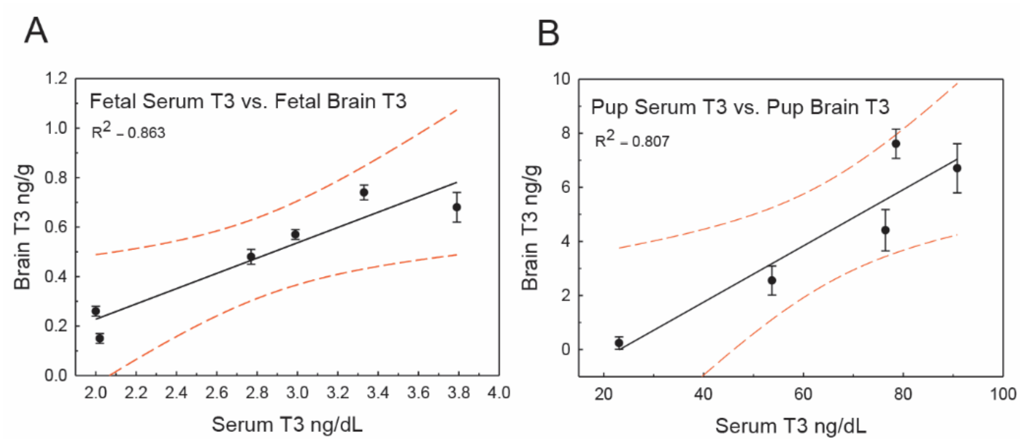
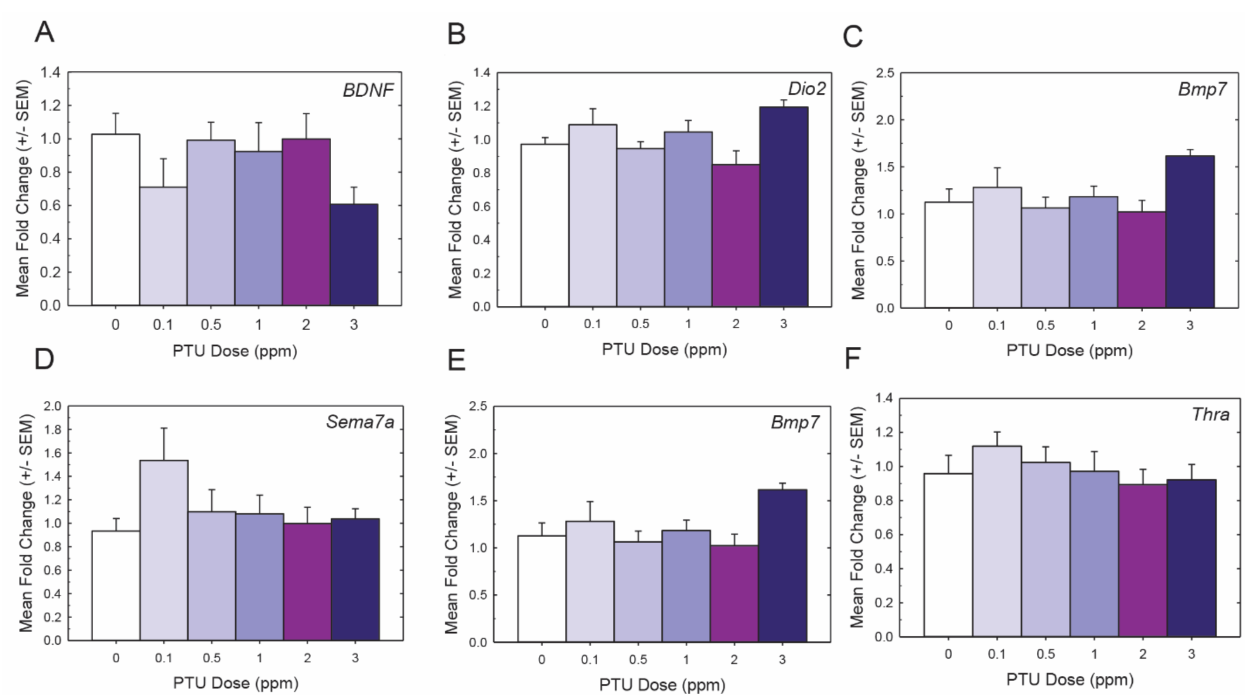
Thyroid hormone disruption in the fetal and neonatal rat: Predictive hormone measures and bioindicators of hormone action in the developing cortex

