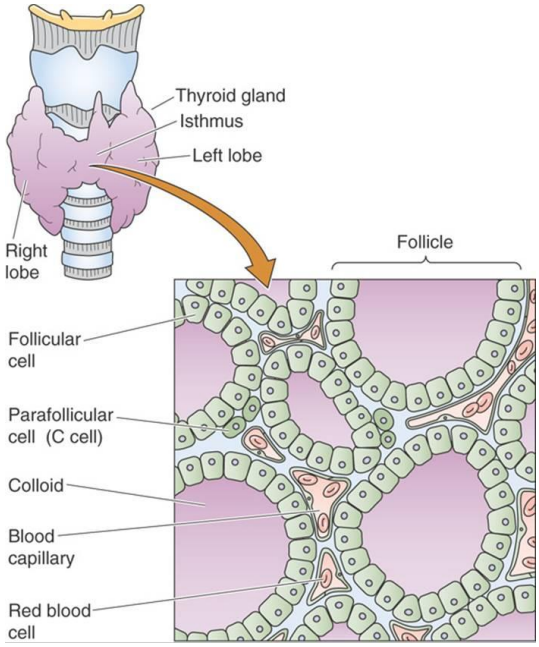
Thyroid Hormone Synthesis

Introduction

The Thyroid Gland is a gland in the neck that consist of 2 lobes and an isthmus in between them connecting them. Inside the Thyroid Gland, there are cells that synthesize the thyroid hormone. Inside the Thyroid Gland, the thyroid cells are surrounding each other in a circle. This circle is called a **Follicle**. The center of the Follicles is **Lumen**. So, in the follicle the lumen is surrounded by thyroid cells in the form of a circle. In the periphery of the follicle, there is blood. The blood is very important as it carries substances that enter in the synthesis of the Thyroid Hormones and the hormones are carried by the blood to the tissues after they are synthesized and released from the thyroid gland. Looking inside the Follicle, the lumen is in its right and the blood is in its left. The layer close to the **blood** is called **Basilar Membrane** or **layer** and the layer close to the **Colloid** is called **Apical Membrane** or **layer**.



Thyroid hormone synthesis

The Iodine is important in synthesis of the thyroid hormones. In the whole body, the iodine level is around 20mg. 80-85% of that iodine are present in the thyroid gland. Only a small ratio of iodine is distributed among other cells like salivary glands, muscles, etc. the cause is that iodine is used in the synthesis of the thyroid hormones.

Iodine is present in the blood in the form of **Iodide I−**. Iodine enters the follicular cell of the thyroid gland through a channel. This channel allows Iodide and Sodium to enter the follicular cell of the thyroid gland. This channel is called **Iodide/ Sodium Co-transport**. Now, both Sodium and Iodide are inside the follicular cell. The iodide moves toward the Apical membrane then cross to the colloid (lumen). In the colloid the **iodide I− will convert to iodine I2** through an enzyme called **Thyroperoxidase**. There are drugs that can inhibit that enzyme like Propylthiouracil which will be discussed later. Thyroperoxidase is an enzyme present in the colloid lumen that convert iodide to iodine. So, now the iodine is ready.

To synthesize thyroid hormones, DNA from the nucleus is needed to form copies of mRNA (messenger RNA) that goes to the Ribosomes and the Rough Endoplasmic Reticulum to form the protein. So, the DNA in the nuclear in the follicular cell is copied into mRNA then goes to Ribosomes and the Rough Endoplasmic Reticulum to form a very important protein called **Thyroglobulin (TG).** This Thyroglobulin is synthesized from follicular epithelial cells. This Thyroglobulin contain a very important amino acid called **Tyrosine**. There is large amount of Tyrosine present in the Thyroglobulin beside some other amino acids. This Thyroglobulin moves out to the colloid.

Both Iodine and Thyroglobulin in the colloid and what remain is to put them together. **Iodine is combined with Thyroglobulin** on its Tyrosine amino acid through an enzyme called **Thyroperoxidase**. So, Thyroperoxidase has 2 functions conversion of Iodide into Iodine and binding of Iodine to Thyroglobulin.

Two iodine molecules + a portion of Thyroglobulin = Diiodotyrosine (DIT).

One molecule of Iodine + a portion of Thyroglobulin = Monoiodotyrosine (MIT).

