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Thyroid Hormone-Clearing Deiodinase 3 Protects from Cranio-Encephalic and Cardiac Congenital Abnormalities

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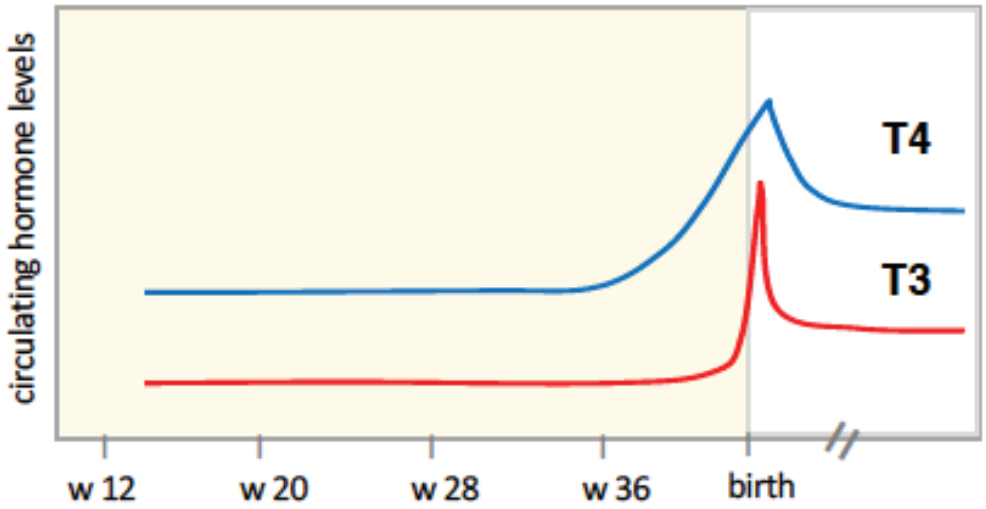
Human thyroid hormones (TH, T4&T3)



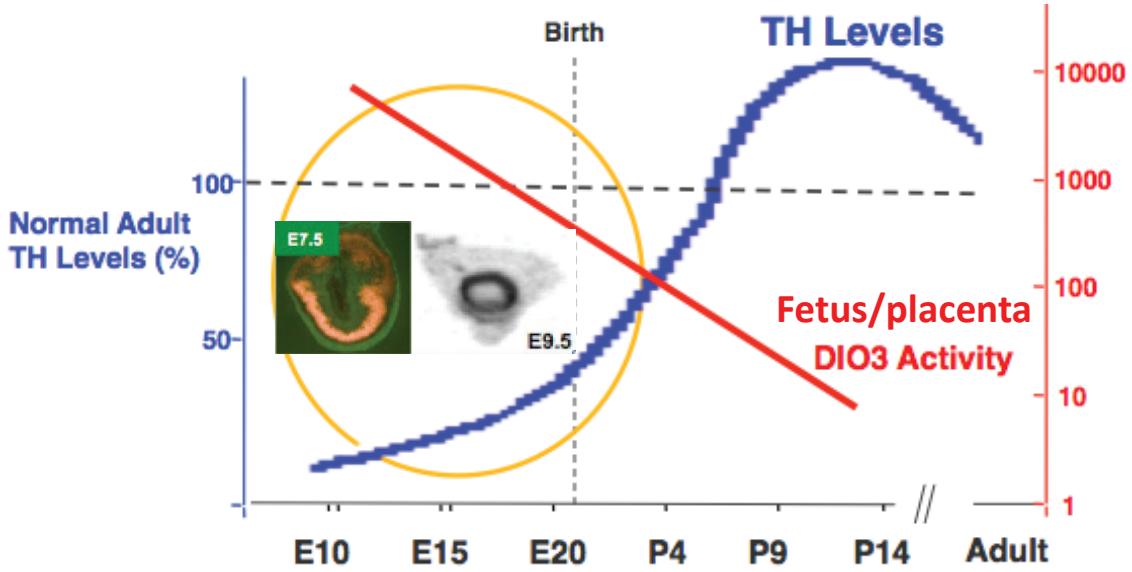
What is the significance of low TH early in development?

Maternal thyroid hyperactivity (Graves' disease) is associated with increases in:

- *Miscarriages*
- *Congenital malformations*

Due to antithyroid drugs?

Mouse thyroid hormones (TH)

