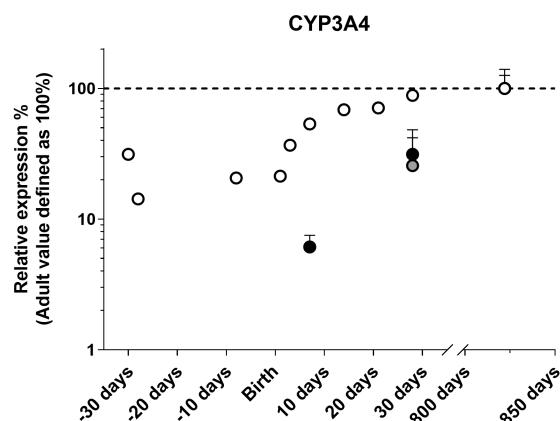




**Q****R****S****T****U****V**

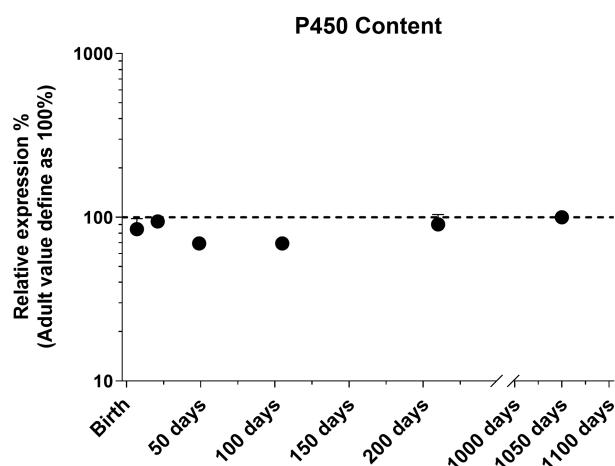
### Supplemental Figure 13.

Literature data on the ontogeny of hepatic CYP3A4 protein expression in the Göttingen minipig. Symbols represent relative protein expression in mixed-gender rat population (open), male rats (grey) and female rats (black) in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative protein expression and the error bars show the standard deviation. See Table 10 for explanation on the ontogeny profiles and literature references.



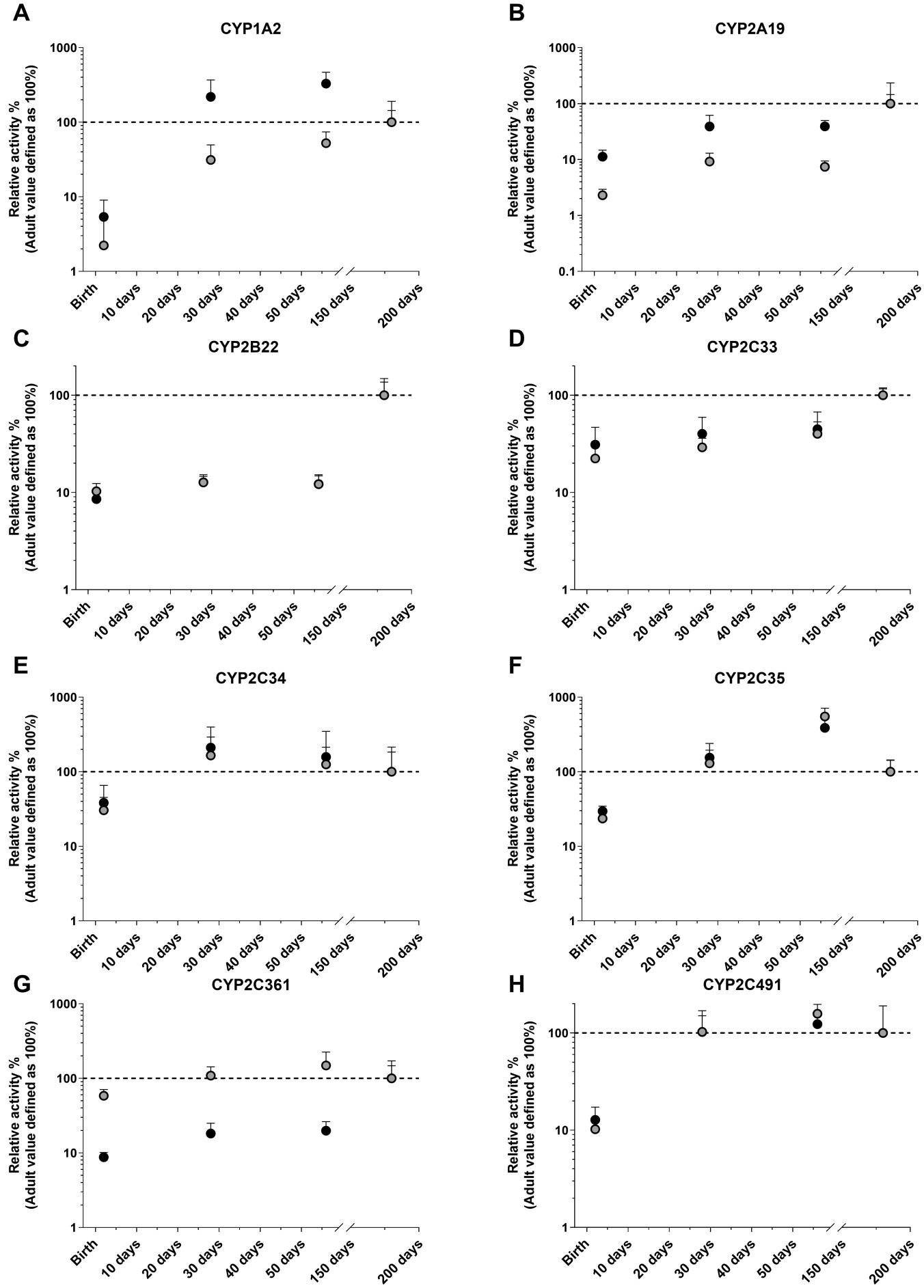
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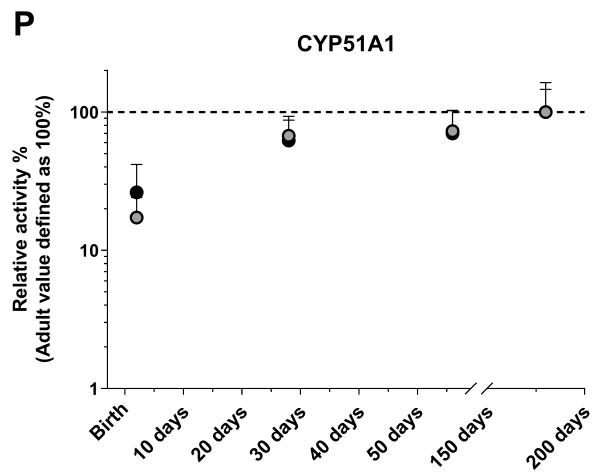
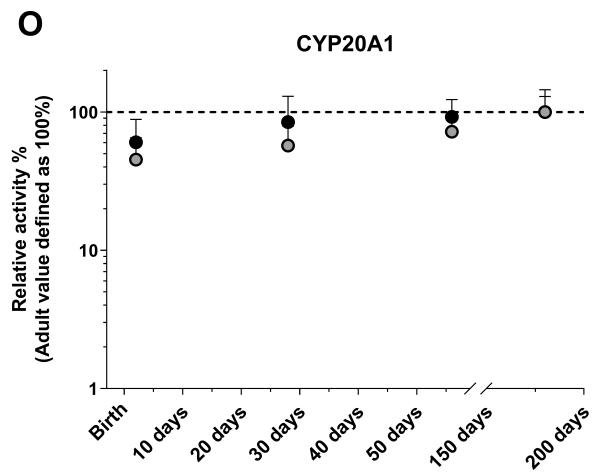
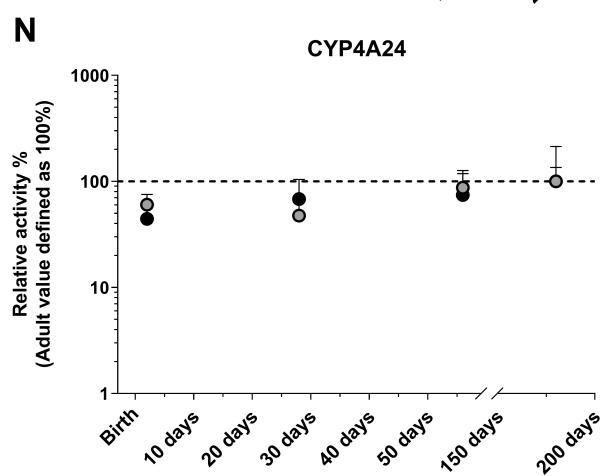
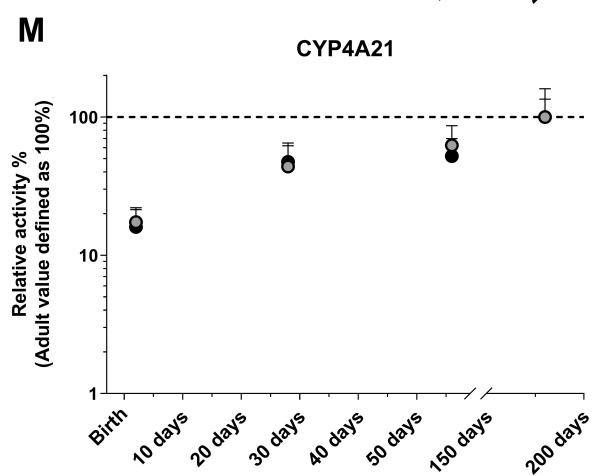
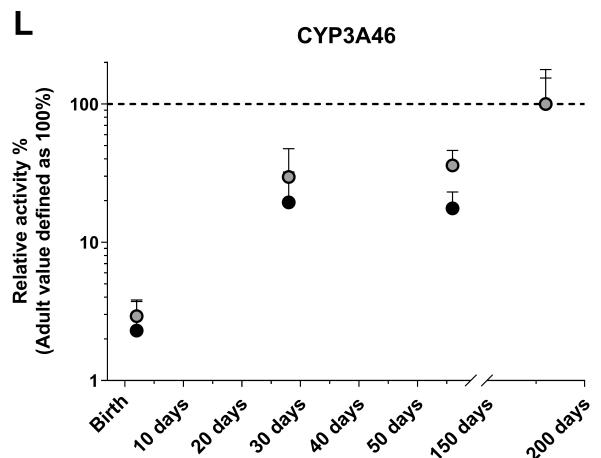
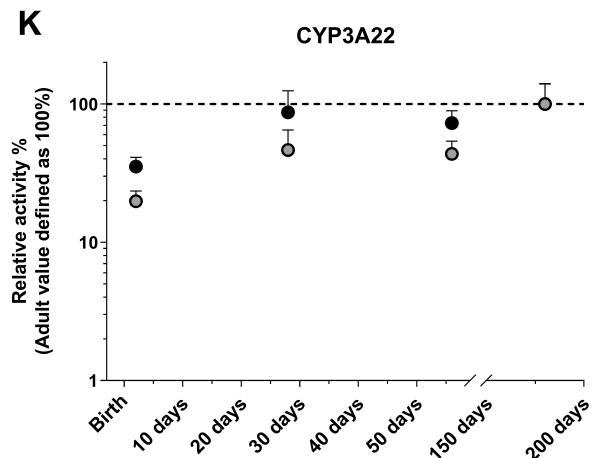
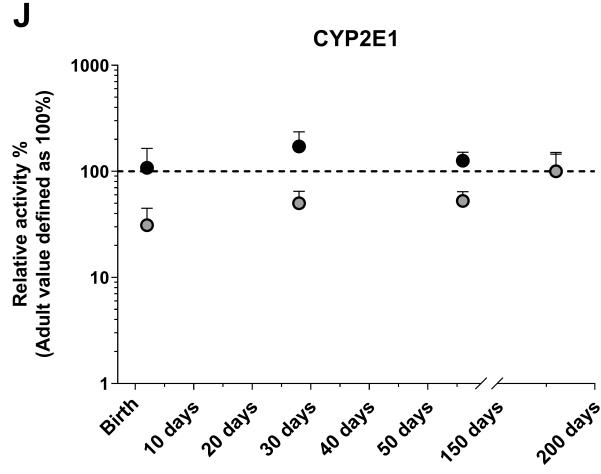
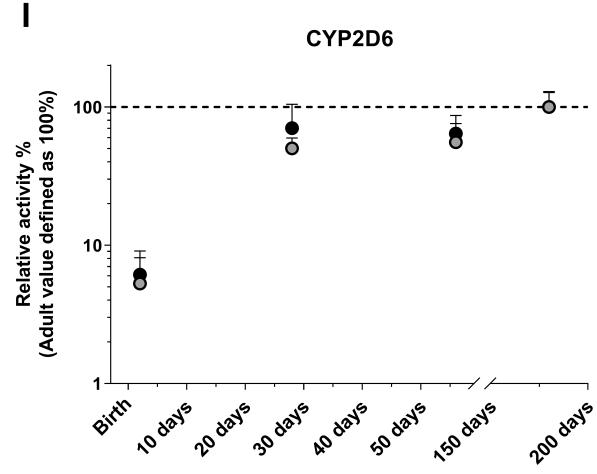
Pooled literature data on the ontogeny of the P450 content in Beagle dog liver microsomes. Symbols represent relative protein expression in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative protein expression and the error bars show the standard deviation. See Table 12 for explanation on the ontogeny profiles and literature references.



### Supplemental Figure 15.

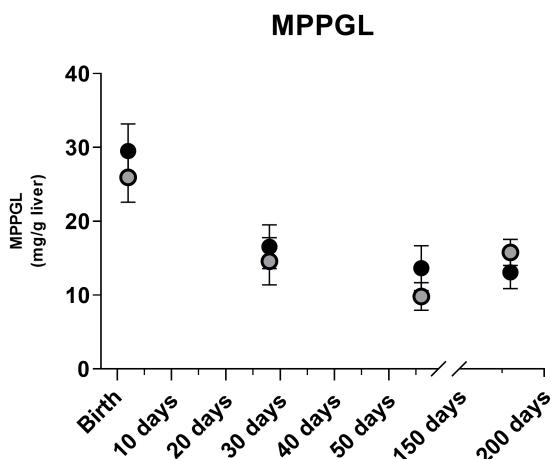
Pooled literature data on the ontogeny of hepatic protein expression levels of phase I drug metabolizing enzymes in domestic pig. Symbols represent relative protein expression in male rats (grey) and female rats (black) in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative protein expression and the error bars show the standard deviation. See Table 13 for explanation on the ontogeny profiles and literature references.





