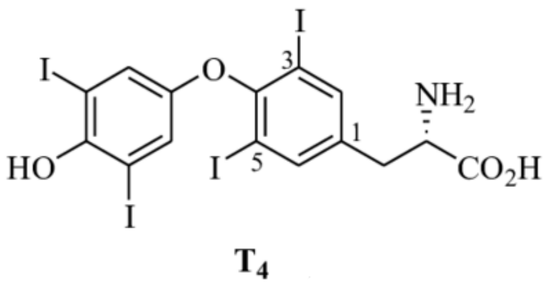
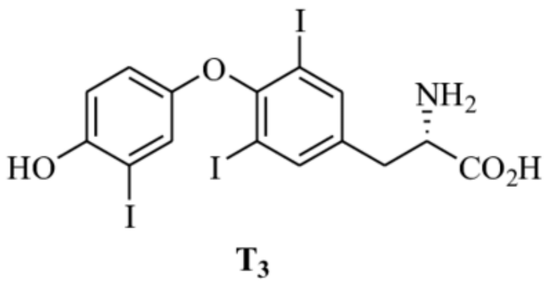
Biochemistry of

Thyroid Hormones

Thyroxine and Triiodothyronine





Jasmine Hartsook // Presented With Permission For Portfolio Purposes

The Thyroid Gland (glandula thyreoidea), a butterfly shaped gland located at the base of your neck, is an important gland in hormone production. It plays a major role in the metabolism, growth and development of the human body which translates to functions like breathing, heart rate, central and peripheral nervous system function, body weight, muscle strength, menstrual cycles, body temperature, and more. It regulates these functions by producing and releasing a steady amount of thyroid hormones into the bloodstream.

The thyroid gland is full of thyroid follicles which are the main site of thyroid hormone synthesis. The follicles are surrounded by a lining of follicular epithelial cells where the multi-step process of thyroid hormone production and release occurs. This is the site where inorganic iodine is actively transported from the bloodstream into the lumen of the cell and joined with tyrosine amino acids gained from thyroglobulin protein and synthesized into **T4 (Thyroxine) or T3 (Triiodothyronine) thyroid hormones** and transported out of the follicular epithelial cells and released to the rest of the body.