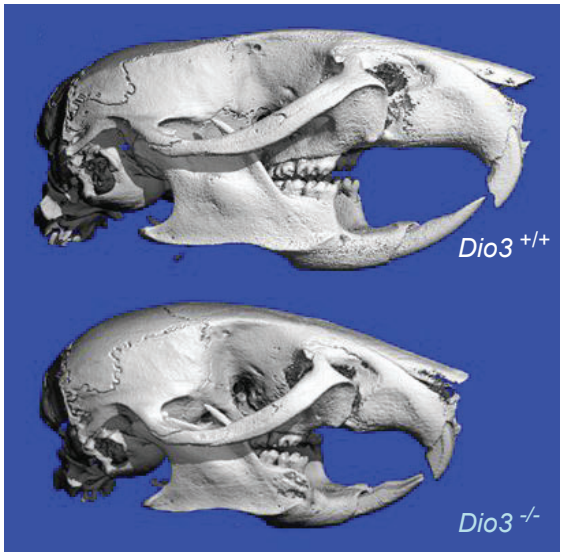


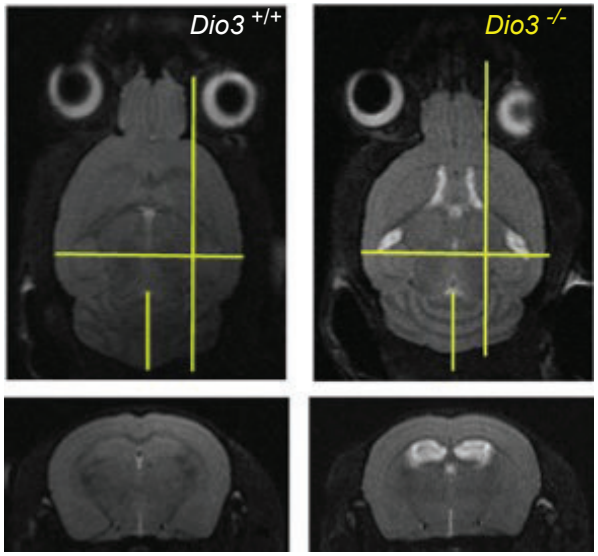
DIO3-deficiency mouse model of Developmental thyrotoxicosis:

40-100% perinatal lethality in homozygous mutants, depending on genetic background ($P<0.001$)

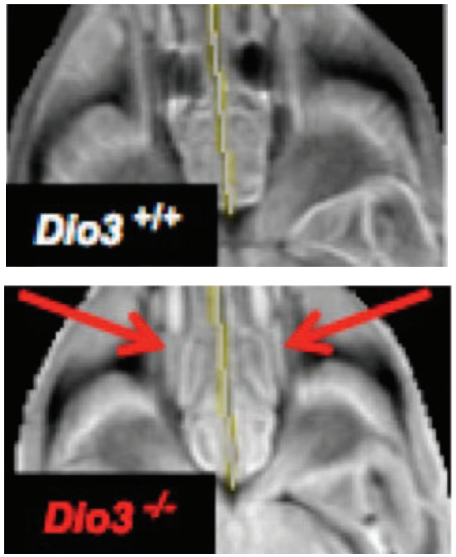
Congenital Abnormalities in DIO3-deficient Mice

Cranial and brain dysmorphism, Hydrocephalus
Cerebellar defects, ⇧ Cx thickness

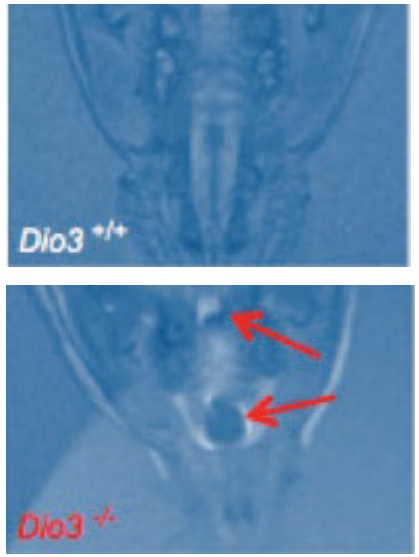




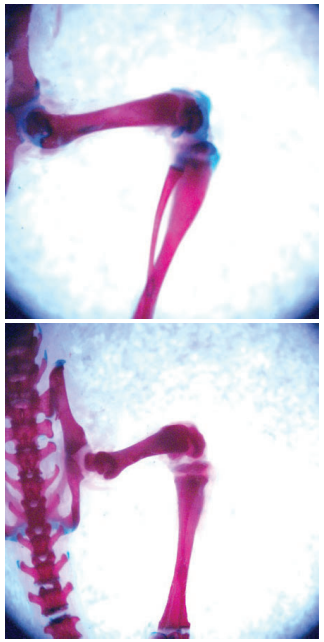
Choanal atresia



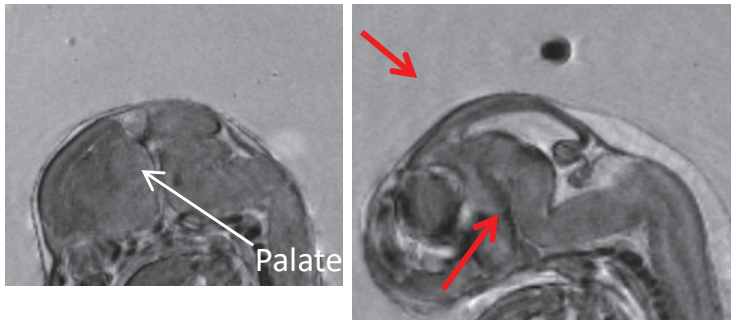
Cleft palate



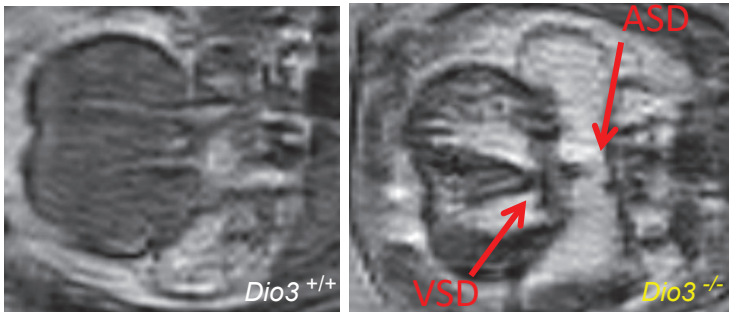
Loss of cartilage



Fetal (E14.5) Cleft face, lack of palate



ASD and VSD



***Conclusion**: TH-clearance by DIO3 is critical for normal craniofacial, encephalic and cardiac development*

***Implications**: Transient overexposure to TH during development may contribute to idiopathic congenital syndromes in humans (cleft palate, hydrocephalus, cardiac and Chiari malformations, others)*

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