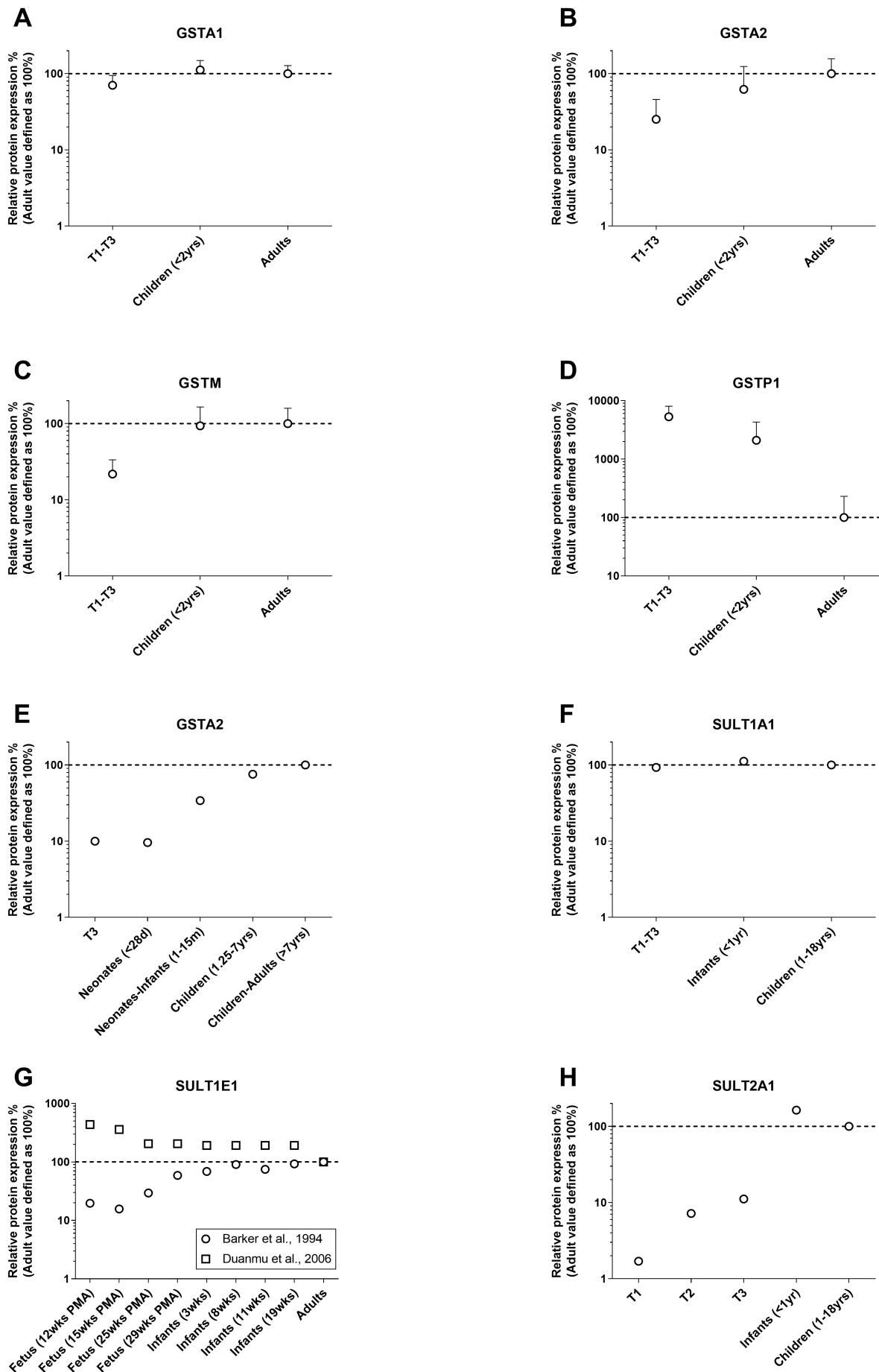
### Supplemental Figure 16.

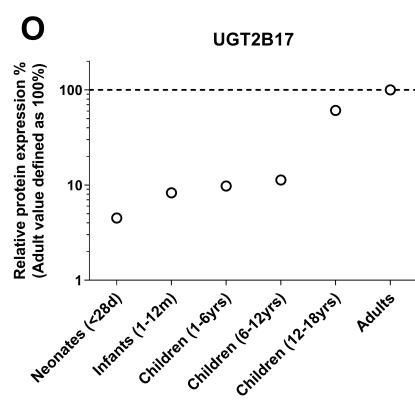
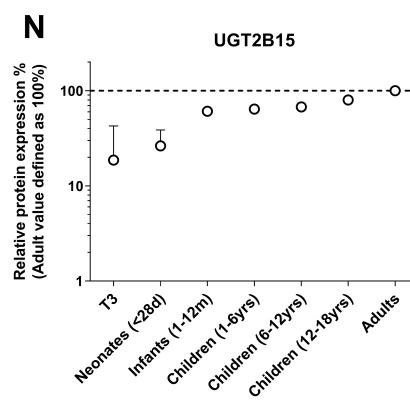
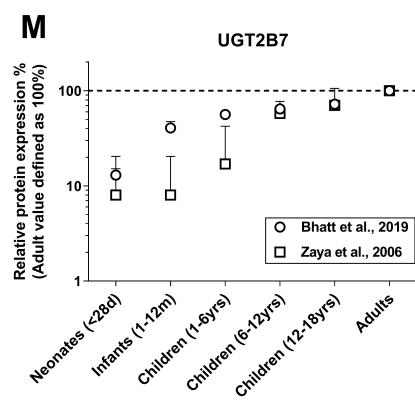
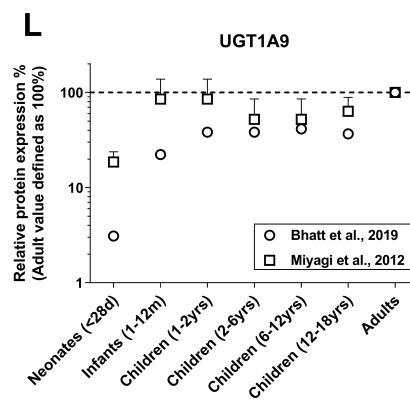
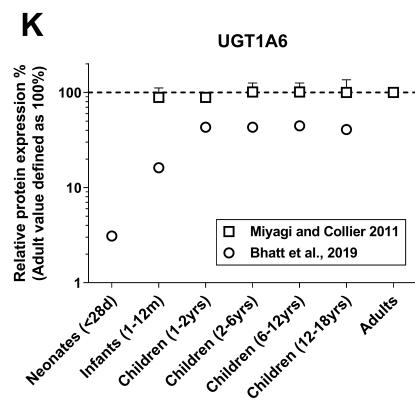
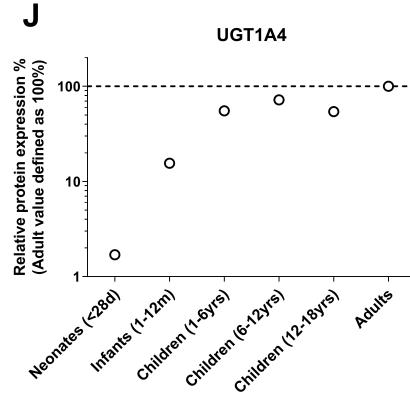
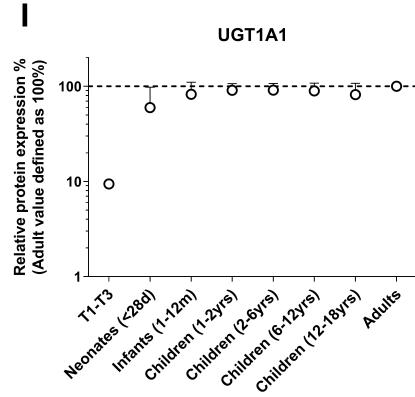
Literature data on the ontogeny of the microsomal protein content in domestic pig. MPPGL = mg protein per gram liver. The symbols represent the relative MPPGL in male rats (grey) and female rats (black) in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative MPPGL and the error bars show the standard deviation. See Table 13 for explanation on the ontogeny profiles and literature references.



### Supplemental Figure 17.

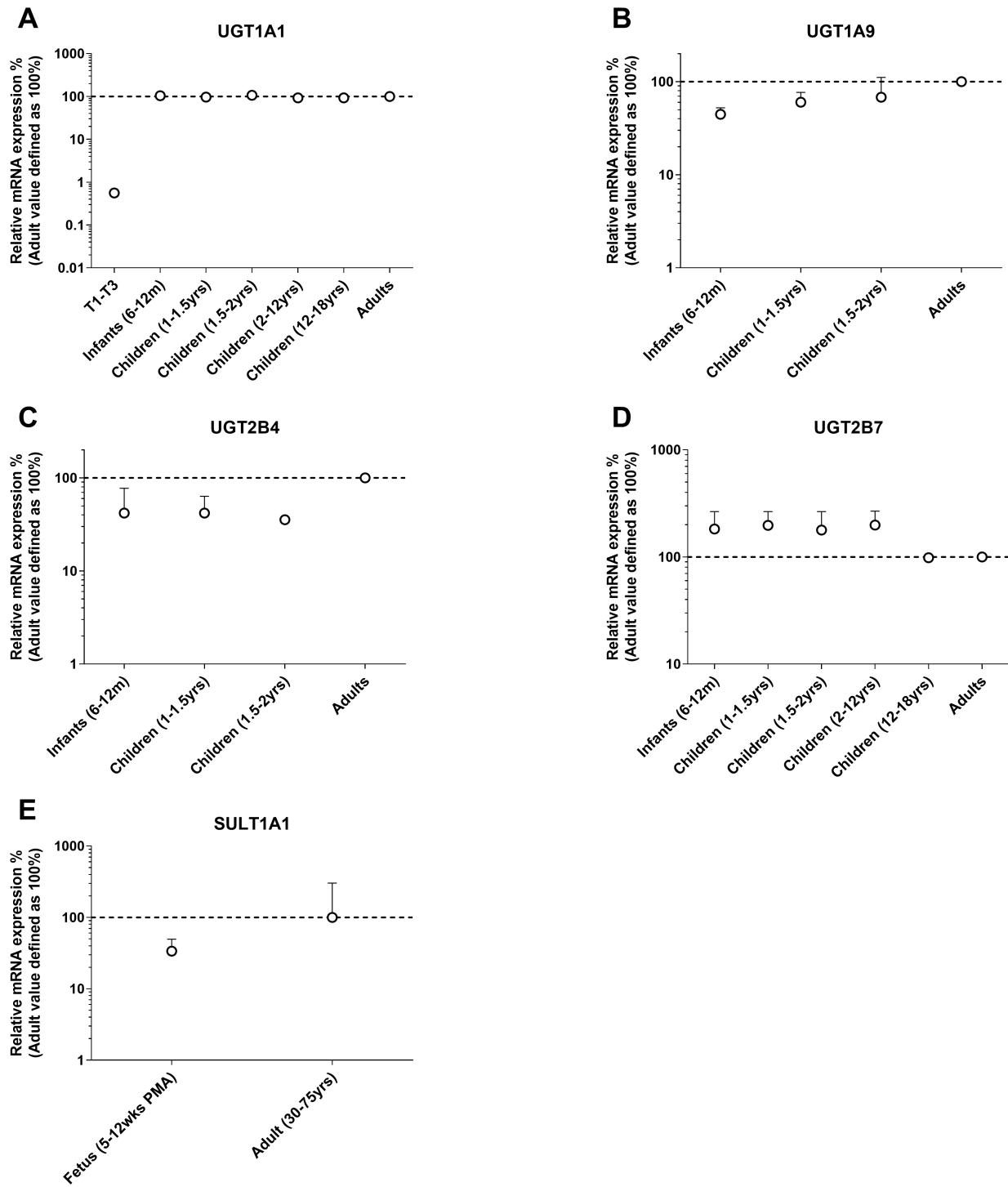
Pooled literature data on the ontogeny of protein expression of phase II drug metabolizing enzymes in humans. The symbols represent the relative protein expression in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative protein expression and the error bars show the standard deviation. See Table 14 for explanation on the ontogeny profiles and literature references.





### Supplemental Figure 18.

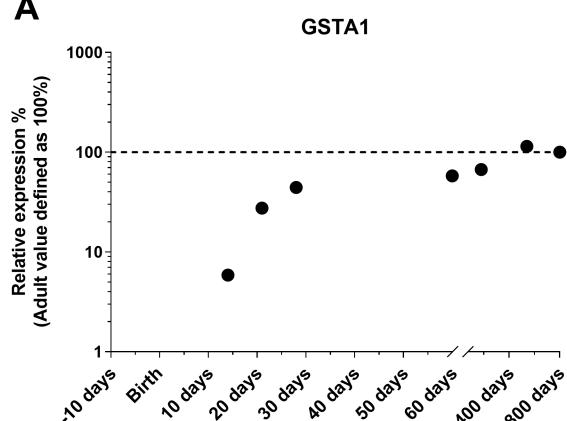
Pooled literature data on the ontogeny of mRNA expression of phase II drug metabolizing enzymes in humans. The symbols represent the relative mRNA expression in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative mRNA expression and the error bars show the standard deviation. See Table 14 for explanation on the ontogeny profiles and literature references.



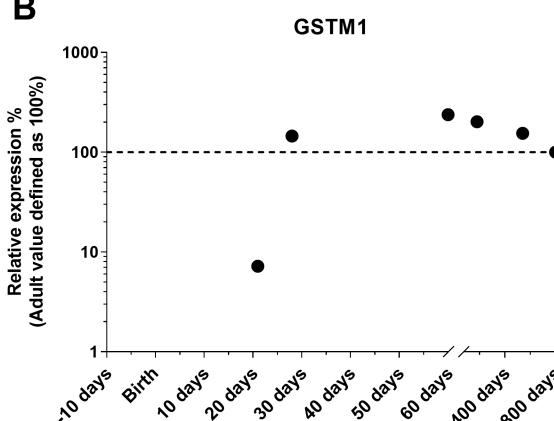
### Supplemental Figure 19.

Pooled literature data on the ontogeny of hepatic protein expression of phase II drug metabolizing enzymes in rats. The symbols represent the relative protein expression in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative protein expression and the error bars show the standard deviation. See Table 15 for explanation on the ontogeny profiles the literature references.