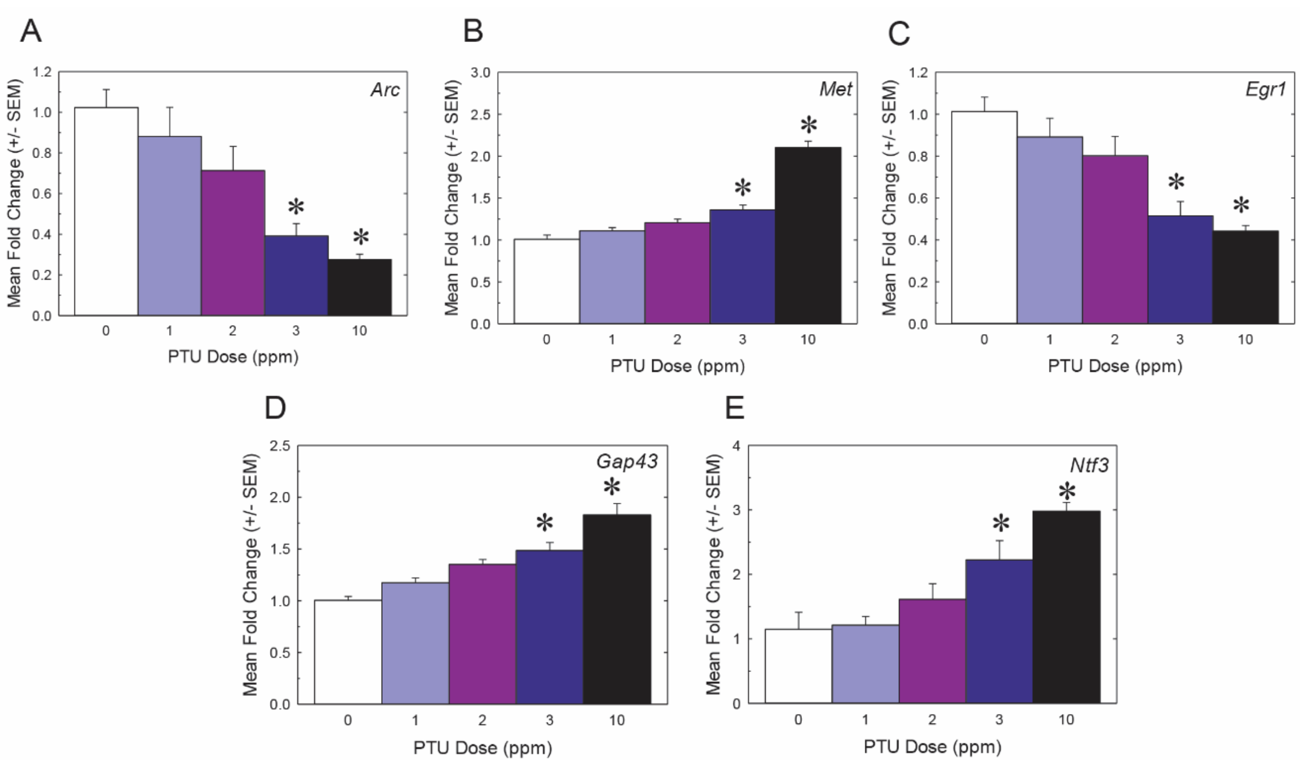
SUPPLEMENTARY INFORMATION



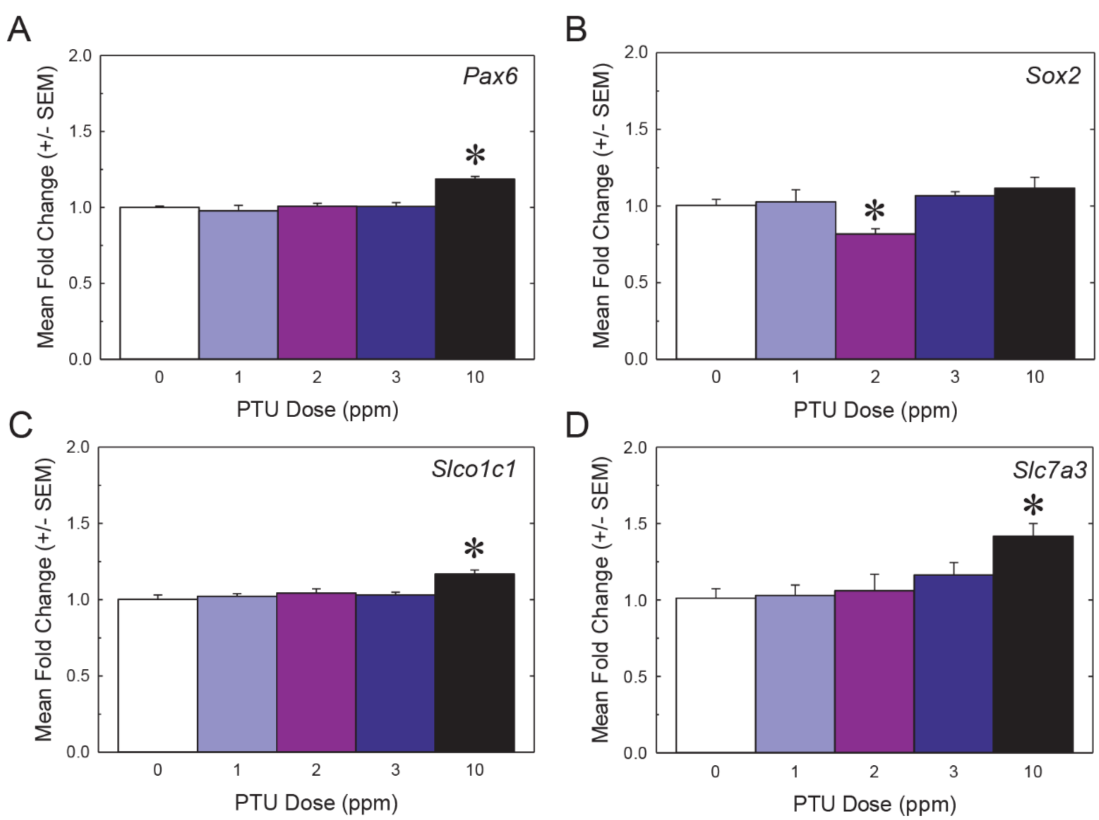
Supplementary Figure 1. Brain T3 expressed as function of serum T3. This relationship in the A) GD20 fetus and B) PN14 pup is linear. However, serum T4 is more highly correlated to brain T3 at both stages (compare to Figure 3C and D). Error bars represent ± SEM, and dashed red lines the 95% confidence interval.