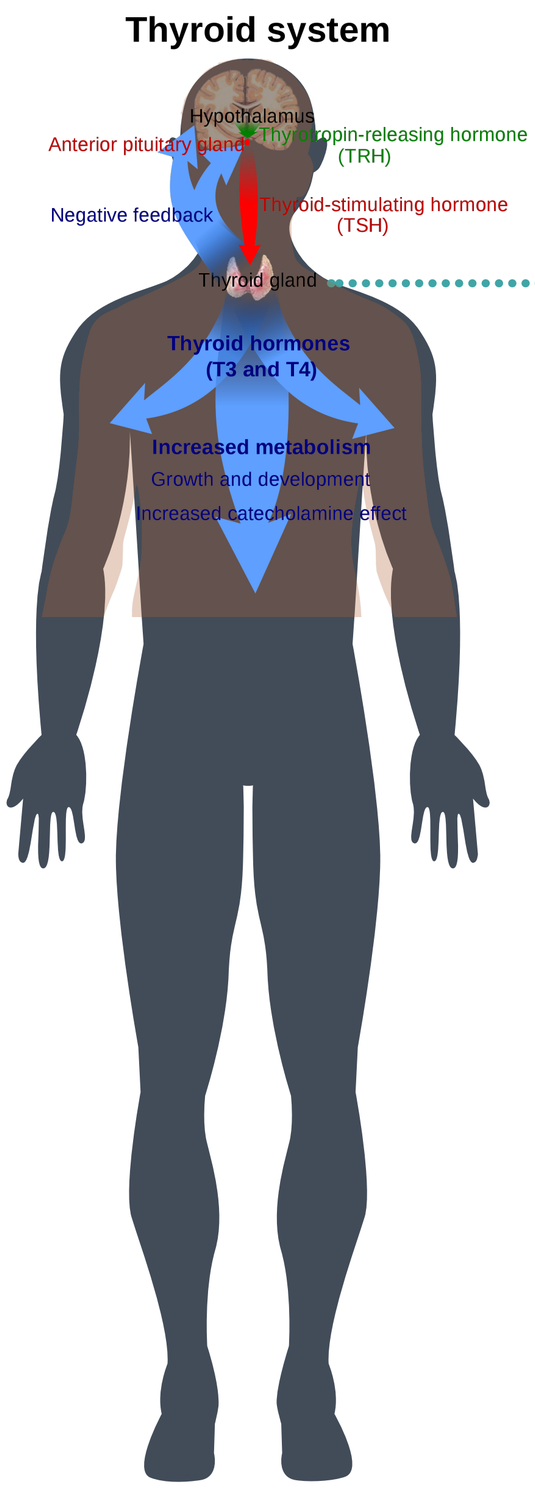


Fig. 1

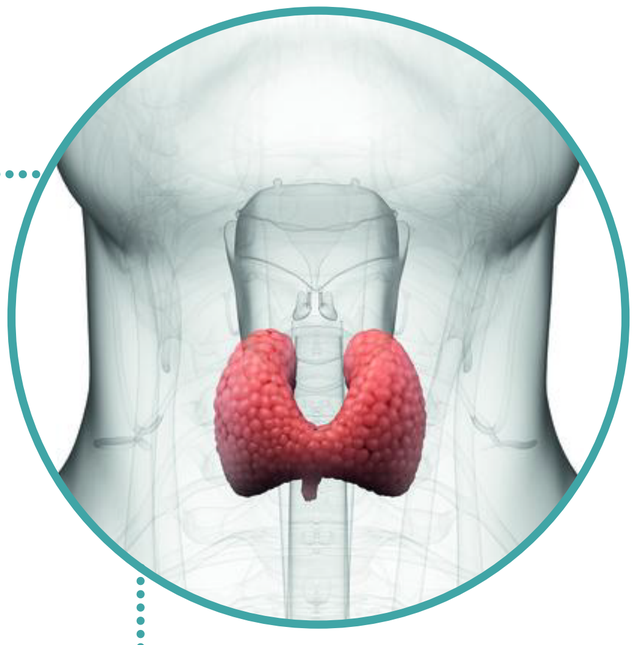


Fig. 2

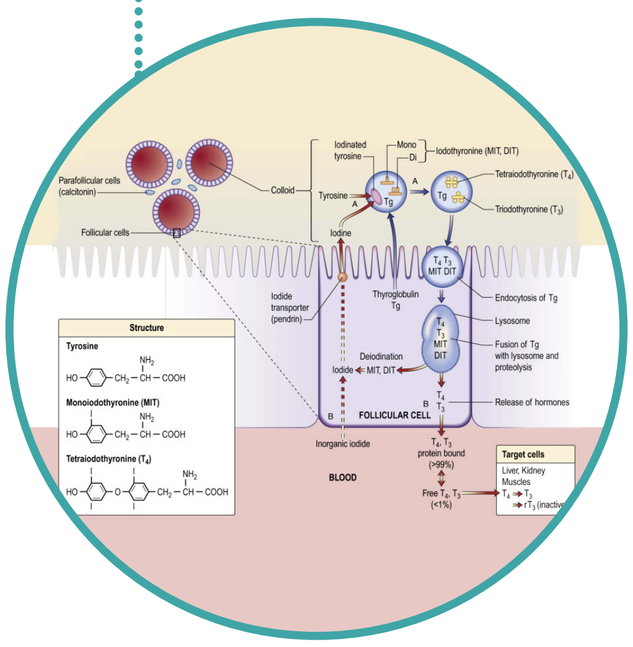


Fig. 3

Fig. 1. The thyroid system overview. Image courtesy of : https://commons.wikimedia.org/wiki/File:Thyroid_system.svg **Fig. 2. The butterfly shaped thyroid gland sits just above the windpipe in the neck.** Image courtesy of: SciencePro, https://www.thenational.ae/lifestyle/well-being/why-the-thyroid-gland-holds-the-key-to-your-energy-levels-1.164478 **Fig. 3. Synthesis of thyroid hormones.** Image courtesy of : https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/thyronine

Iodine Transport-
Iodine is one of the main building blocks of both hormones. Our bodies can't produce this trace element, so we need to obtain iodine from our food and absorb it into the bloodstream. Large amounts of iodine are required for thyroid hormone synthesis. Once in the bloodstream, iodine (I-) is actively transported into the follicular lumen by the Follicular Epithelial Cells. This explains why iodine is highly concentrated in this gland in comparison to the rest of the body.

Thyroglobulin Synthesis-
Thyroglobulin is a protein that contains large numbers of the amino acid tyrosine. These become the building blocks of individual thyroid hormone molecules. Thyroglobulin is synthesized in the follicular epithelial cells and secreted into the follicular lumen.

Thyroid Peroxidase-
This enzyme located in the follicular lumen performs several key reactions. Thyroid Peroxidase first generates I2 and then organifies I2 the by covalently linking it with tyrosine residues present in Thyroglobulin. It produces either single or double iodinated species of tyrosine called Monoiodotyrosine (MIT) or Diiodotyrosine (DIT). Thyroid Peroxidase then combines the MIT and DIT residues to generate T3 or T4 within the Thyroglobulin protein. This process is called "coupling". T4 is produced by combining two DIT residues whereas T3 is produced by combining a DIT residue with an MIT residue. Peroxidase is more efficient at combining DIT residues explaining why the gland primarily produces the T4 species. The secretion ratio is about 14:1 T4 to T3. Although the T4 is more favored in secretion from the thyroid, T3 is considered to be the biologically active form of the hormone. The bulk of T3 is derived by deiodination of T4 in peripheral tissues, especially liver and kidney. Some of the MIT and DIT residues do not get coupled and will be retained in the processed thyroglobulin.

Endocytosis of Peroxidase-processed Thyroglobulin-
When the thyroid gland is stimulated to release thyroid hormones into circulation, Peroxidase-processed thyroglobulin is endocytosed by follicular epithelial cells. Within the follicle, it can act as a reservoir for thyroid hormones for release when needed.

