**Short Communication**
Volume 08:02, 2024

Reports in Thyroid Research

ISSN: 2684-4273 Open Access

# Molecular Mechanisms of Thyroid Hormone Action

**Senem Manera***

*Department of Thyroid Research, Health Sciences University, Gazi Yasargil Education and Research Hospital, 21090 Diyarbakir, Turkey*

## Introduction

Thyroid hormones play a crucial role in regulating numerous physiological processes, including metabolism, growth, and development. The primary hormones produced by the thyroid gland, Thyroxine (T4) and Triiodothyronine (T3), exert their effects through complex molecular mechanisms that involve interactions with specific nuclear receptors. This effect is critical for thermogenesis, particularly in brown adipose tissue. Additionally, thyroid hormones can influence ion transport across cellular membranes and modulate intracellular signalling pathways such as the Phosphatidylinositol 3-kinase (PI3K) and Mitogen-Activated Protein Kinase (MAPK) pathways, which are involved in cell growth, differentiation, and apoptosis [1]. The interplay between genomic and non-genomic actions of thyroid hormones ensures a comprehensive regulation of cellular metabolism and physiological functions. These interactions influence the expression of various genes, thereby modulating metabolic pathways and cellular functions. Understanding the molecular mechanisms of thyroid hormone action is essential for elucidating how these hormones maintain homeostasis and how dysregulation can lead to thyroid-related disorders.

## Description

The molecular mechanisms of thyroid hormone action primarily involve the binding of T3, the active form of thyroid hormone, to Thyroid Hormone Receptors (TRs) located in the nucleus of target cells. These receptors, which belong to the nuclear receptor superfamily, function as transcription factors. Upon binding T3, TRs undergo a conformational change that allows them to regulate the transcription of target genes [2]. This process begins with T4 being converted to T3 by deiodinase enzymes in peripheral tissues. T3 then enters the nucleus and binds to TRs, which are often already bound to Thyroid Hormone Response Elements (TREs) in the promoter regions of target genes. Thyroid hormones, primarily thyroxine and triiodothyronine are critical regulators of metabolism, development, and growth, exerting their effects through complex molecular mechanisms. The synthesis and secretion of these hormones are controlled by the Hypothalamic-Pituitary-Thyroid (HPT) axis, where the hypothalamus releases Thyrotropin-releasing hormone, stimulating the pituitary gland to produce Thyroid-Stimulating Hormone (TSH), which in turn promotes thyroid hormone production in the thyroid gland.

Once secreted into the bloodstream, T4 and T3 are transported to target tissues, predominantly bound to plasma proteins such as Thyroxine-Binding Globulin (TBG), transthyretin, and albumin. T4, the more abundant but less active form, is converted into the more potent T3 within cells by deiodinase enzymes. T3 then enters the nucleus of target cells, where it binds to Thyroid Hormone Receptors (TRs) that are part of the nuclear receptor superfamily. These receptors function as ligand-activated transcription factors, modulating the expression of specific genes involved in metabolic processes, differentiation, and development. The TRs exist in two main isoforms, TR$\alpha$ and TR$\beta$, which are encoded by separate genes and have distinct tissue distribution patterns and physiological roles [3]. Binding of T3 to TRs induces a conformational change in the receptor, facilitating its interaction with thyroid hormone response elements (TREs) in the promoter regions of target genes. This interaction recruits coactivators or corepressors, depending on the presence of T3, thereby modulating gene transcription. The genes regulated by thyroid hormones encompass a wide array of functions, including those involved in basal metabolic rate, thermogenesis, lipid and carbohydrate metabolism, cardiac function, and central nervous system development.

In addition to these genomic effects, thyroid hormones also exert non-genomic actions by interacting with cytoplasmic or mitochondrial proteins, influencing cellular functions such as ion transport, oxidative phosphorylation, and mitochondrial biogenesis [4]. The T3-TR complex recruits coactivator proteins and promotes the transcription of genes involved in metabolic processes, such as those regulating glucose and lipid metabolism, thermogenesis, and protein synthesis. Additionally, thyroid hormones can exert non-genomic actions through interactions with mitochondrial proteins and plasma membrane receptors, influencing cellular functions rapidly and independently of gene transcription. These non-genomic effects include modulation of mitochondrial respiration, ion transport, and signal transduction pathways. Thyroid hormones also influence gene expression indirectly by interacting with other transcription factors and signaling pathways. For instance, they can modulate the activity of the peroxisome Proliferator-activated Receptor (PPAR) family, which plays a crucial role in lipid metabolism and inflammation. Furthermore, thyroid hormones can affect the expression of genes involved in the oxidative stress response and cellular differentiation, highlighting their broad regulatory capabilities.