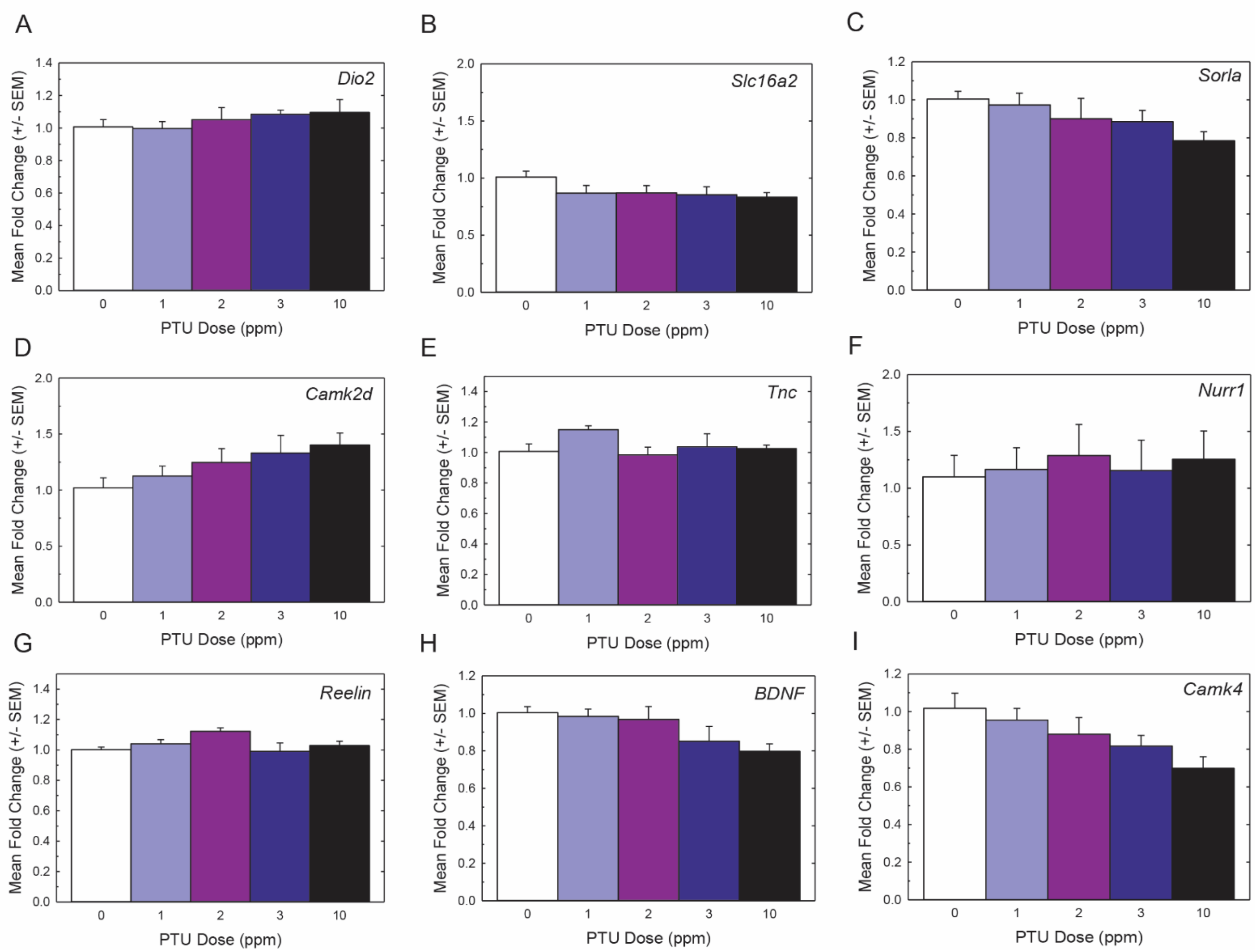
Supplementary Figure 2. Subset of genes not differentially expressed in the GD20 forebrain. All PTU doses represent the maternal dose administered. Error bars represent ± SEM.



Supplementary Figure 3. Genes differentially expressed only in response to 3 and 10 ppm PTU in PN14 neocortex. All PTU doses represent the maternal dose administered. In all panels error bars represent ± SEM.



Supplementary Figure 4. Genes differentially expressed in the PN14 brain in response to a single dose of PTU. All PTU doses represent the maternal dose administered. In all panels error bars represent ± SEM.



Supplementary Figure 5. Genes not differentially expressed in the PN14 neocortex. All PTU doses represent the maternal dose administered. In all panels error bars represent ± SEM.

Stage Analyzed	Gene name	Gene Symbol	NCBI Gene ID	References
GD20	Bone morphogenetic protein 7	*Bmp7*	85272	(Shiraki *et al.*, 2014)
GD20	Roundabout guidance receptor 1	*Robo1*	58946	(Gil-Ibanez *et al.*, 2017)
GD20	Slit guidance ligand 2	*Slit2*	360272	(Gil-Ibanez, Garcia-Garcia, Dopazo, Bernal and Morte, 2017; Morte *et al.*, 2010; Shiraki, Saito, Akane, Takeyoshi, Imatanaka, Itahashi, Yoshida and Shibutani, 2014)
