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# ROLE OF PERSONALIZED MEDICINE IN THYROID CANCER: LATEST ASPECTS

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## ABSTRACT

Thyroid cancer is the prevalent endocrine cancers, and its incidence is growing all over the world, according to the World Health Organization. About 5–10 per cent of individuals with differentiated thyroid carcinoma may experience destructive behavior and metastasis, and their disease will be refractory to therapeutic techniques such as radiation therapy for an unknown cause, despite the favorable prognosis. Most aggressive, deadly, and unresponsive type of the cancer is thyroid carcinoma. Regrettably, existing treatments are not specific and are thus considered poor in treating thyroid malignancies. Consequently, mortality in this malignancy despite progress in diagnosis and treatment is a prominent issue in medicine. evidence linking cellular, molecular, and genetic to a diagnostic and therapeutic simplification. With the new idea of personalized therapy for thyroid cancer diagnosis, arranging the treatment, discovering the success of the treatment and assessing the visualization has improved in the last ten years. Personalized medicine treatment for thyroid cancer is supported by these studies. According to the findings of this review, cellular and molecular processes of cancer will lay concrete on the way for the development of narrative biomarkers for personalized medicine that take individual variations into account.

**KEYWORDS:** Personalized Medicine, Carcinoma, Endocrine, Metastasis.

## INTRODUCTION

Personalized medicine is described as identifying individual according to their biological details in order to separate them into various subpopulations, who then get distinct treatments, diagnoses, and predicted response to disease(1). Precise medicines, stratification drugs, and P4 drugs are used for precautionary drugs (2). Personalized treatment focuses on treating each patient differently, taking into account each individual's distinct genetic information. Tumor therapy that is subset of personalized medicine in context of genetic-variation helps to identify more effective preventive, early diagnosis, and treatment options for cancers(3). Completion of the Human Genome Project (HGP) revealed that about 99.9% of the human genome sequence is the same among people, but there is a 0.1% difference in the genetic variants that determine a person's risk of disease, severity, and response to treatment (4,5). Thyroid cancer is the most frequent endocrine risk, the prevalence of papillary thyroid cancer (PTC) has been steadily growing for a very long period as a result of improved detection and treatment methods (6,7).

The majority of thyroid cancers are epithelium tumors that develop from follicle thyroid cells; this is the most common type of primary thyroid cancer. Increases the attention in the subject of personalized medication have occurred in recent years. Indeed, one has to speculate whether personalized medicine will get out of hand as genomic testing becomes increasingly available directly to the consumer. Ultimately, it must be remembered that despite all these technological advances, several tumor syndromes can be detected through rigorous clinical analysis. In the case of endocrine-related neoplasia in particular, the doctor must pay attention to the phenomena or phenotypic profile associated with the series of inheritable endocrine tumor syndromes. Unsurprisingly, several of the hereditary tumor syndromes were originally described and named long before genetic causes were recognized. In reality, it should be dominant to the healthcare professionals to use meticulous observation the findings to decision on treatment options and, far more importantly, to give priority on medical genetic testing (8).

## HISTOLOGICAL FEATURES OF THYROID CANCER

Thyroid cancers are classified into papillary carcinoma (PTC), follicular carcinoma (FTC), medullary thyroid carcinoma (MTC), anaplastic thyroid carcinoma (ATC), primary thyroid cancer (ATC), primary thyroid cancer primary thyroid sarcoma (PST). The PTC accounts to 80% of all thyroid malignancies (9), FTC, on the other hand, are the second most frequent malignancy. The MTC accounts for around 3% of all thyroid cancers (12). ATC is the type of TC, accounting for around 2 percent of all cases, whereas PLT and PST are extremely rare. In fact, PTC happens more commonly in children and patients under the age age of 50 (11), FTC happens more commonly in patients under the age of 60 (9), and ATC occurs more frequently in patients between the ages of 60 and 70 (13).