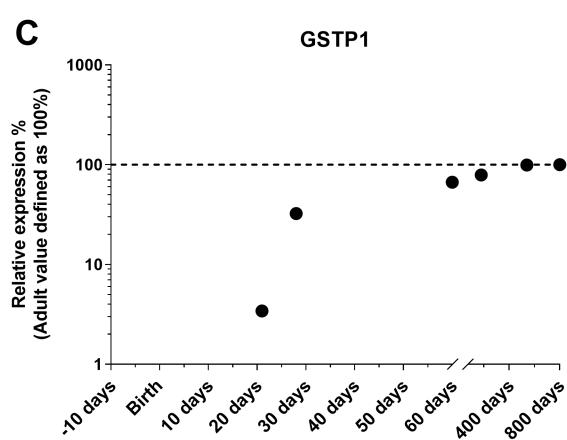
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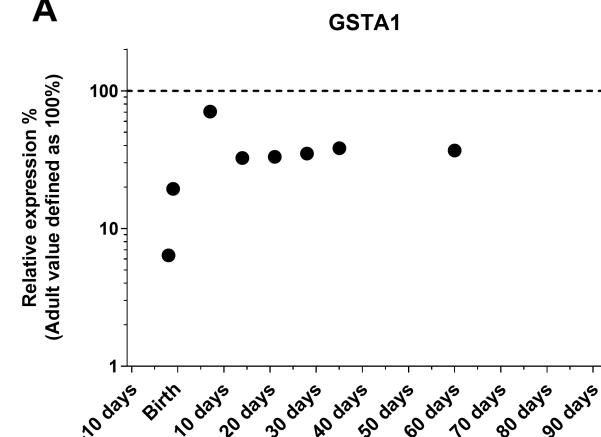
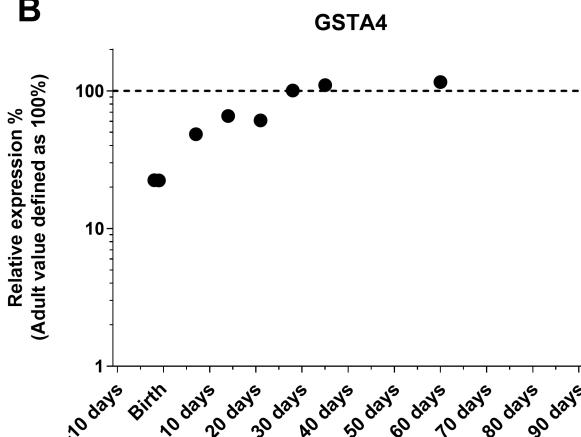
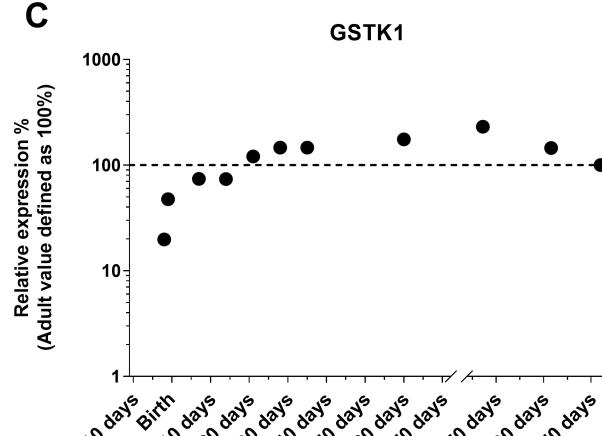
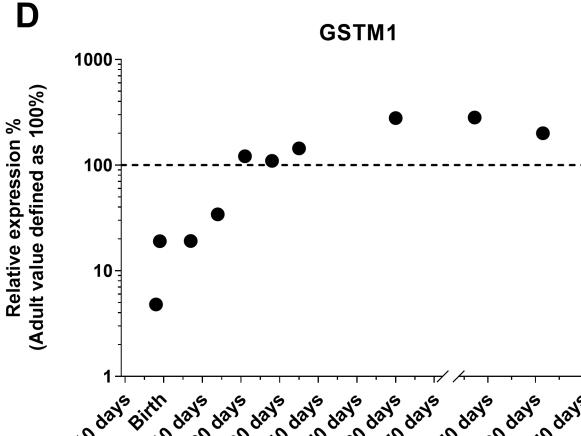
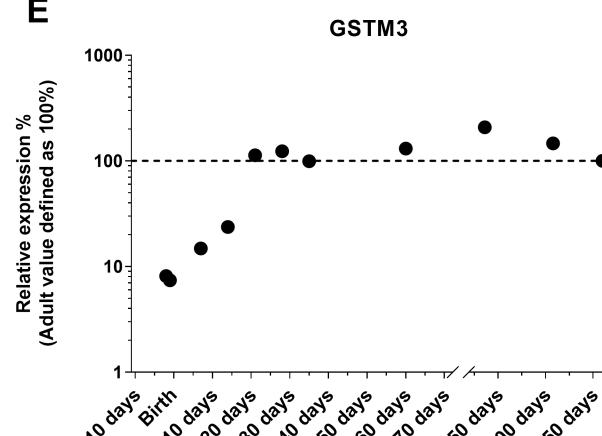
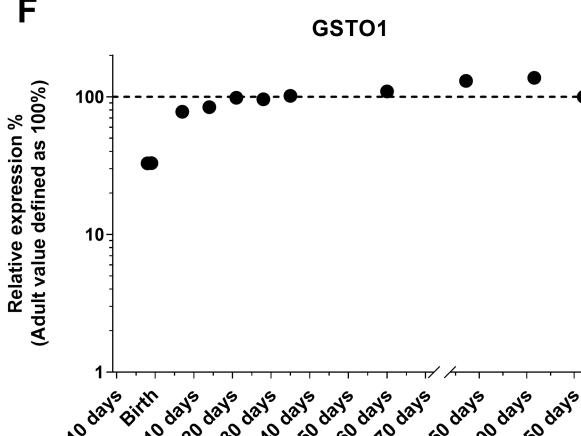
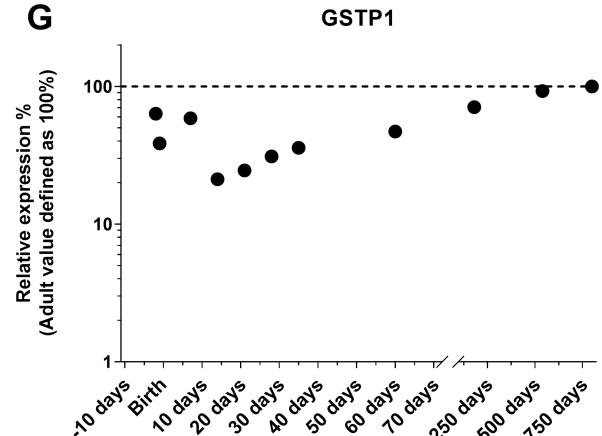
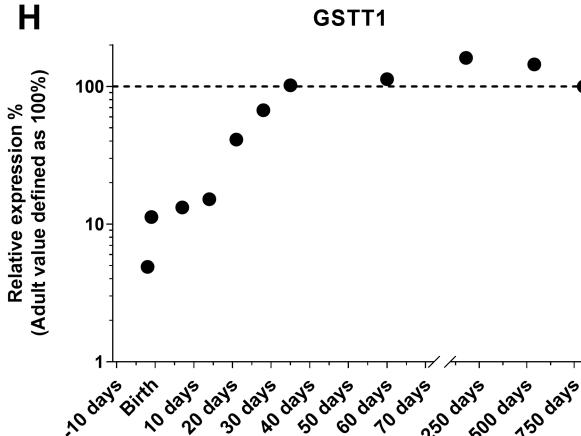


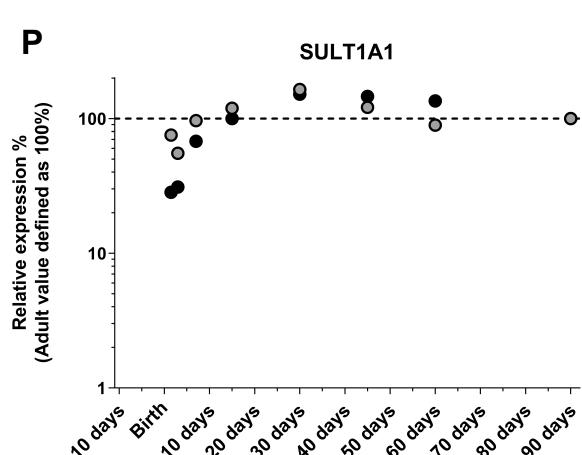
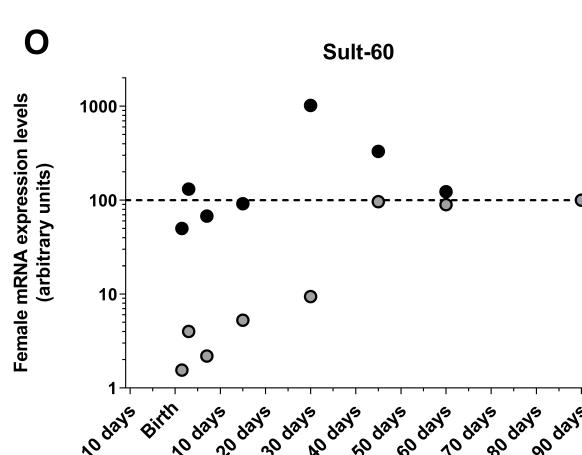
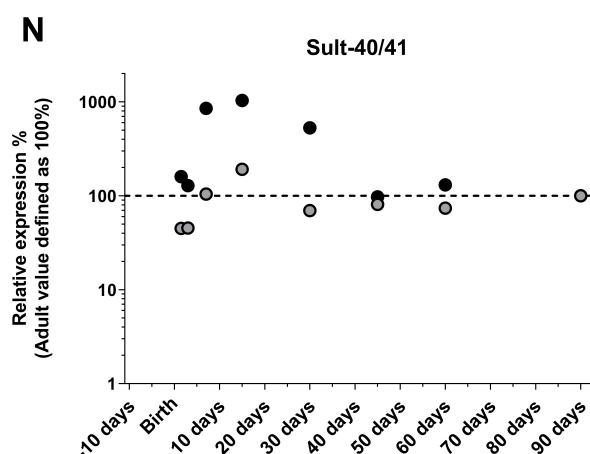
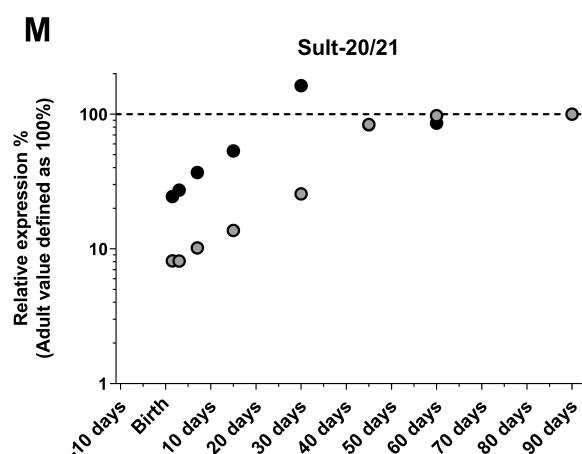
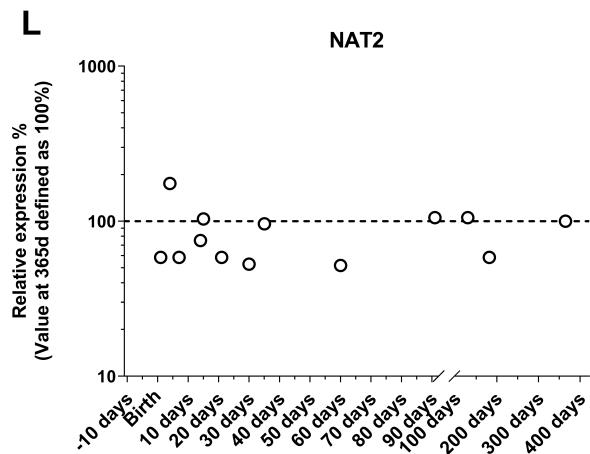
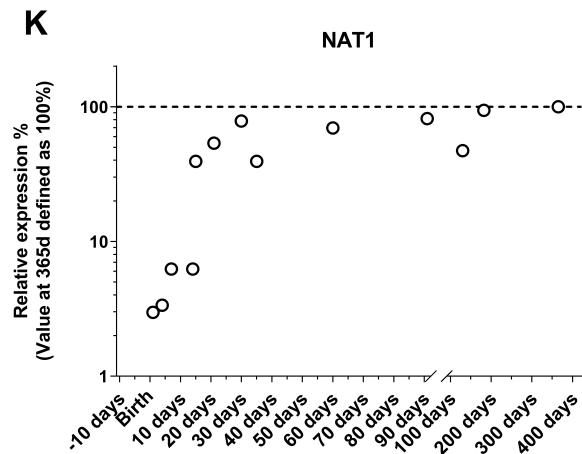
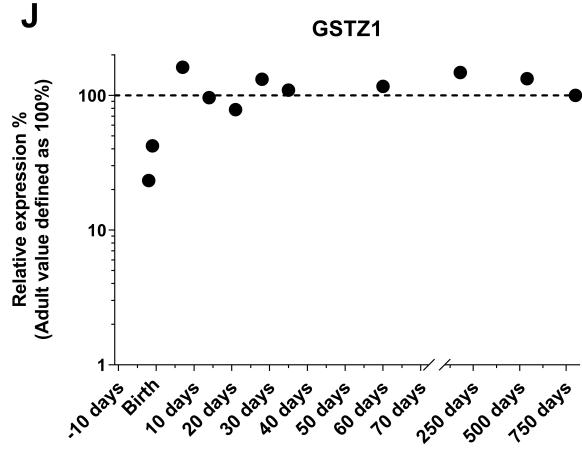
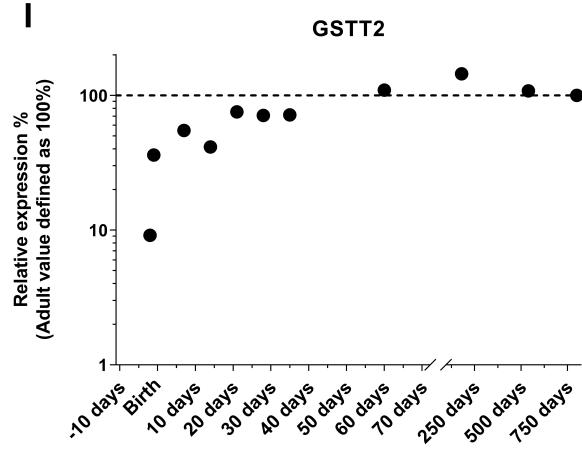
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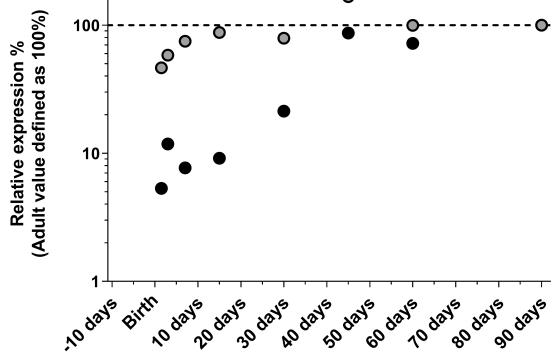
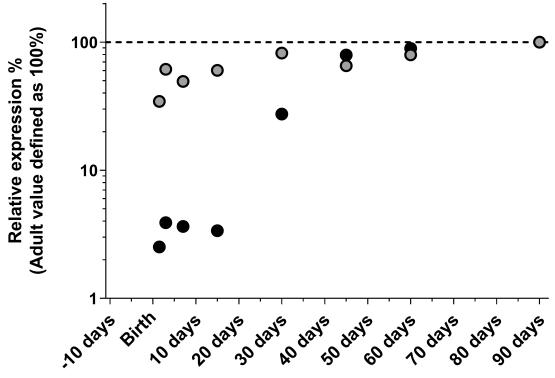
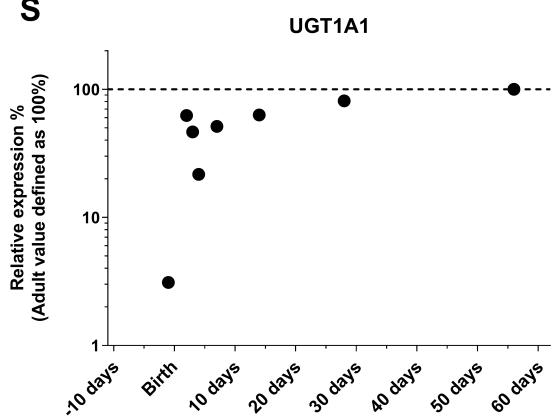
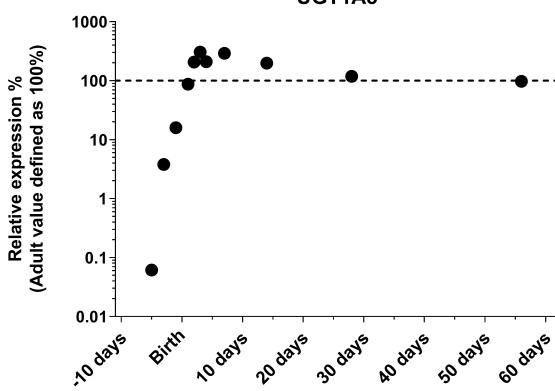
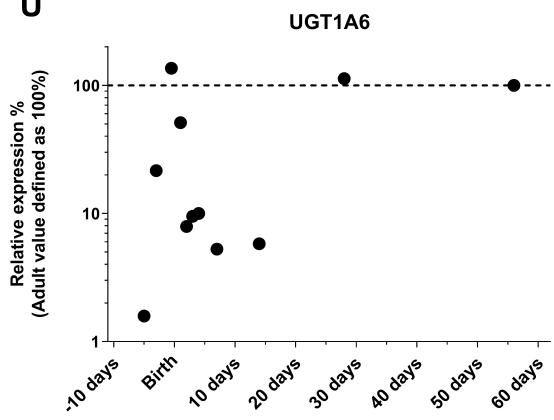
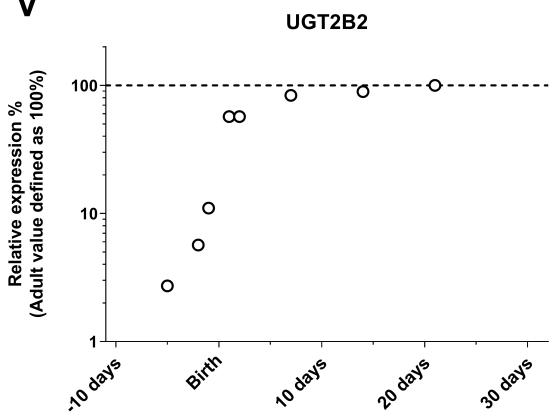