GD20	Neurofilament medium polypeptide	*Nefm*	24588	(Gil-Ibanez *et al.*, 2014; Morte, Diez, Auso, Belinchon, Gil-Ibanez, Grijota-Martinez, Navarro, de Escobar, Berbel and Bernal, 2010)
GD20	Sonic hedgehog	*Shh*	29499	(Desouza *et al.*, 2011; Gil-Ibanez, Bernal and Morte, 2014; Gil-Ibanez, Garcia-Garcia, Dopazo, Bernal and Morte, 2017; Hasebe *et al.*, 2008; Wang *et al.*, 2014; Yu *et al.*, 2015)
GD20	Thyroid receptor alpha	*Thra* (TRα)	81812	(Gil-Ibanez *et al.*, 2013)
GD20	Thyroid receptor beta	*Thrb* (TRβ)	24831	(Chatonnet *et al.*, 2013; Gil-Ibanez, Morte and Bernal, 2013)
GD20, PN14	Calcium -dependent protein kinase type IV	*Camk4*	25050	(Gil-Ibanez, Garcia-Garcia, Dopazo, Bernal and Morte, 2017; Krebs *et al.*, 1996; Morte, Diez, Auso, Belinchon, Gil-Ibanez, Grijota-Martinez, Navarro, de Escobar, Berbel and Bernal, 2010; Shiraki, Saito, Akane, Takeyoshi, Imatanaka, Itahashi, Yoshida and Shibutani, 2014)
GD20, PN14	Reelin	*Reln*	24718	(Gil-Ibanez, Garcia-Garcia, Dopazo, Bernal and Morte, 2017; Pathak *et al.*, 2011;