So, a long chain of Thyroglobulin consists of multiple Diiodotyrosine (DIT) and Monoiodotyrosine (MIT). Diiodotyrosine (DIT) and Monoiodotyrosine (MIT) can combine to form Triiodotyrosine (T3).

So, **T3 is formed from one Diiodotyrosine (DIT) and one Monoiodotyrosine (MIT)**. This process is called **Organification**.

Combination of two Diiodotyrosine (DIT) together to form Tetraiodotyrosine (T4) is a process called **Coupling Reaction**.

Now, hormones that are attached to each other on the Thyroglobulin protein and they are still ion the colloid (lumen).

How these hormones reach the blood.?

The full Thyroglobulin is **endocytoced** into the follicular cells through a process called **Endocytosis**. On the endocytoced Thyroglobulin, there are T3,T4 , DIT and MIT. Both the Endosome (with Thyroglobulin bound hormones) and the Lysosome fuse together. The lysosome breakdown the Thyroglobulin bound hormones to T3 and T4 (Active forms) and some DIT and MIT (inactive forms). Both T3 and T4 are released to the blood. But DIT and MIT are recycled back to be reused in synthesis of more T3 and T4.

Both T3 and T4 are released to the blood under the regulation of other hormones like TSH, which will be explained later.

This is the process of synthesis of the thyroid hormones.

Summary

1. Iodide reached the blood from the GIT from food like fish and other food that contains iodide.
2. Iodide is absorbed to the blood.
3. Iodides enter along with the Sodium to the Follicular cell.
4. Iodide moves to the colloid and is converted to Iodine through Thyroperoxidase.
5. The nucleus DNA is copied into mRNA that goes to the Ribosomes and the Rough Endoplasmic Reticulum to form the Thyroglobulin with multiple Tyrosine.
6. Thyroglobulin moves to the colloid where the Iodine gets attached to it forming Diiodotyrosine (DIT) and Monoiodotyrosine (MIT).
    a. 2 Iodine molecules + a portion of Thyroglobulin = Diiodotyrosine (DIT).
    b. One molecule of Iodine + a portion of Thyroglobulin = Monoiodotyrosine (MIT).
    c. DIT+ MIT bind together forming T3 through Organification.
    d. DIT+ DIT bind together forming T4 through Coupling Reaction
7. The full Thyroglobulin with the hormones undergo Endocytosis and enter the follicular cell back.
8. Both the Endosome (with Thyroglobulin bound hormones) and the Lysosome fuse together.
9. The lysosome breakdown the Thyroglobulin bound hormones to T3 and T4 (Active forms) (large amount) and some DIT and MIT (inactive forms)(tiny amount).

* Sometimes, a piece of TG without hormones is cut and reach the blood. It means that the Thyroid gland is functioning.

* In patients who underwent surgical removal of the thyroid gland and are given External T3 and T4, they will not have TG in their blood as the thyroid gland is not functioning.

Thyroid Hormone Synthesis Important Notes:

- Iodide is absorbed to the blood. Iodide enter along with the Sodium to the Follicular cell. Iodide moved to the colloid and is converted to Iodine through Thyroperoxidase enzyme.
- In the same time, the nucleus DNA is copied into mRNA that goes to the Ribosomes and the Rough Endoplasmic Reticulum to form the Thyroglobulin with multiple Tyrosine.
- Thyroglobulin moves to the colloid where the Iodine get's attached to it forming Diiodotyrosine (DIT) and Monoiodotyrosine (MIT).
  - Two Iodine molecules + a portion of Thyroglobulin = Diiodotyrosine (DIT).
  - One molecule of Iodine + a portion of Thyroglobulin = Monoiodotyrosine (MIT).
- DIT+ MIT bind together forming T3 through Organification.
- DIT+ DIT bind together forming T4 through Coupling Reaction
- The full Thyroglobulin with the hormones undergo Endocytosis and enter the follicular cell back.
- Both the Endosome (with Thyroglobulin bound hormones) and the Lysosome fuse together. The lysosome breakdown the Thyroglobulin bound hormones to T3 and T4 (Active forms) (large amount) and some DIT and MIT (inactive forms)(tiny amount).
- Free TG in the blood means a Functioning Thyroid Gland