## Supplemental Figure 20.

Pooled literature data on the ontogeny of hepatic mRNA expression of phase II drug metabolizing enzymes in rats. The symbols represent the relative mRNA expression in mixed-gender rat population (open), male rats (grey) and female rats (black) in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative mRNA expression and the error bars show the standard deviation. See Table 15 for explanation on the ontogeny profiles and literature references.

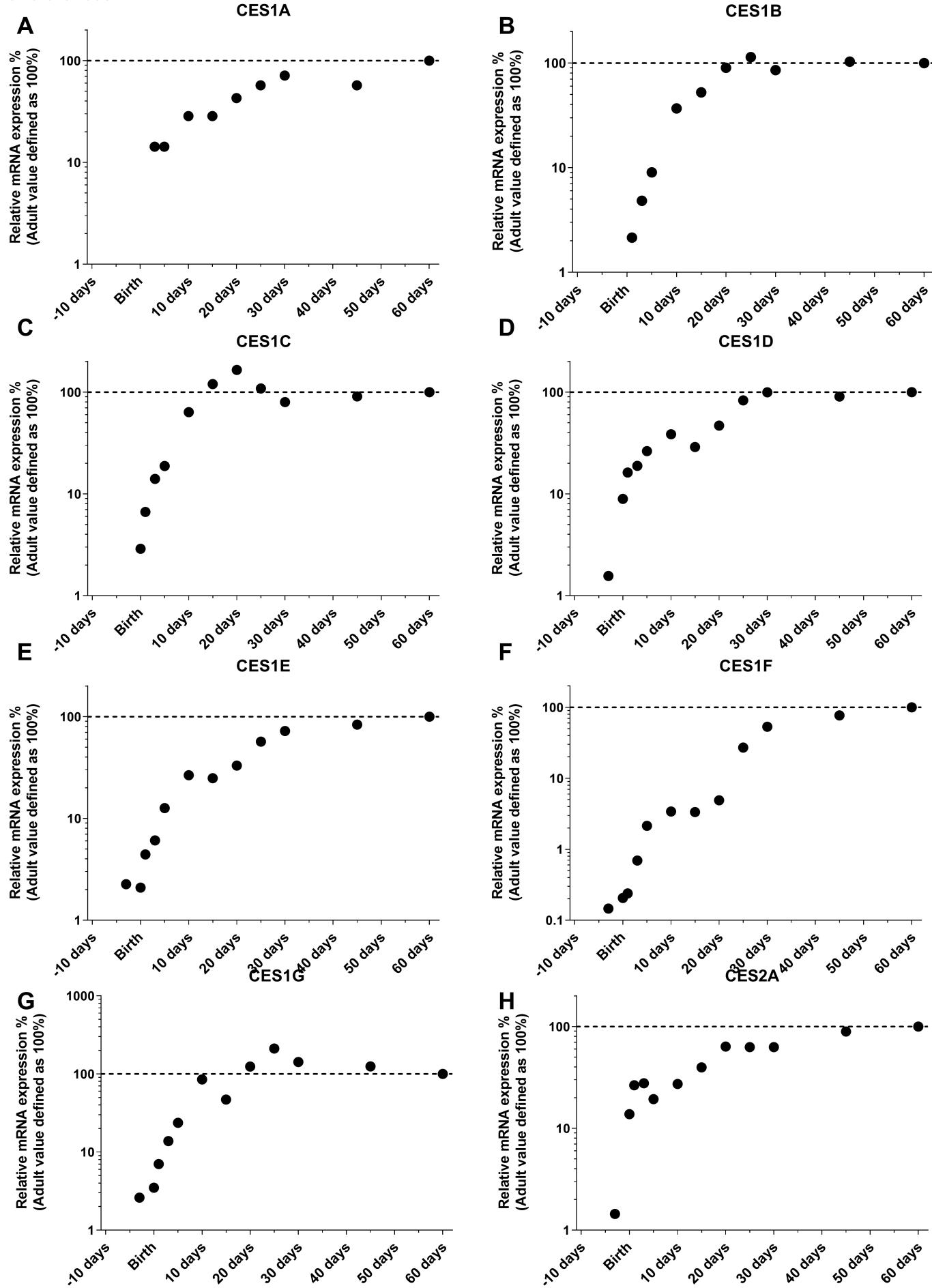
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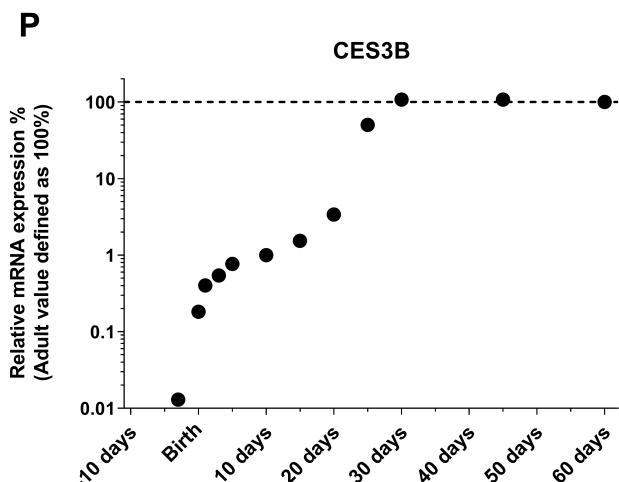
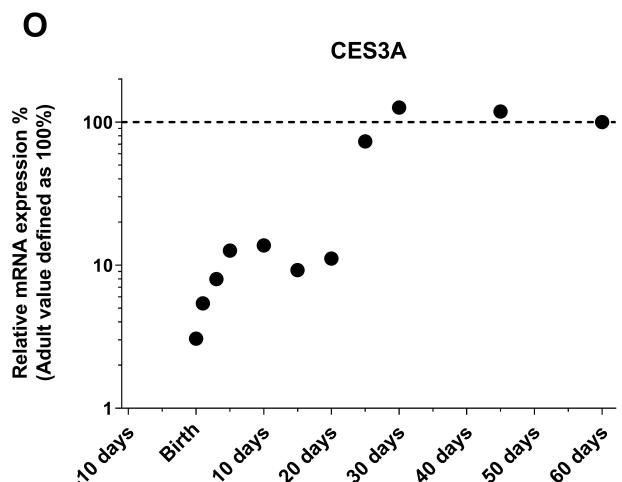
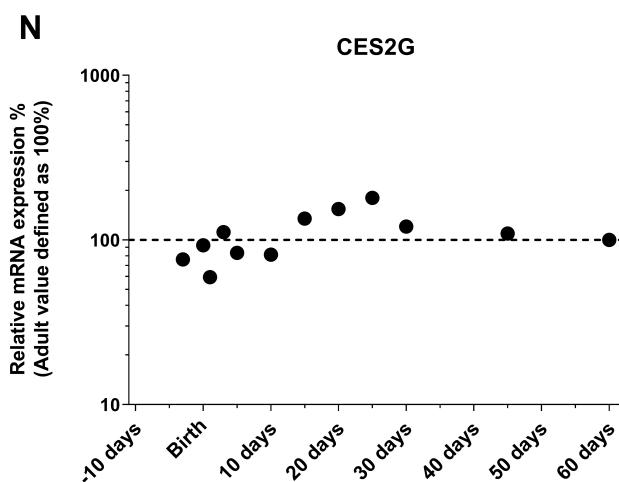
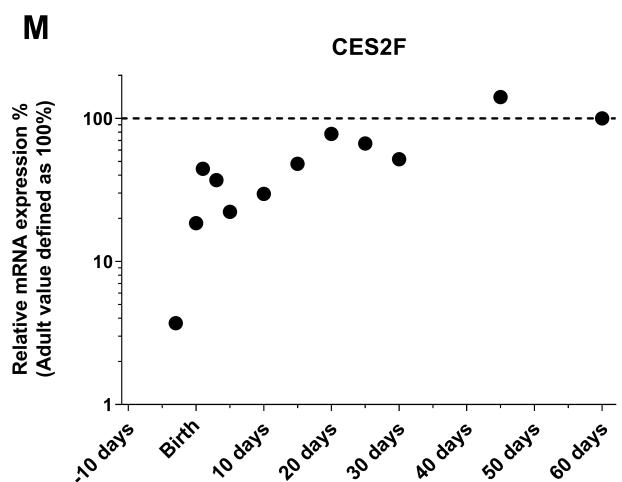
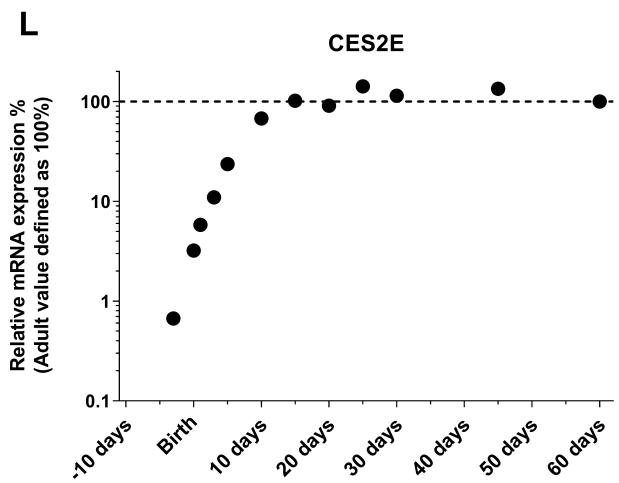
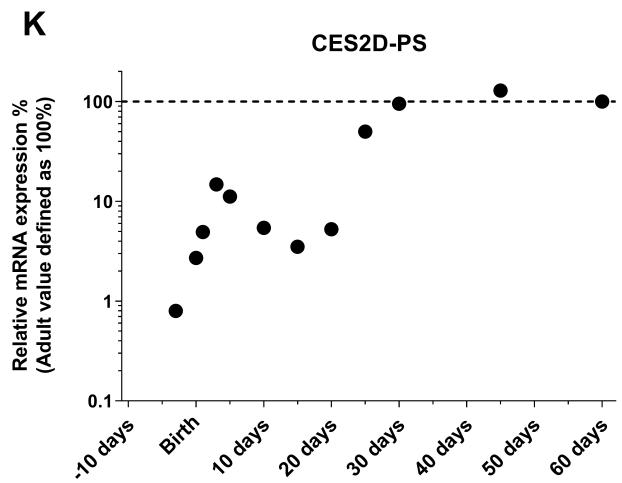
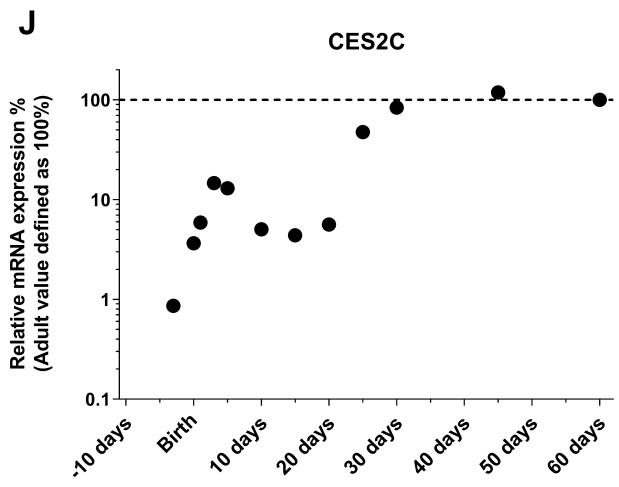
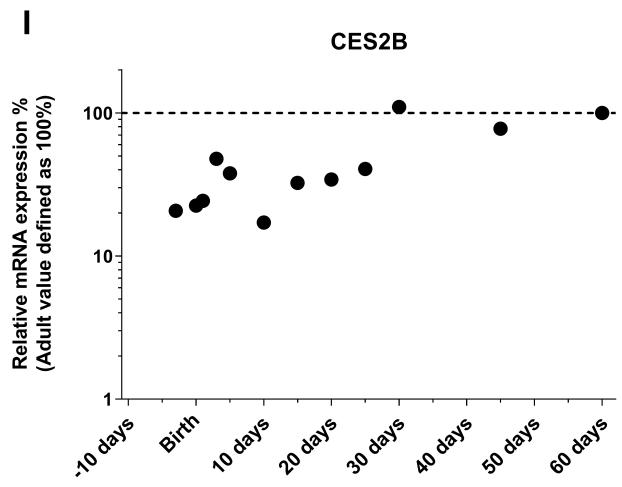