				Shiraki, Saito, Akane, Takeyoshi, Imatanaka, Itahashi, Yoshida and Shibutani, 2014; Sui and Li, 2010)
GD20, PN14	Semaphorin 7a	*Sema7a*	315711	(Gil-Ibanez, Garcia-Garcia, Dopazo, Bernal and Morte, 2017; Shiraki, Saito, Akane, Takeyoshi, Imatanaka, Itahashi, Yoshida and Shibutani, 2014)
GD20, PN14	Hairless	*Hr*	60563	(Chatonnet, Guyot, Benoit and Flamant, 2013; Del Carmen Grijota-Martinez *et al.*, 2008; Gil-Ibanez, Bernal and Morte, 2014; Gil-Ibanez, Garcia-Garcia, Dopazo, Bernal and Morte, 2017; Mayerl *et al.*, 2012; Morte, Diez, Auso, Belinchon, Gil-Ibanez, Grijota-Martinez, Navarro, de Escobar, Berbel and Bernal, 2010; Potter *et al.*, 2002; Royland *et al.*, 2008a; Shiraki, Saito, Akane, Takeyoshi, Imatanaka, Itahashi, Yoshida and Shibutani, 2014; Yu, Iwasaki, Xu, Lesmana, Xiong, Shimokawa, Chin and Koibuchi, 2015)
GD20, PN14	Nerve growth factor	*Ngf*	310738	(Gilbert *et al.*, 2016; Neveu and Arenas, 1996; O'Hare *et al.*, 2015; Roskoden *et al.*, 1999; Zhang *et al.*, 2009)}
GD20, PN14	Inter-Alpha-Trypsin Inhibitor Heavy Chain 3	*Itih3*	50693	(Gil-Ibanez, Bernal and Morte, 2014; Royland, Parker and Gilbert, 2008a)
GD20, PN14	Prepronociceptin	*Pnoc*	25516	(Gil-Ibanez, Garcia-Garcia, Dopazo, Bernal and Morte, 2017; Morte, Diez, Auso, Belinchon, Gil-Ibanez, Grijota-Martinez, Navarro, de Escobar, Berbel and Bernal, 2010)

GD20, PN14	Deiodonase II	*Dio2*	65162	(Gil-Ibanez, Garcia-Garcia, Dopazo, Bernal and Morte, 2017{Barez-Lopez, 2017 #204; Sharlin *et al.*, 2010)
GD20, PN14	Brain derived neurotophic factor total	*BDNF-t*	24225	(Chakraborty *et al.*, 2012; Gilbert, Sanchez-Huerta and Wood, 2016; Neveu and Arenas, 1996; Shiraki, Saito, Akane, Takeyoshi, Imatanaka, Itahashi, Yoshida and Shibutani, 2014; Sui and Li, 2010; Yu, Iwasaki, Xu, Lesmana, Xiong, Shimokawa, Chin and Koibuchi, 2015)
GD20, PN14	Kruppel like factor 9	*Klf9*	117560	(Chatonnet, Guyot, Benoit and Flamant, 2013; Denver and Williamson, 2009; Gil-Ibanez, Bernal and Morte, 2014; Gil-Ibanez, Garcia-Garcia, Dopazo, Bernal and Morte, 2017; Gilbert, Sanchez-Huerta and Wood, 2016; Morte, Diez, Auso, Belinchon, Gil-Ibanez, Grijota-Martinez, Navarro, de Escobar, Berbel and Bernal, 2010; Royland, Parker and Gilbert, 2008a; Shiraki, Saito, Akane, Takeyoshi, Imatanaka, Itahashi, Yoshida and Shibutani, 2014)
GD20, PN14	SRY-box 2	*Sox2*	499593	(Lemkine *et al.*, 2005; Lopez-Juarez *et al.*, 2012)
PN14	Monocarboxylate transporter 8	*Slc16a2*	259248	(Gil-Ibanez, Garcia-Garcia, Dopazo, Bernal and Morte, 2017; Sharlin, Gilbert, Taylor, Ferguson and Zoeller, 2010)
PN14	Organic anion transporter polypeptide 1C	*Slco1c1*	84511	(Mayerl, Visser, Darras, Horn and Heuer, 2012)
PN14	Solute Carrier Family 7 Member 3	*Slc7a3*	64554	(Grijota-Martinez *et al.*, 2011; Morte, Diez, Auso, Belinchon, Gil-Ibanez, Grijota-

