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Costas T. Lambrew Research Retreat 2021

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

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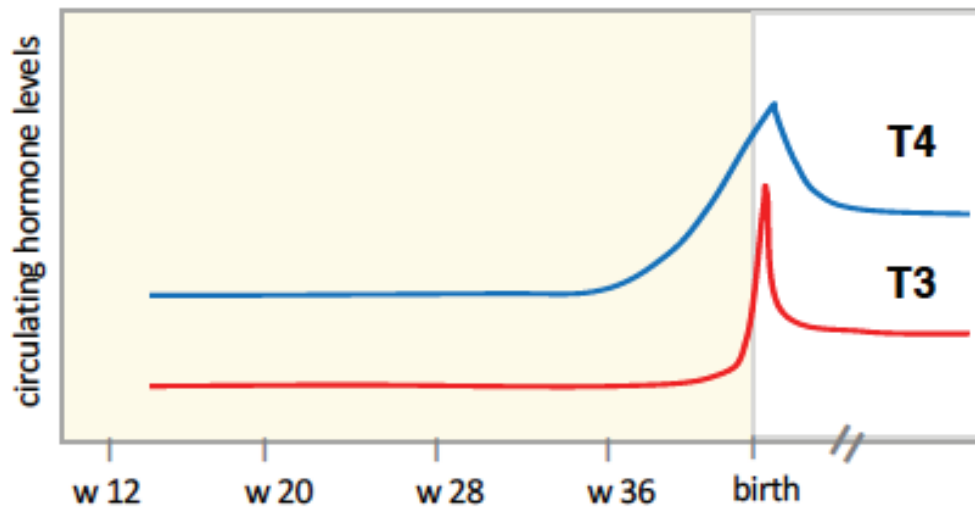
Hernandez, Arturo; Martinez, M Elena; Pinz, Ilka; Preda, Marilena; and Gridley, Thomas, "Thyroid Hormone-Clearing Deiodinase 3 Protects from Cranio- Encephalic and Cardiac Congenital Abnormalities" (2021).
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Thyroid Hormone-Clearing Deiodinase 3 Protects from Cranio-Encephalic and Cardiac Congenital Abnormalities

Arturo Hernandez, M. Elena Martinez, Ilka Pinz, Marilena Preda and Thomas Gridley

Human thyroid hormones (TH, T4&T3)



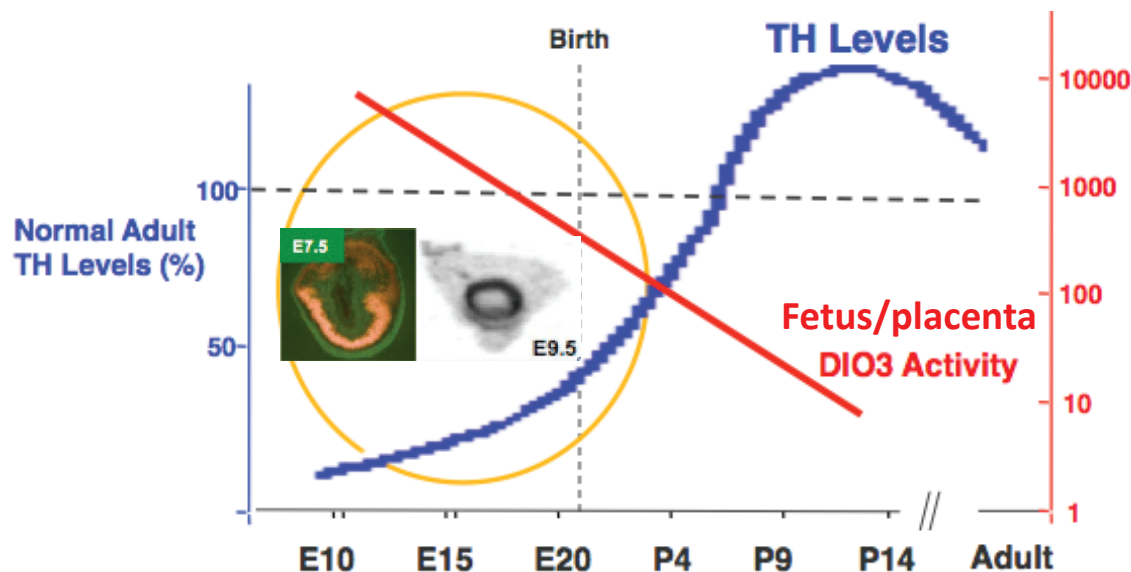
What is the significance of low TH early in development?

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

- Miscarriages
- Congenital malformations

Due to antithyroid drugs?