## MOLECULAR CHARACTERISTICS OF THYROID CANCER

There are a variety of hereditary modifications associated with ATC that specifically cause dysfunction in the ERK1 / 2-MEK1 / 2 and PI3K-AKT flagging pathways(14) and BRAF able to target downstream target molecules such as MEK and ERK (15). In, MAPK signaling pathway, BRAF is an intermediary product, and transcription factors that are required for cell growth and differentiation, as well as proliferation and endurance, are formed. The RAS mutation is another significant frequent variation in thyroid cancer that has to be highlighted. Ras proteins are proto-oncogenes that have been found to be frequently altered in a various type of human cancers. These GTPases implicated in the cell growth and cell endurance pathways. Point mutations at codon twelve, thirteen or sixty-one of the RAS gene aassociated with cell-proliferation along with tumor growth, respectively (17).

The MAPK signaling pathway plays a central role in the guideline on cell expansion and endurance and in human tumorigenesis. Thyroid malignancies are associated with increased phosphorylation of AKT, which is a marker of the PI3KAKT signaling pathway. RAS adaptation has been shown to specifically stimulate the PI3KAKT signaling pathway in thyrocyte's, indicated by the relationship among RAS variations and AKT phosphorylation (18). However, the phosphoinositide 3-kinase protein kinase B/Akt (PI3K-PKB/AKT) pathway, a critical signaling route in the development of many organisms. Its unregulated activation as a result of many alterations in receptor tyrosine kinases (RTKs) have a cell-proliferation in carcinogenesis, which has been observed in thyroid cancer (19). Hereditary alterations have been found to activate the PI3KAKT gene which are the genetic cause of follicular thyroid cell tumor, which began with Cowden's disease and has progressed to the present (20,21).

Phosphatidylinositol 4,5-bisphosphate-3-kinase (PI3K) have been occupied in thyroid cancers such as FTC, PDTC, and ATC, and have been used in a number of cases of thyroid cancers such as PDTC and ATC(22,23,24). Besides catenin (cadherin-associated protein), there is a long list of additional altered genes in thyroid tumorigenesis, such as P53 alterations, which are detected in 14 percent of malignant thyroid tumors, with the frequency being higher in inefficiently separated and anaplastic thyroid cancers.Fareed, et al. 2001 investigated the rate of change of p53 as a proportion of the genomic instability (hypermutability) of harmful thyroid tumors (49). The thyroid epithelial cells (thyrocytes) undergo epigenetic changes that differ from hereditary changes. These epigenetic changes include DNA-methylation, variety of histones, and micro-RNA, all of which could affect chromosome transformation along with the quality of articulation structure without a change in the exact DNA sequence (46). It is essential to select between these epigenetic alterations because they may represent potential therapeutic strategies for the treating of thyroid cancer that can be personalized patien t(25).

## SOME DRUGS THAT TARGETING IN ATC

Much longer endurance was found in mouse models of BRAFV600E-positive ATCs with dabrafenib/trametinib (in contrast to BRAF inhibitor-treated models)(42). A paper showed an 81-year-old man who had a developing neck masses and who is sent for additional surgery because of an analysis of MTC (medullary thyroid cancer). Dabrafenib is a drug used to treat cancers with BRAF mutations. To diminish that predicament, the BRAF inhibitor dabrafenib was administered along with the MEK inhibitor trametinib, given to prevent the development of confrontation to dabrafenib or other BRAF inhibitors (43). In a work published in 2004, Kurata et al. (44) investigated the efficacy of inhibiting the started RAS/RAF/MEK pathway in 4 human ATC cell-lines (ACT-1, OCUT-2, OCUT-4, and OCUT-6) in order to determine whether or not the inhibition was effective.ACT-1 and OCUT-6 were transformed with wild-type BRAF and NRAS mutations, OCUT-4 was transformed with a BRAF mutation, and OCUT-2 was transformed with BRAF and PI3KCA mutations. Dabrafenib inhibited the suitability of BRAF-transformed cells through the G0/G1-capture, which

decreased the phosphorylation of MEK and ERK in the cells. Through the downregulation of ERK phosphorylation, Trametinib reduced the cell ability to survive. The double bar created by dabrafenib and trametinib showed cytostatic effects on the four ATC cell lines tested in this study (45).