				Martinez, Navarro, de Escobar, Berbel and Bernal, 2010)
PN14	Neurotrophin-3	*Ntf3*	81737	(Del Carmen Grijota-Martinez, Ortega and Bernal, 2008; Gil-Ibanez, Garcia-Garcia, Dopazo, Bernal and Morte, 2017; Royland and Kodavanti, 2008)
PN14	Growth Associated Protein 43	*Gap43*	29423	(Shiraki, Saito, Akane, Takeyoshi, Imatanaka, Itahashi, Yoshida and Shibutani, 2014)
PN14	Paired box 6	*Pax6*	25509	(Shiraki, Saito, Akane, Takeyoshi, Imatanaka, Itahashi, Yoshida and Shibutani, 2014)
PN14	Calcium/calmodulin-dependent protein kinase type II	*Camk2d*	24246	(Royland and Kodavanti, 2008)
PN14	Early growth response protein 1	*Egr1/Cuzd1*	24330	(Kobayashi *et al.*, 2009; Royland, Parker and Gilbert, 2008a)
PN14	Activity regulated cytoskeleton associated protein	*Arc*	54323	(Gilbert, Sanchez-Huerta and Wood, 2016; Kobayashi, Akune, Sumida, Saito, Yoshioka and Tsuji, 2009; Royland, Parker and Gilbert, 2008a; Royland *et al.*, 2008b)
PN14	Angiotensinogen	*Agt*	24179	(Royland, Parker and Gilbert, 2008a)
PN14	Tenascin C	*Tnc*	116640	(Royland, Parker and Gilbert, 2008a)
PN14	Gap junction beta 6	*Gjb6*	84403	(Royland, Parker and Gilbert, 2008a; Shiraki, Saito, Akane, Takeyoshi, Imatanaka, Itahashi, Yoshida and Shibutani, 2014)
PN14	Collagen type XI alpha 2 chain	*Col11a2*	294279	(Royland, Parker and Gilbert, 2008a; Shiraki, Saito, Akane, Takeyoshi, Imatanaka,

				Itahashi, Yoshida and Shibutani, 2014)
PN14	Hop homeobox	*Hopx*	171160	(Royland, Parker and Gilbert, 2008a)
PN14	Nuclear receptor related 1 protein	*Nurr1*	54278	(Royland, Wu, Zawia and Kodavanti, 2008b)
PN14	Myelin oligodendrocyte glycoprotein	*Mog*	24558	(Kobayashi, Akune, Sumida, Saito, Yoshioka and Tsuji, 2009; Royland, Parker and Gilbert, 2008a; Royland, Wu, Zawia and Kodavanti, 2008b)
PN14	Parvalbumin	*Parv*	25269	(Gilbert *et al.*, 2007; Royland, Parker and Gilbert, 2008a; Shiraki, Saito, Akane, Takeyoshi, Imatanaka, Itahashi, Yoshida and Shibutani, 2014)}
PN14	Mesenchymal-epithelial transition factor	*Met*	24553	(Gil-Ibanez, Garcia-Garcia, Dopazo, Bernal and Morte, 2017)
PN14	Sortilin Related Receptor 1	*Sorla*	300652	(Gil-Ibanez, Garcia-Garcia, Dopazo, Bernal and Morte, 2017)

Supplementary Table 1. Extended version of Table 4. Complete list of genes interrogated in this study, in addition to select references that previously reported that these transcripts were differentially regulated in the developing brain by THs; preference was given to studies using rodent models, or human cell lines, which is represented by the provided references. It is noted that these studies may have used severe anti-thyroid exposures to induce hormone insufficiency, and/or analyzed different stages than what was presented in this study.

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