Mouse thyroid hormones (TH)

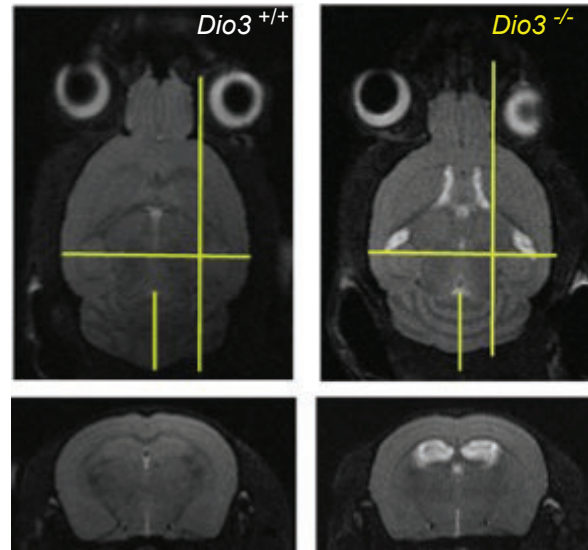
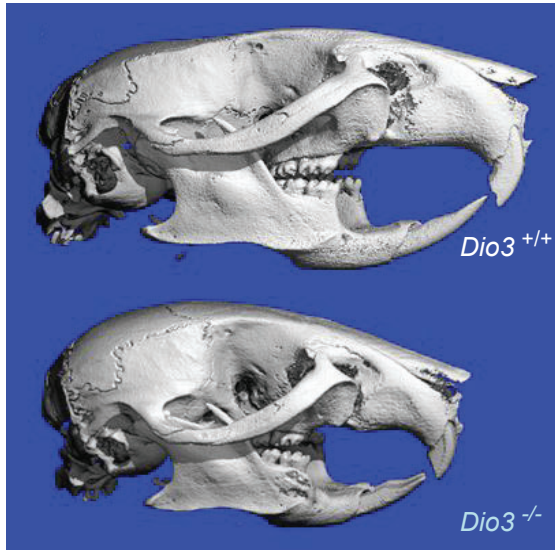


DIO3-deficiency mouse model of Developmental thyrotoxicosis:

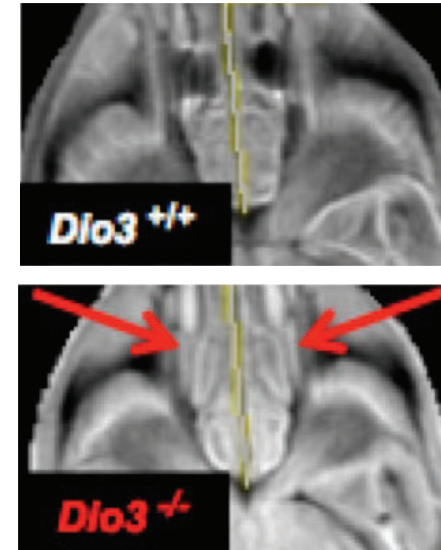
40-100% perinatal lethality in homozygous mutants, depending on genetic background ($P < 0.001$)

Congenital Abnormalities in *DIO3*-deficient Mice

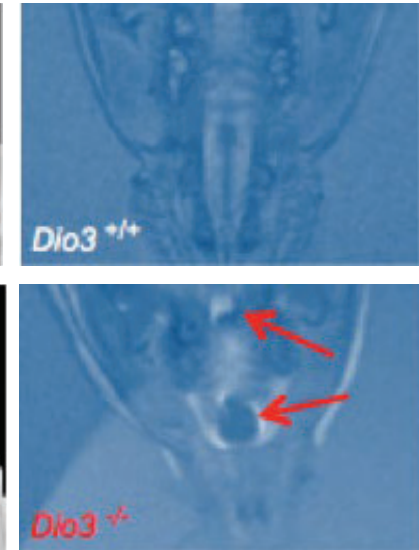
*Cranial and brain dysmorphism, Hydrocephalus
Cerebellar defects, ↑ Cx thickness*



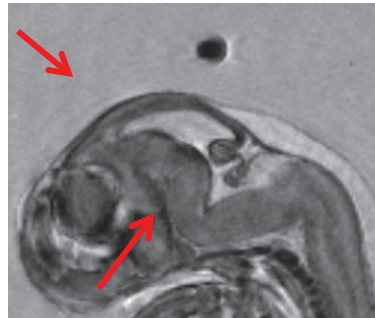
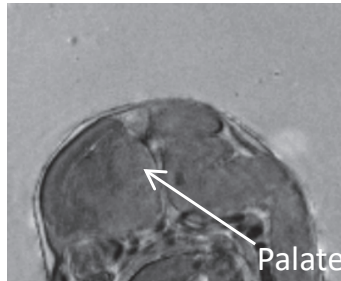
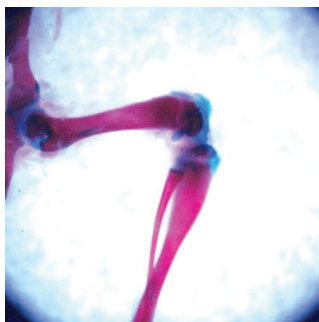
Choanal atresia



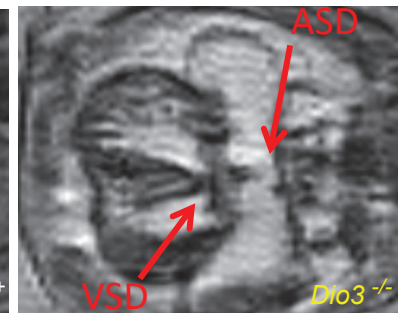
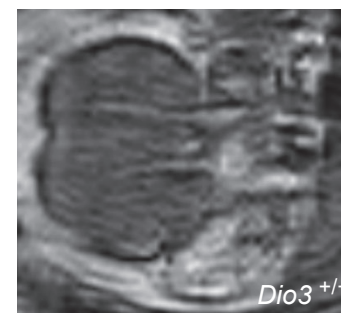
Cleft palate



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)