Release of T4 and T3 from Thyroglobulin-
Once inside the follicular epithelial cell, thyroglobulin is broken down by lysosomes and releases the attached T4, T3, MIT, and DIT. T4 and T3 are then transported out of the cells into the bloodstream for circulation.

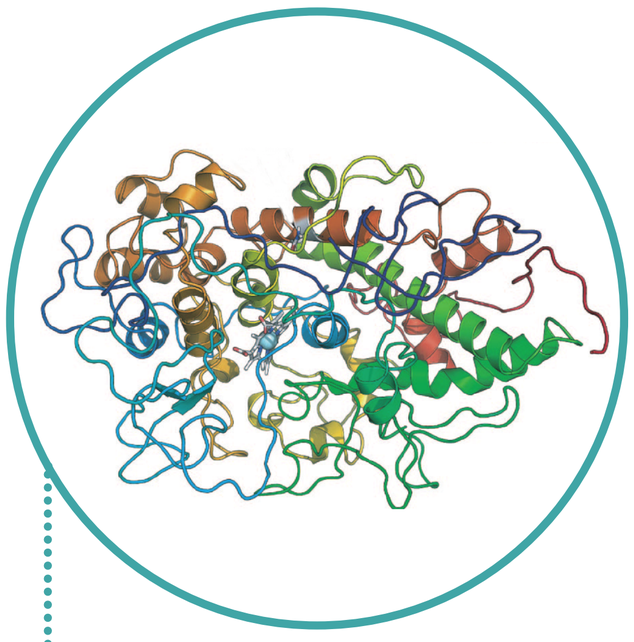


Fig. 4

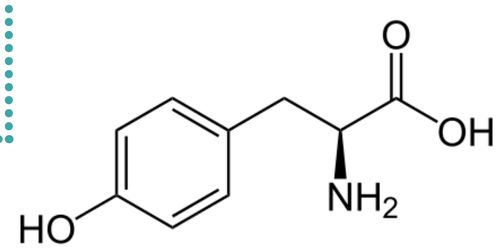


Fig. 5

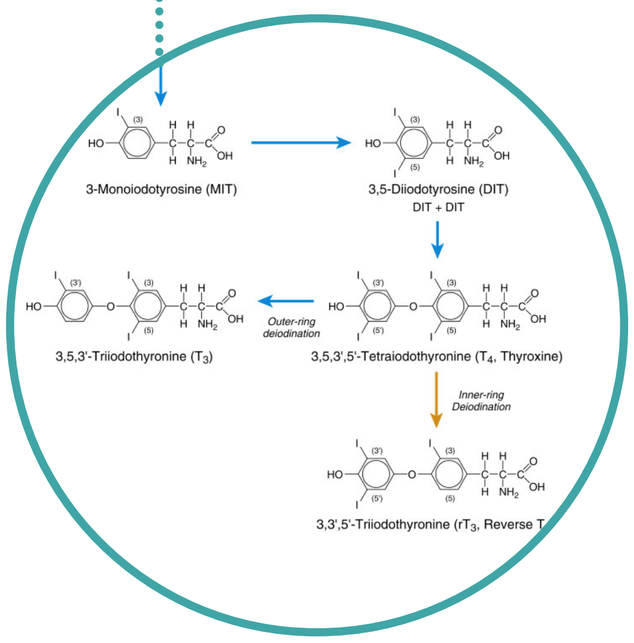


Fig. 6

Fig. 4. Ribbon representation of the modeled structure of TPO protein structure. Image courtesy of : https://www.researchgate.net/-figure/The-TPO-structure-A-Schematic-view-of-the-human-TPO-structure-plain-arrows-indicate_fig2_5818743 **Fig. 5. Chemical structure of amino acid Tyrosine, a precursor for thyroid hormone production. Fig. 6. Synthesis of MIT, DIT, T4, and conversion of T4 to T3 and rT3.** Image courtesy of : https://www.sciencedirect.-com/topics/neuroscience/thyronine

References

(2019). Retrieved 27 November 2019, from https://www.researchgate.net/-figure/The-TPO-structure-A-Schematic-view-of-the-human-TPO-structure-plain-arrows-indicate_fig2_581874 3

Bridget Brady MD, F. (2019). Thyroid Gland: Overview. Retrieved 26 November 2019, from https://www.endocrineweb.com/conditions/thyroid-nodules/-thyroid-gland-controls-bodys-metabolism-how-it-works-symptoms-hyperthyroid

Thyroid Hormone Synthesis. (2019). Retrieved 26 November 2019, from http://www.pathwaymedicine.org/thyroid-hormone-synthesis

Thyronine - an overview | ScienceDirect Topics. (2019). Retrieved 26 November 2019, from https://www.sciencedirect.com/topics/neuroscience/thyronine

How does the thyroid gland work?. (2019). Retrieved 26 November 2019, from https://www.ncbi.nlm.nih.gov/books/NBK279388/