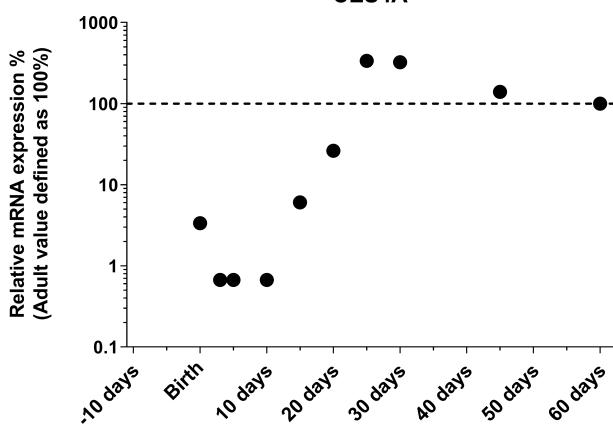
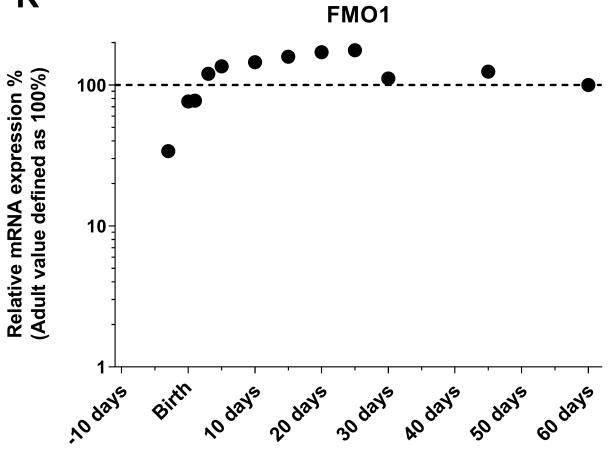
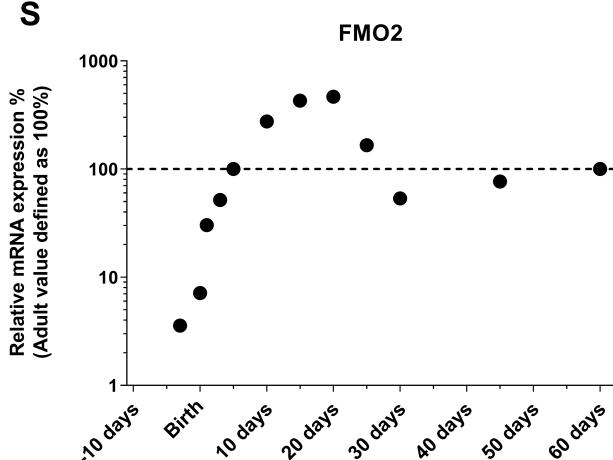
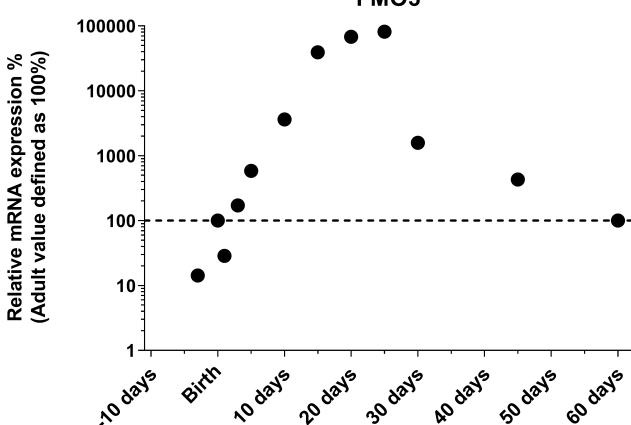
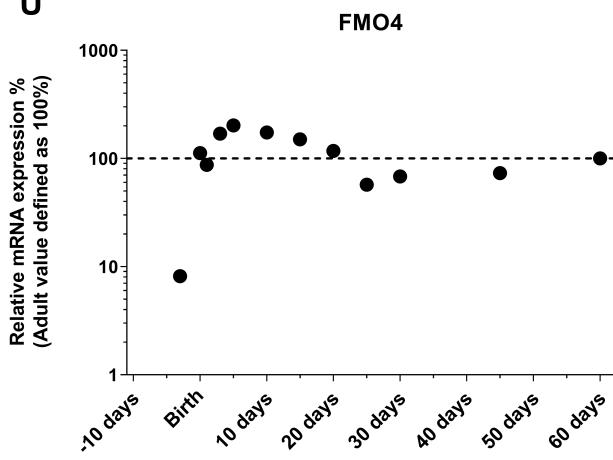
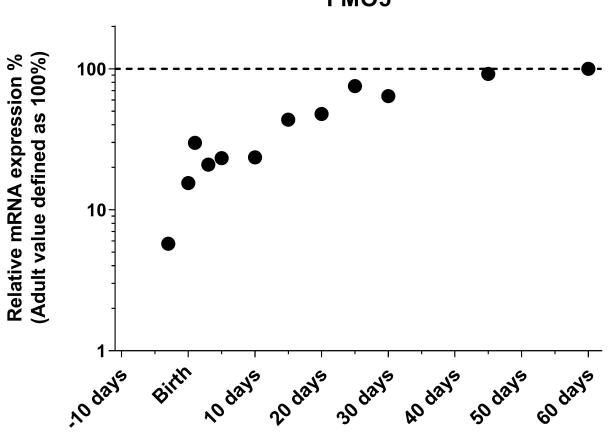
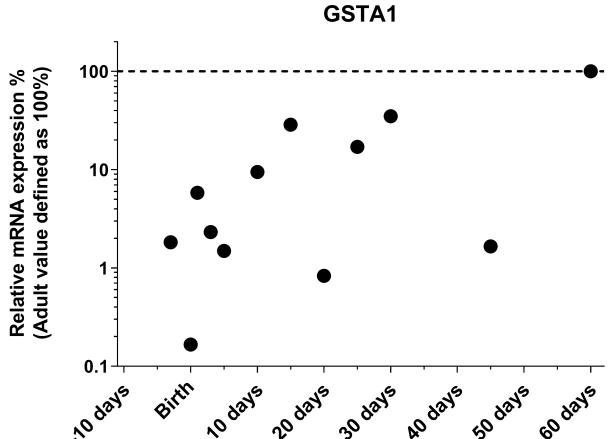
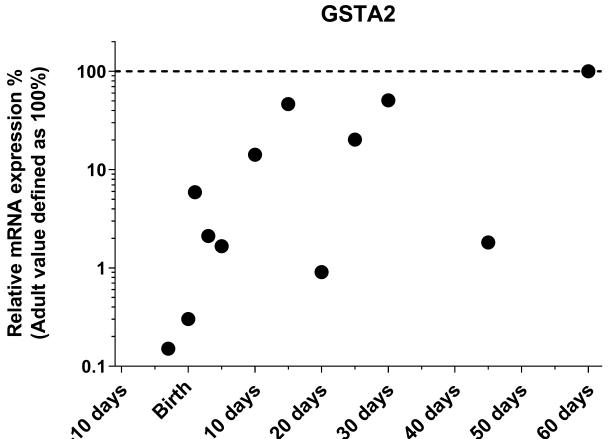
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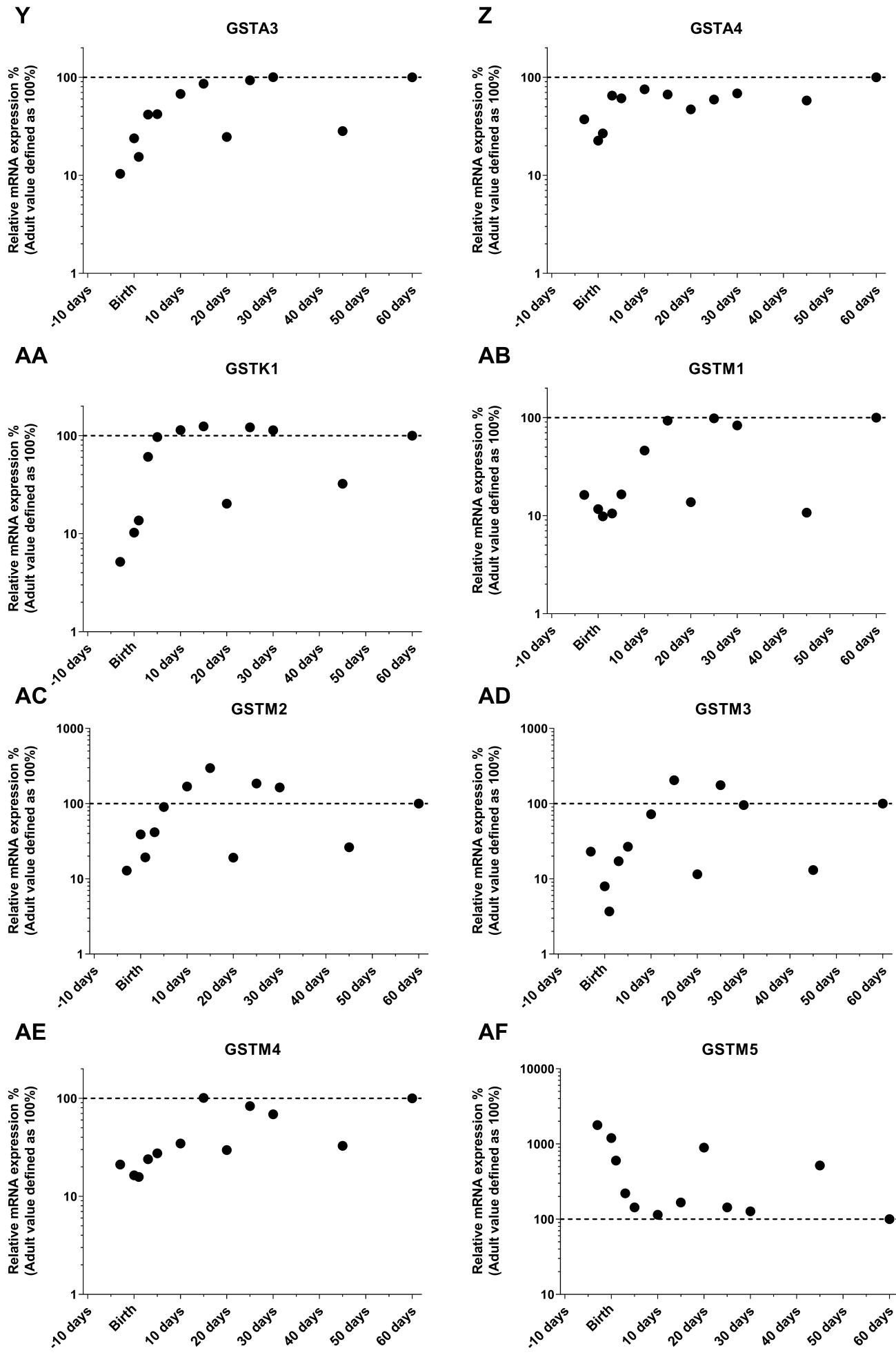
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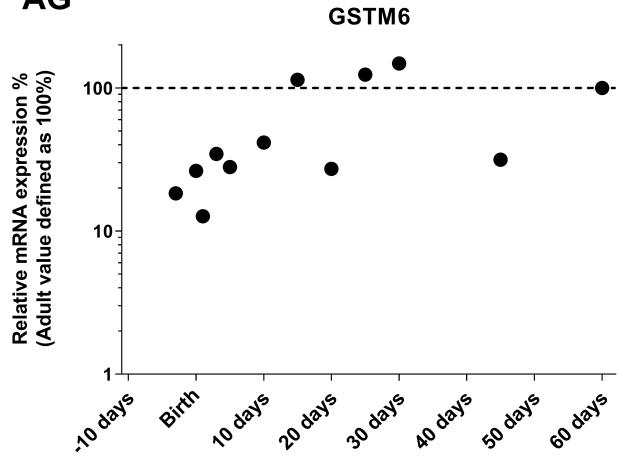
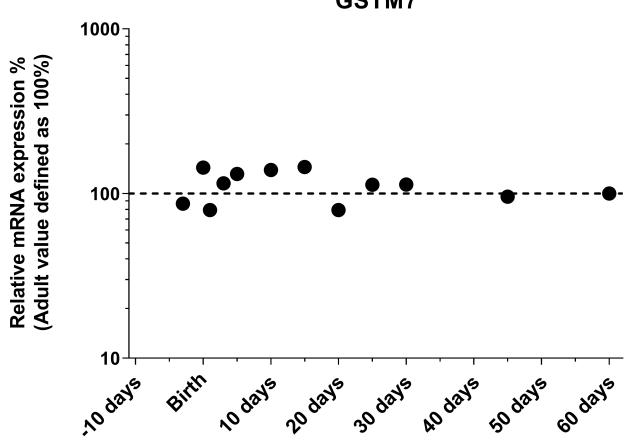
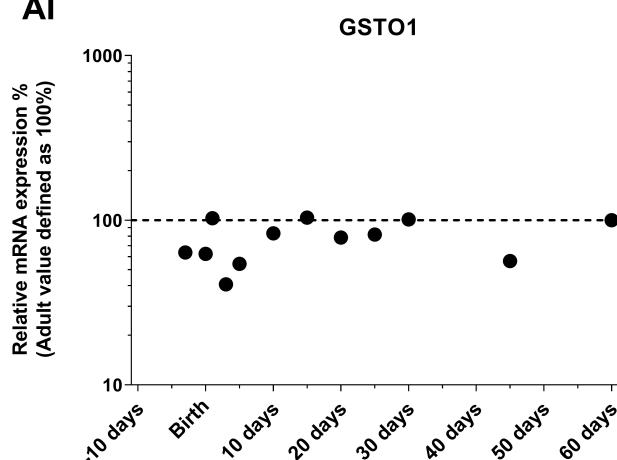
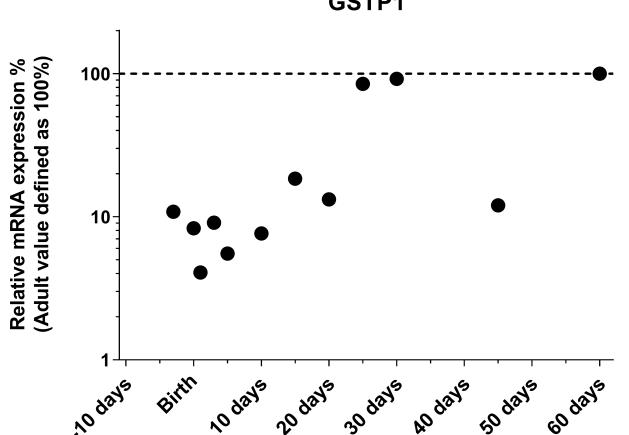
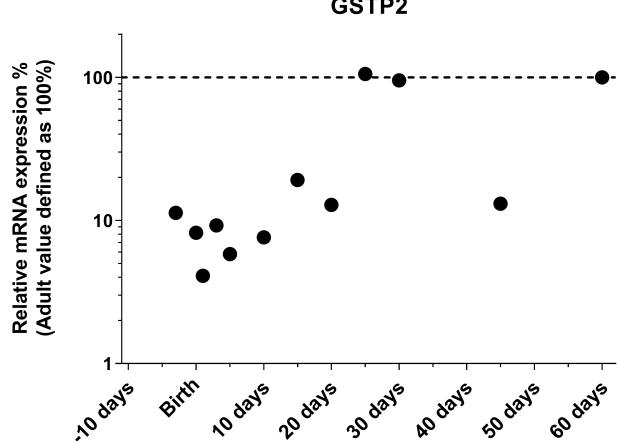
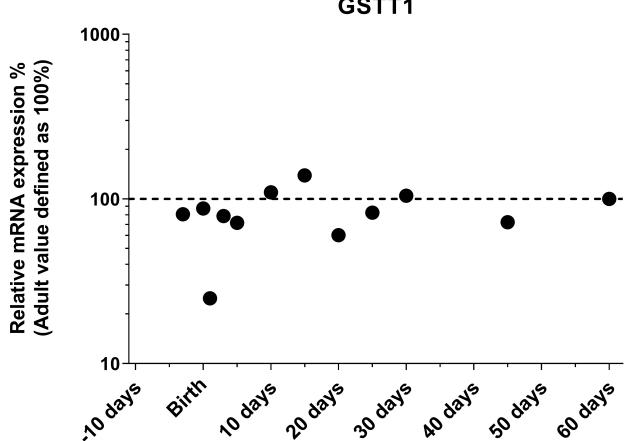
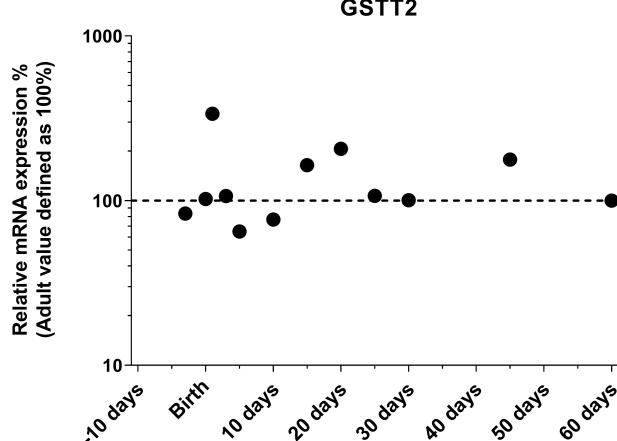
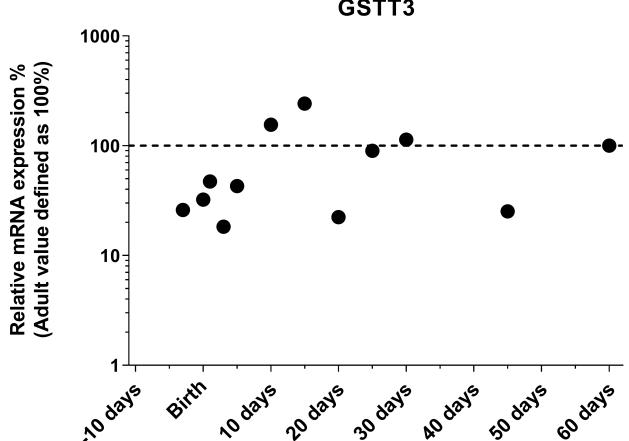
Pooled literature data on the ontogeny of hepatic mRNA expression of phase II drug metabolizing enzymes in mice. Symbols represent relative mRNA expression in male rats (grey) and female rats (black) in each age group and the dotted line indicates the adult value defined as 100%. If multiple values were obtained for the same age group, the symbols represent the average relative mRNA expression and the error bars show the standard deviation. See Table 16 for explanation on the ontogeny profiles and literature references.