In addition to their genomic actions, thyroid hormones exert non-genomic effects that do not involve direct regulation of gene transcription. These non-genomic actions occur rapidly and are mediated through interactions with mitochondrial proteins and plasma membrane receptors [5]. For example, T3 can bind to a specific receptor on the mitochondrial membrane, enhancing mitochondrial respiration and ATP production. Thyroid hormone action is tightly regulated at multiple levels, including hormone synthesis and release, peripheral conversion of T4 to T3, cellular uptake of hormones, and the intracellular availability of TRs. Dysregulation of any of these processes can lead to thyroid disorders such as hypothyroidism or hyperthyroidism, with widespread systemic effects. Advances in molecular biology have elucidated various components of thyroid hormone action, including the identification of deiodinase isoenzymes that regulate local T3 availability and the discovery of TR co-regulators that modulate receptor activity. Understanding these mechanisms has important clinical implications, particularly in the development of targeted therapies for thyroid-related diseases.

## Conclusion

Thyroid hormones exert their physiological effects through intricate molecular mechanisms involving both genomic and non-genomic pathways. By binding to nuclear thyroid hormone receptors and regulating gene transcription, as well as interacting with mitochondrial and membrane proteins, thyroid hormones influence a wide range of metabolic and cellular processes. Understanding these mechanisms is crucial for comprehending how thyroid hormones maintain metabolic homeostasis and for developing therapeutic strategies to address thyroid-related disorders. On-going research continues to unravel the complexities of thyroid hormone action, providing deeper insights into their role in health and disease. The molecular

***Address for Correspondence:** Senem Manera, Department of Thyroid Research, Health Sciences University, Gazi Yasargil Education and Research Hospital, 21090 Diyarbakir, Turkey E-mail: senem@manera.com*



**Received:** 29 May, 2024, Manuscript No. rtr-24-143701; **Editor Assigned:** 31 May, 2024, PreQC No. P-143701; **Reviewed:** 14 June, 2024, QC No. Q-143701; **Revised:** 20 June, 2024, Manuscript No. R-143701; **Published:** 28 June, 2024, DOI: 10.37421/2684-4273.2024.8.69

mechanisms of thyroid hormone action are fundamental to understanding their pervasive influence on human physiology. These mechanisms involve a complex network of regulatory steps, from hormone synthesis and release to intracellular signalling pathways that modulate gene expression and cellular metabolism. Thyroid hormones, through their interaction with nuclear receptors, control a vast array of physiological processes, highlighting their essential role in maintaining metabolic homeostasis and promoting growth and development.

The intricate regulation of thyroid hormone activity, including the conversion of T4 to T3 and the fine-tuning of receptor interactions, underscores the precision required for proper endocrine function. Disruptions in these mechanisms can lead to significant clinical manifestations, reinforcing the importance of on-going research to elucidate these pathways fully. Advances in our understanding of thyroid hormone action at the molecular level have the potential to inform the development of novel therapeutic approaches for thyroid disorders, improving patient outcomes and expanding our knowledge of endocrine regulation. The continued exploration of these molecular pathways promises to reveal further insights into the intricate balance of hormonal control and its impact on health and disease.

## Acknowledgement

None.

## Conflict of Interest

None

## References

1. Sinha, Rohit A., Brijesh K. Singh and Paul M. Yen. "Direct effects of thyroid hormones on hepatic lipid metabolism." *Nat Rev Endocrinol* 14 (2018): 259-269.
2. Ritter, Megan J., Izuki Amano and Anthony N. Hollenberg. "Thyroid hormone signaling and the liver." *Hepatology* 72 (2020): 742-752.
3. Zucchi, Riccardo. "Thyroid hormone analogues: an update." *Thyroid* 30 (2020): 1099-1105.
4. Reinke, Hans, and Gad Asher. "Circadian clock control of liver metabolic functions." *Gastroenterology* 150 (2016): 574-580.
5. Philippe, Jacques, and Charna Dibner. "Thyroid circadian timing: Roles in physiology and thyroid malignancies." *J Biol Rhythm* 30 (2015): 76-83.

***How to cite this article:*** Manera, Senem. "Molecular Mechanisms of Thyroid Hormone Action." *Rep Thyroid Res* 8 (2024): 69.