

electrolyte disturbance (OR 6.12, $p < 0.001$) and those with a neurologic disorder (OR 2.46, $p = 0.002$). Admitted patients with a concomitant psychological disorder had lower odds of death (OR 0.38, $p = 0.03$).

Conclusions: This study identified clinical characteristics associated with TS-related admission including female gender, age 30-59, Caucasian race, and urban populations. Higher mortality was associated with patients 30-59 years and >60 years of age, electrolyte disturbances, blood disease, weight loss, paralysis, cancer, renal disease, and male gender.

Thyroid

THYROID HORMONE METABOLISM AND ACTION

Dio2-CreErt2 Knockin Model to Identify T3-Generating Cells That Express Type 2 Deiodinase in Tissues

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Background: Thyroid hormone promotes many developmental and homeostatic functions. Apart from adequate circulating levels, the concentration of the active hormone T3 within tissues may be amplified by type 2 deiodinase (Dio2) by conversion from the precursor T4. Dio2 is critical in auditory development, bone maturation, brain function and control of the hypothalamic-pituitary-thyroid axis. Despite its crucial role, an obstacle to studying Dio2 is that the protein has a short half-life, is at low levels and is often transiently expressed, making it difficult to identify Dio2 in tissues at cellular resolution. **Methods:** We derived a Dio2-CreERT2 knockin mouse that expresses tamoxifen-dependent Cre recombinase from the endogenous Dio2 gene. When crossed onto Ai6 reporter mice, following tamoxifen treatment, Dio2-CreERT2 expression is detected as fluorescent signal in specific cells in brain regions, pituitary, and other tissues. We showed previously that Dio2 is essential for hearing with rising expression levels in the cochlea prior to onset of hearing. The Dio2-CreERT2 model identified positive cell types in the cochlear spiral ligament, septal divisions and modiolus around the sensory epithelium. Dio2-positive fibrocytes were adjacent to and extended projections around blood capillary networks, the source of T4 supply. Transcriptome analysis of isolated positive cells revealed bone lineage-related origins for many of these cells. **Conclusion:** The Dio2-CreERT2 model detects Dio2 expression sensitively at cellular resolution. In the cochlea, Dio2-positive cell types reside in vascularized support tissues, suggesting combined endocrine and paracrine-like control of the T3 supply. Analysis of cell origins suggests novel interactions between endocrine and skeletal systems in promoting T3 action required for hearing.

Thyroid

THYROID HORMONE METABOLISM AND ACTION

Identification of Cell Types that Express Dio3 Deiodinase, a Thyroid Hormone-Inactivating Enzyme, Using a Dio3-CreERT2 Reporter System

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Background: Thyroid hormone promotes development, growth and metabolism. The level of thyroid hormone ligand (triiodothyronine, T3) in tissues depends not only on circulating levels but also upon tight regulation by activating and inactivating deiodinases within tissues. Type 3 deiodinase (Dio3) inactivates T3 and its precursor thyroxine (T4) and mediates many functions including in neurodevelopmental, sensory and reproductive systems. Dio3 is subject to genomic imprinting. Despite its critical functions, Dio3 is often expressed transiently and at low levels in restricted cell populations making it difficult to detect in natural tissues. **Methods:** To visualize Dio3 expression at cellular resolution, we derived a Dio3-CreERT2 knockin allele that expresses tamoxifen-dependent Cre recombinase from the endogenous Dio3 gene. When crossed with Ai6 reporter mice, Dio3-CreERT2-positive cells display fluorescent signals. When tamoxifen-treated at neonatal ages, Dio3-CreERT2 recapitulates endogenous Dio3 expression as previously reported in brain: in the bed nucleus of the stria terminalis and preoptic nuclei. In addition, we uncovered several positive cell groups in the hypothalamus, brain stem, pituitary and other tissues. Drastic differences were observed for Dio3-CreERT2 as a paternally versus maternally inherited allele, revealing imprinting effect in specific cell types. Dio3-CreERT2 activity is enhanced by T3 administration, in accordance with Dio3 as a T3-inducible gene. **Conclusion:** The Dio3-CreERT2 model sensitively reveals Dio3-expressing cell types in tissues. The model is useful for studying expression patterns, imprinting and lineage tracing of Dio3-positive cells during development and homeostatic challenges.

Thyroid

THYROID HORMONE METABOLISM AND ACTION

iPSC-Derived Human Hepatocytes as a Novel Model to Investigate Thyroid Hormone Action and Signaling

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Thyroid hormone (TH) actions are essential to normal metabolism and neurologic function. Abnormal TH levels can lead to significant morbidity including metabolic abnormalities, cardiac disease, and obesity. TH action is mediated by the thyroid hormone receptor (TR) isoforms and their coregulators. In the disease models of Resistance to Thyroid Hormone (RTH) it is clear that the TR isoforms play tissue-specific roles in humans, however a platform for drug discovery to potentially treat the diseases does not exist. We hypothesize that human hepatocytes (iHeps) derived from induced pluripotent stem cells (iPSCs) will serve as an ideal model to study TH signaling and to delineate mechanisms of TH diseases in humans. To investigate the TH action in humans, we have developed a serum free human iPSC hepatic differentiation protocol that utilizes sequential exposure to growth factors to mimic actual