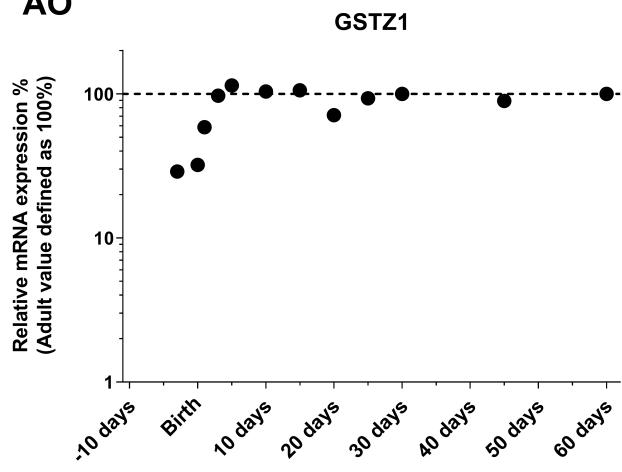
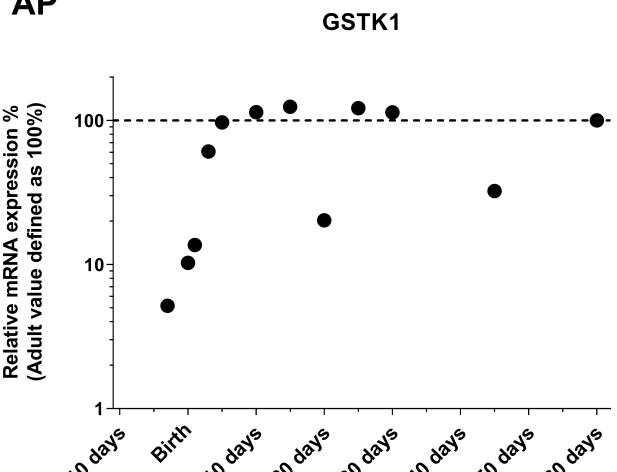
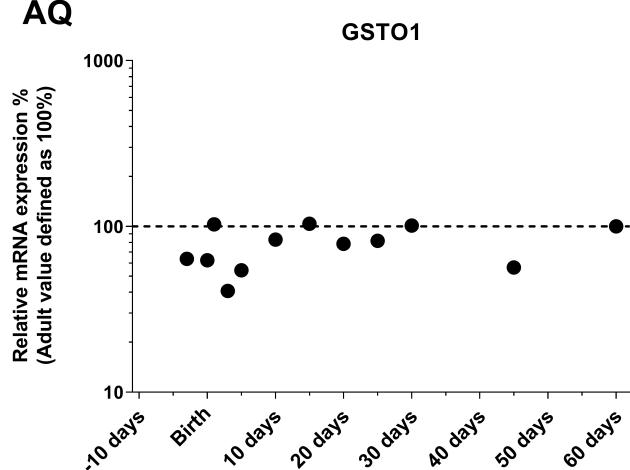
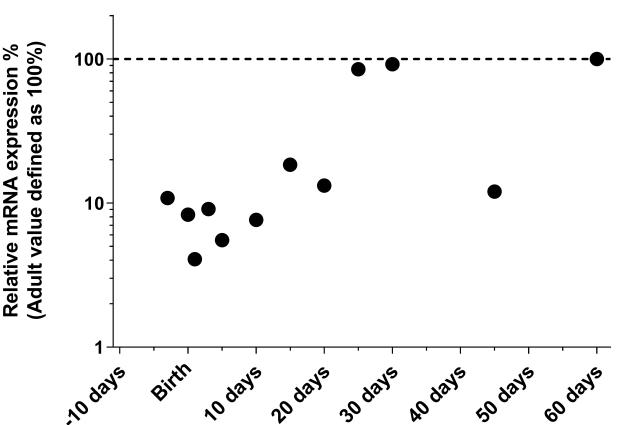
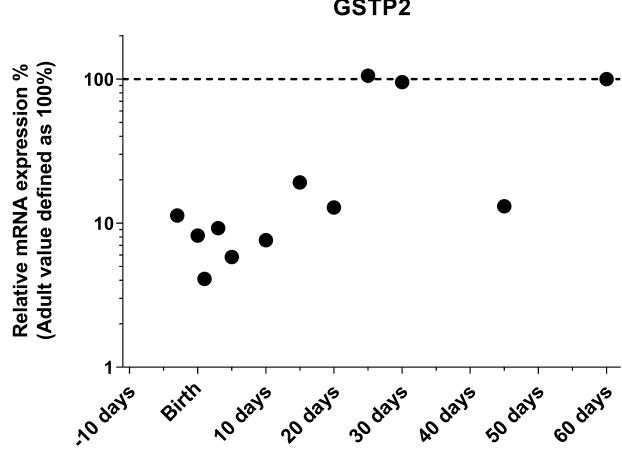
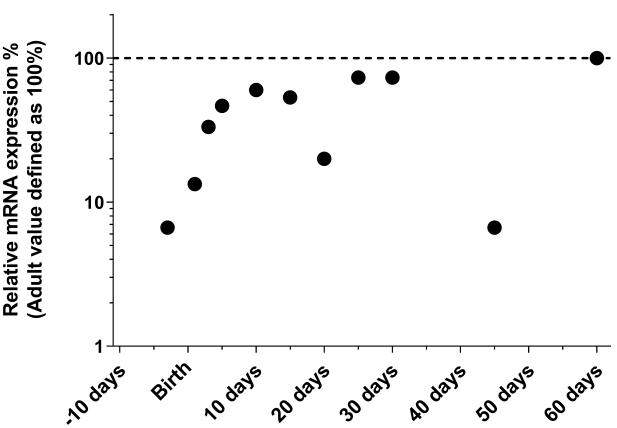
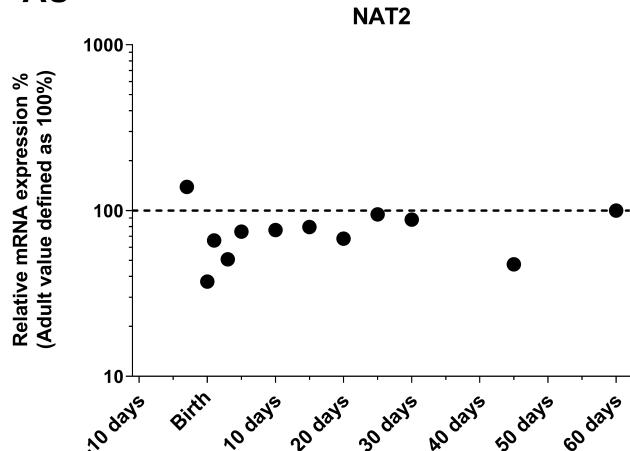
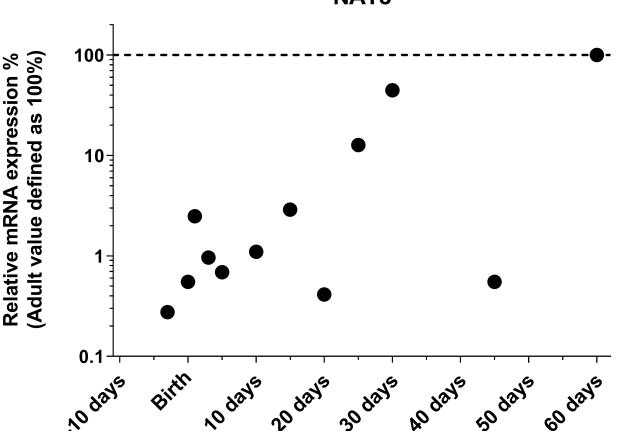


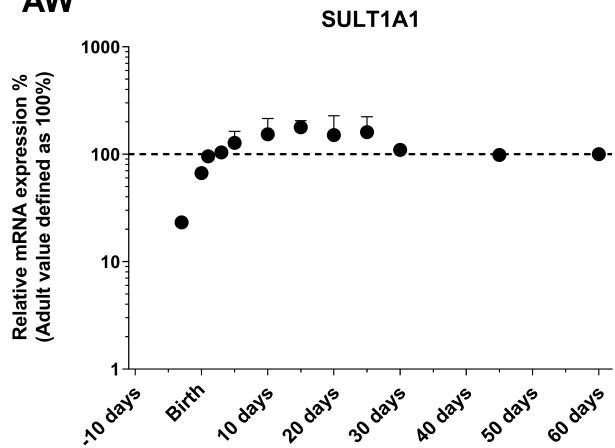
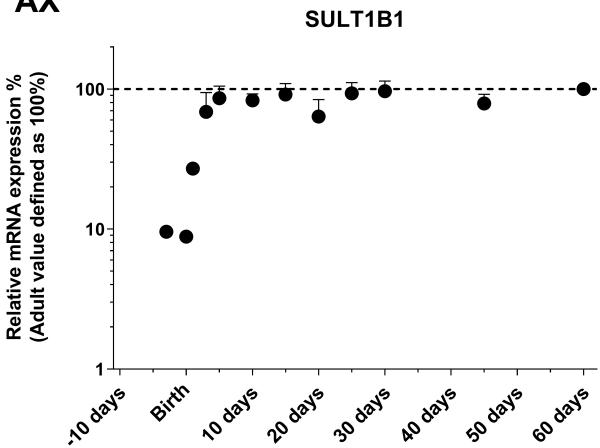
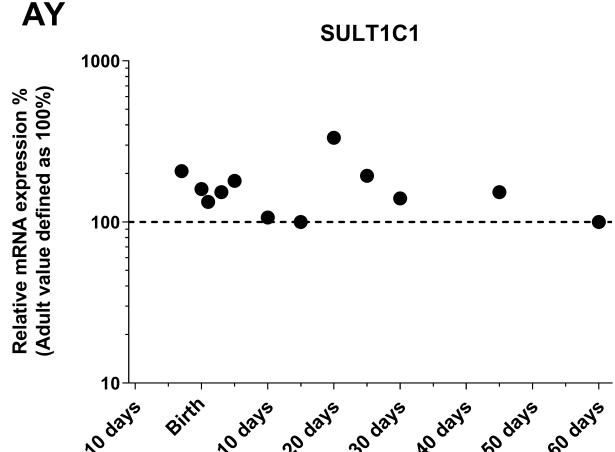
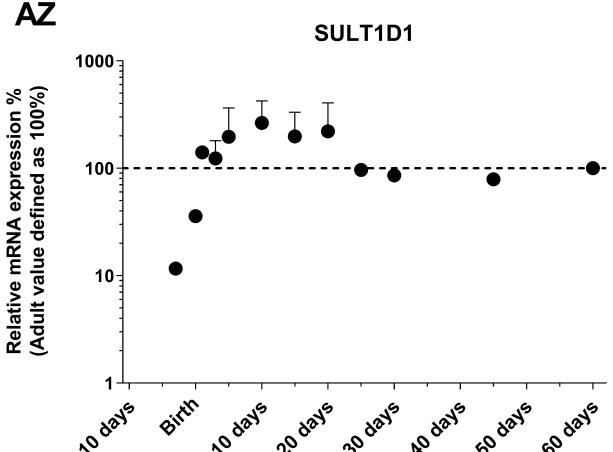
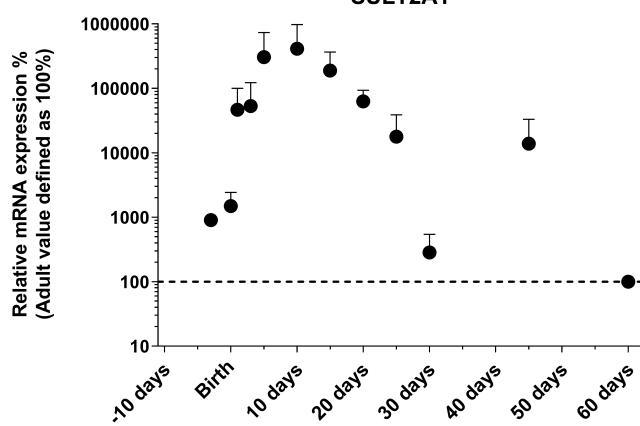
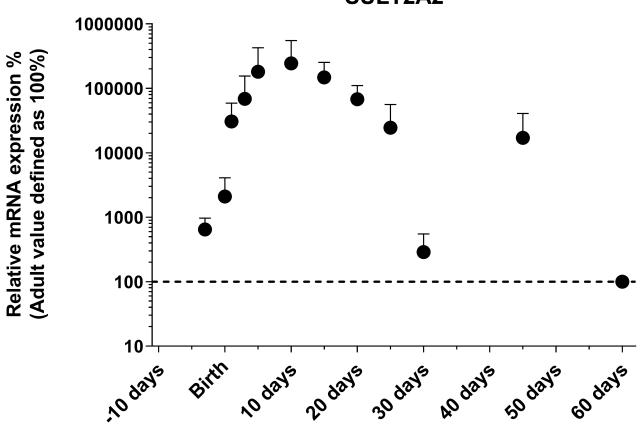
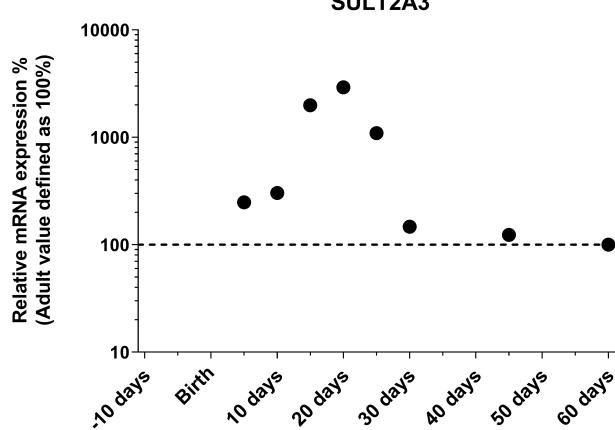
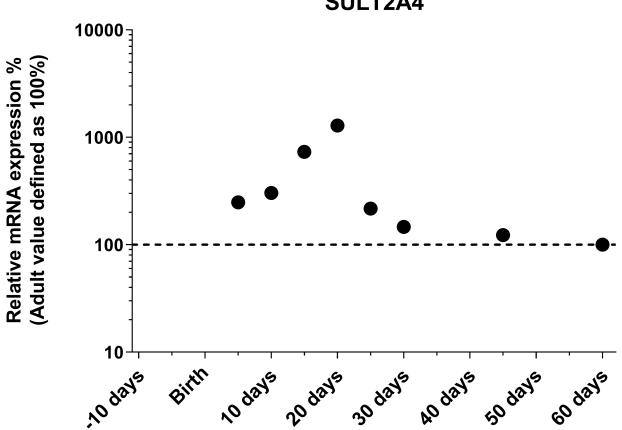


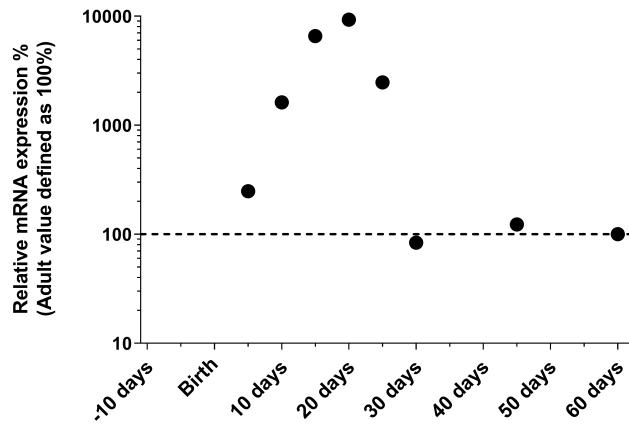
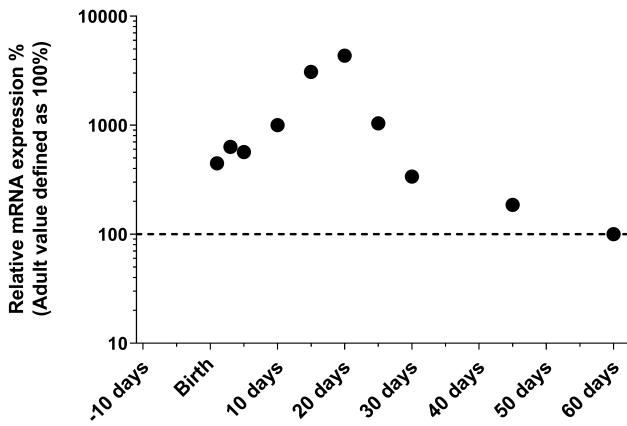
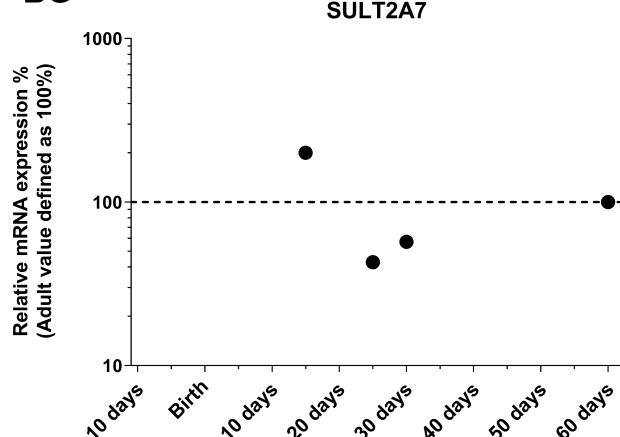
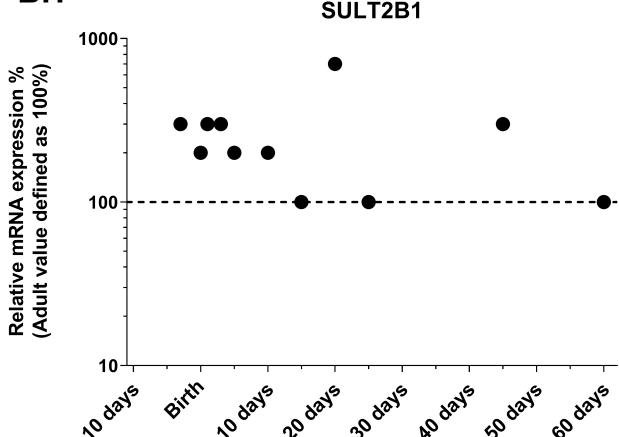
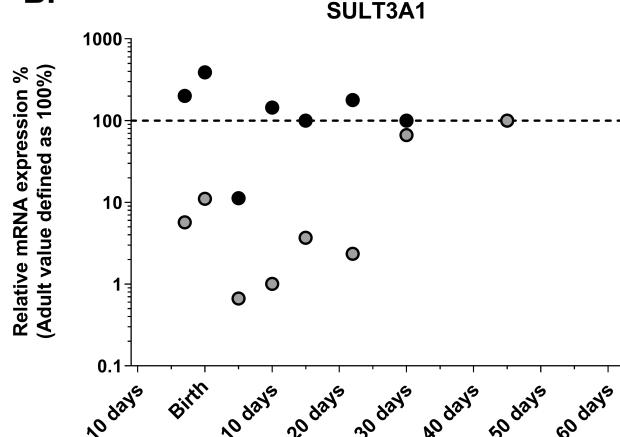
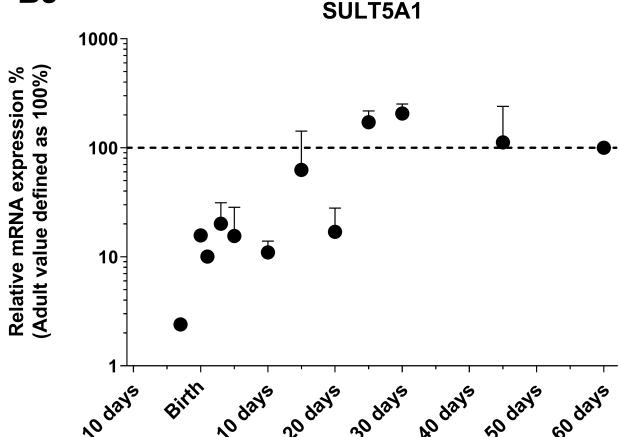
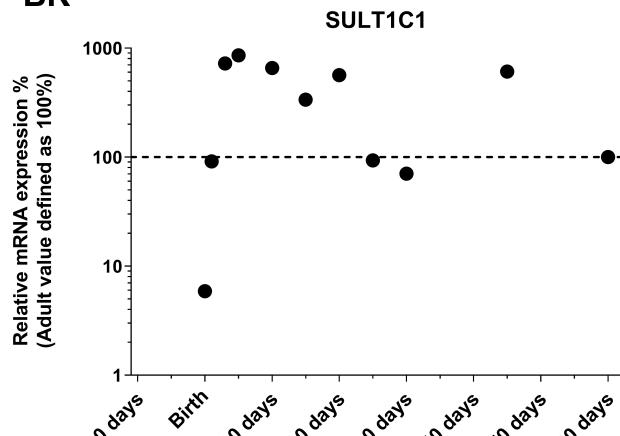
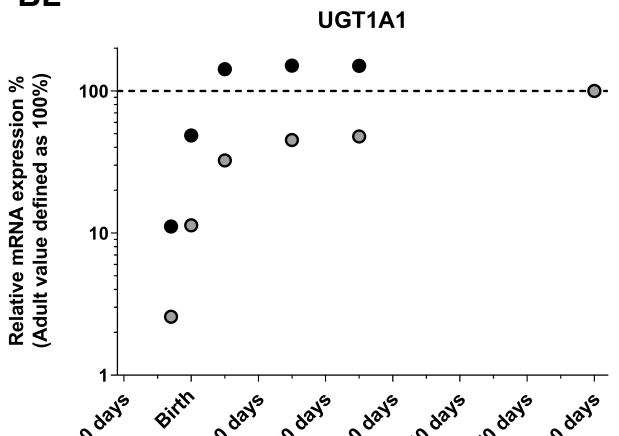
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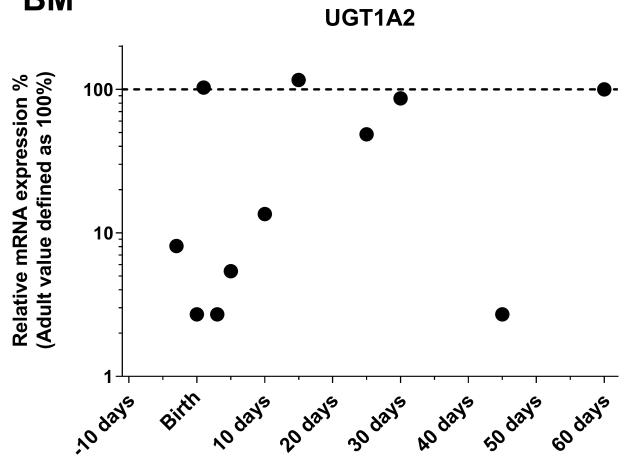
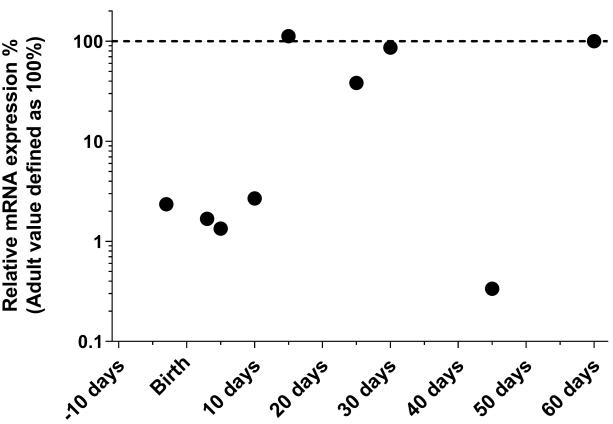
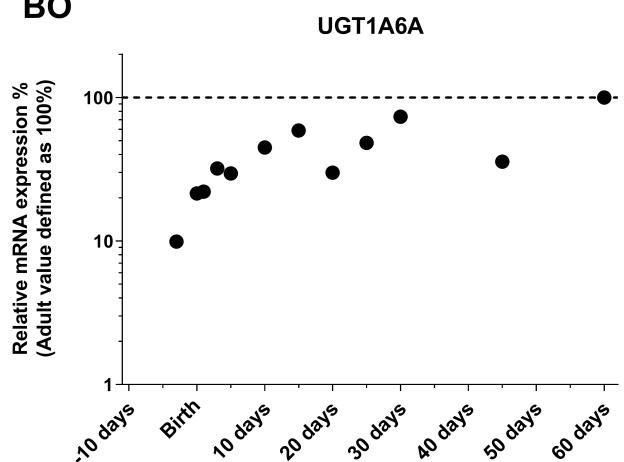
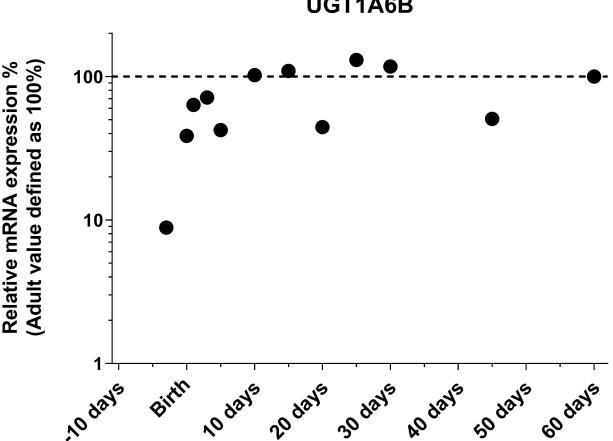
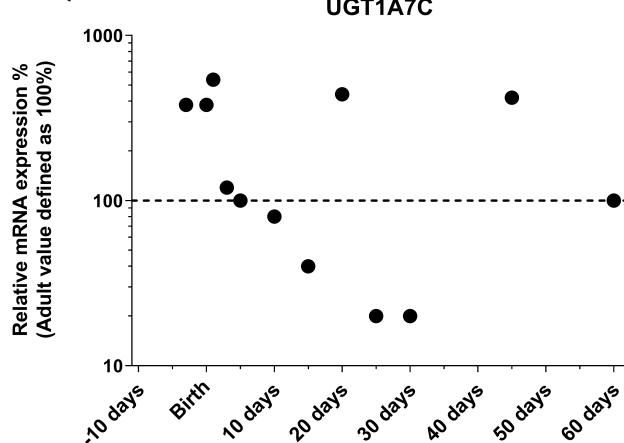
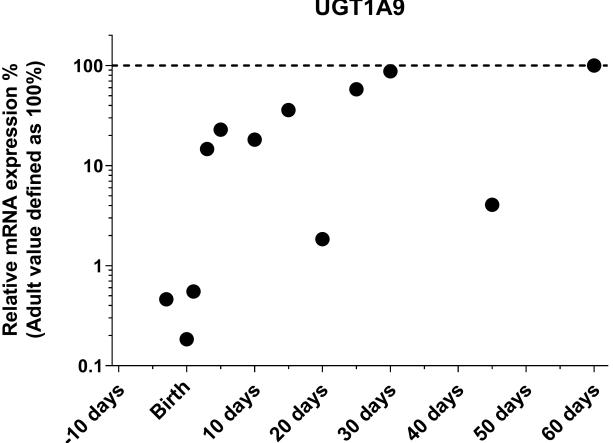
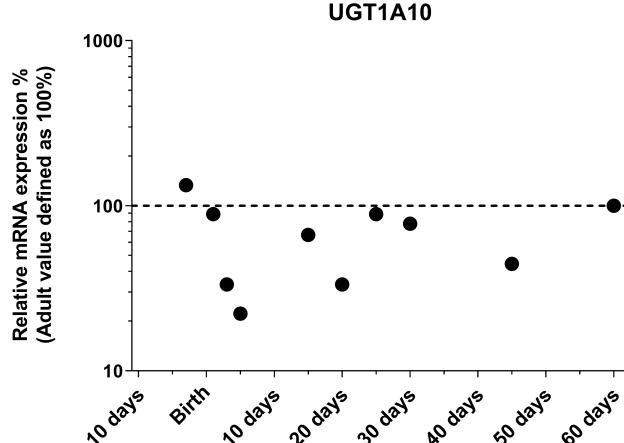
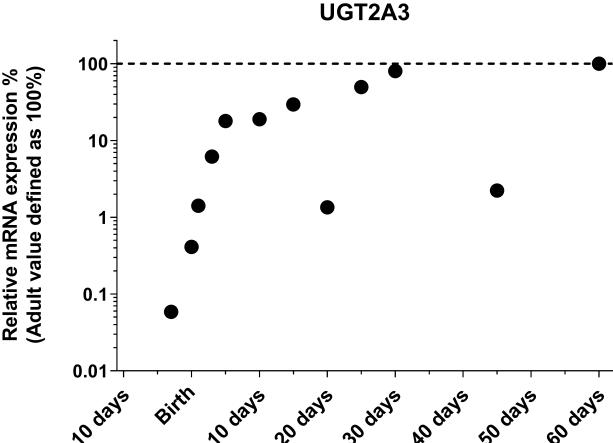


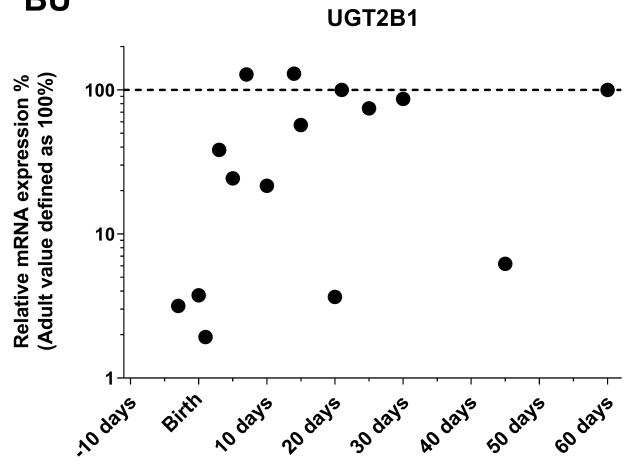
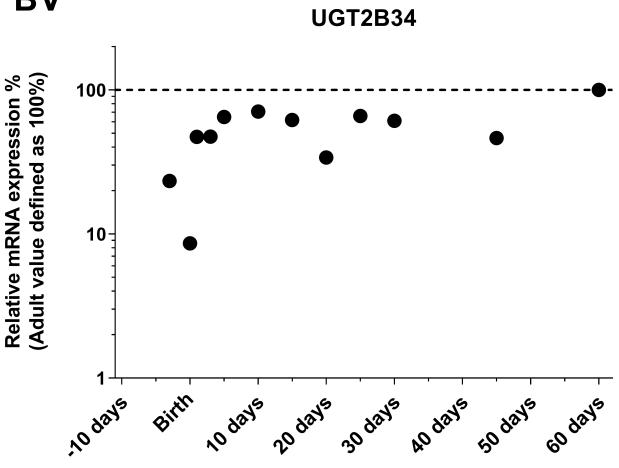
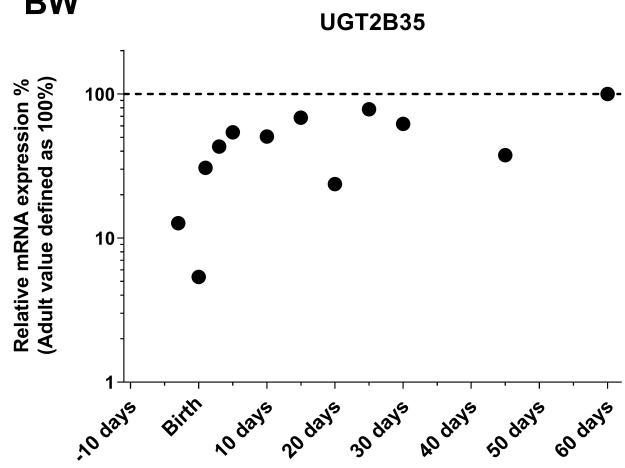
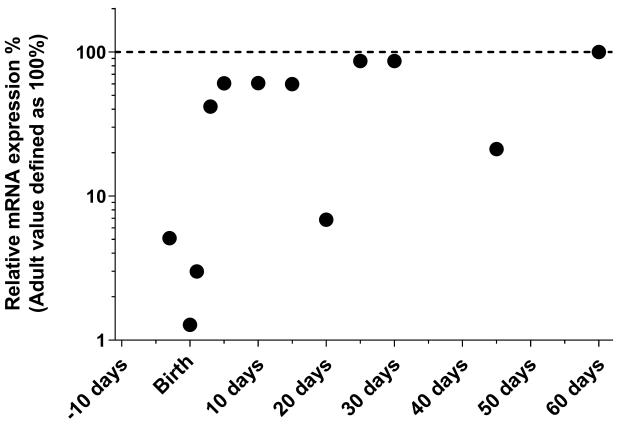
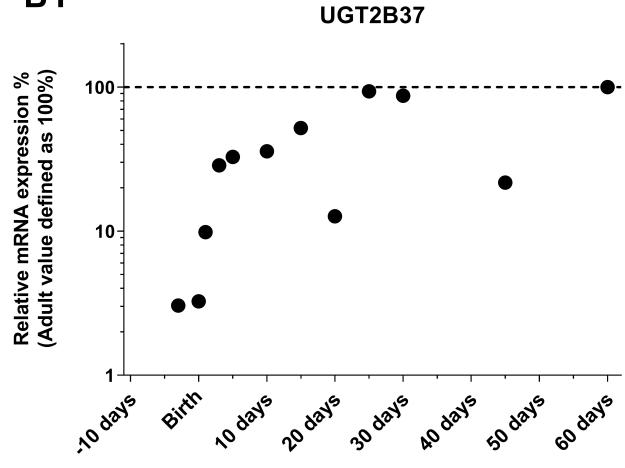
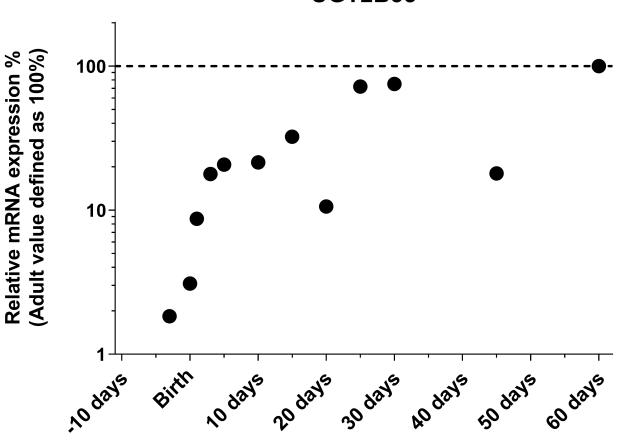
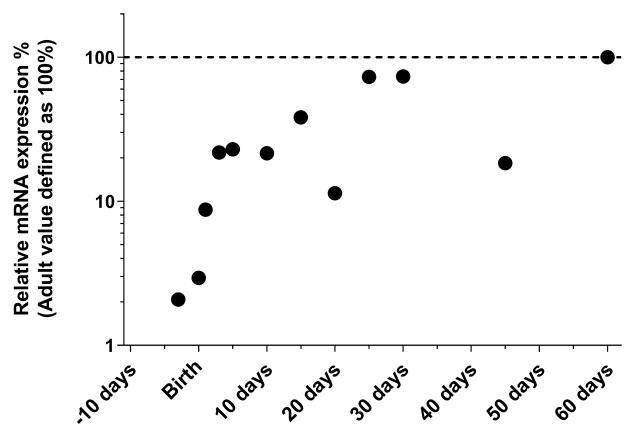
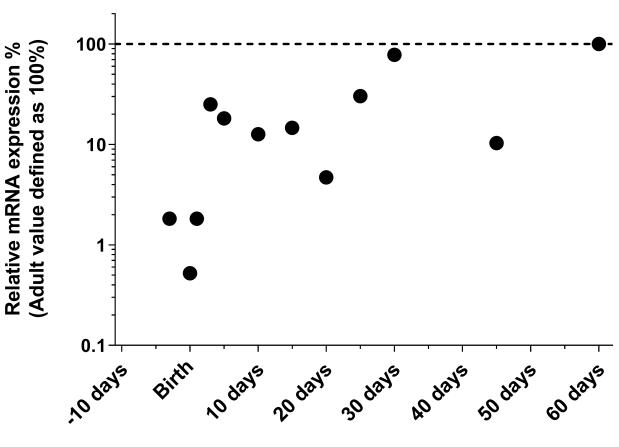
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