## MORTALITY

Despite a considerable increase in the number of cases, the mortality rate for TC iss not greater than before in a respective manner. It appears to be twice as common in females, with annual mortality rates between 0.4 - 2.8 and 0.2 - 1.2/100 for both genders, respectively, compared to male participants (26).

## RISK FACTORS

People at risk for TC have a multifactor etiology, which is the consequence of multiple genetic and environmental variables interacting in their environment. The following significant risk variables have been identified through epidemiological investigations.

## GENDER AND AGE

Thyroid cancer (TC) is 2-4 times further likely to occur in women, which are often better predictors of malignant development than men, who are at higher risk of developing malignant masses. It is extremely uncommon in patients under the age of 16 years, with an annual incidence of 0.02–0.3/100, and exceptionally uncommon in patients under the age of 10 years (27,28,29). The prevalence of the disease rises with age, and the typical age of diagnosis is 45–50 years. Still, it is necessary to emphasize the following points:

(1) While it is uncommon, the incidence of TC in infancy is associated with a more advanced state of illness at the time of diagnosis;

(2) It has been shown that people over the age of 60 have an increased chance of developing thyroid nodules that are cancerous.

## RACIAL DIFFERENCES

TC rate is divided according to geography and ethnicity. It occurs more frequently in certain countries, such as Iceland, Hawaii, Philippines, Japan, and Israel, than in other countries, such as North America, Canada, and the United States. In the United States, Caucasian plunging subjects had a higher risk of recurrence than Afro-American, Hispanic, Hawaiian, Chinese, or Japanese females, who still have a recurrence rate that is twice as high in their countries of origin. This research suggests that such variations may be caused by both environmental and genetic variables, and that should be taken into consideration (27,28,29,30).

## ENVIRONMENTAL FACTORS

This section examines the importance of several factors.

(1) Ionizing radiation exposure

(2) Age when the exposure occurred

(3) A past history of benign and malignant thyroid cancer

(4) Amount of iodine intake

(5) BMI: determining weight-related issues, and

(6) Biochemical functions

## A. PREVIOUS REVELATION TO IONIZING RADIATION

Exposure has been known to play a role in thyroid cancer since the first atomic bomb detonated in Japan in 1950. Thyroid nodules, whether benign or malignant, are more common in people who have previously been exposed to ionizing radiation for exterior irradiation of neck, and palpable nodules are seen in 20 percent to 30 percent of those who have been exposed to the radiation (31). Hematological cancers such as lymphoma or leukemia often suffer from radiation-induced damages (32,33). The bas baseline age for clinical confirmation of thyroid cancer has been determined to be somewhere between 4 and 5 years old, and is peaking far ahead of time. For dosages between 10 and 1500 cGy, the linear cancer risk rises. The risk of radio-induced cell necrosis increases with greater dosages.

## B. AGE AT THE TIME OF IRRADIATION

After fifteen to twenty years, there is no longer any increased risk. The excess risk for TCa in children exposed to 1Gy doses is equal to 7.7 time's superior than in the common population (34). Post-Chernobyl have shown a higher prevalence of thyroid cancer in people ages 5 months to 10 years (35).The age at which TCa is diagnosed is similar for both genders. Recurring histopathological findings included robust as well as follicular variants of PTC. In the early stages of the disease, lymph node and lung tumors had developed, and the disease was more commonly associated with autoimmune thyroiditis (35,36).

## PERSONALIZED ASPECTS IN THYROID CANCER

Personalized medication is the innovative practice of patient treatment in which physicians select medications based on their expertise and genetics. Cluster CGH and next-generation sequencing (NGS) have assisted researchers in conducting high-throughput change screening and genome wide duplicate number examination.N. Pozdeyev and

companions completed a large scope inquiry to describe the hereditary scenes of ATCT and to understand hereditary alterations of various analytic, prognosis, and therapeutic implications (37). The thyroid malignant growth therapy method includes inventive based approaches that concentrate on iodine reuptake pathways (38,39). Barbolosi and colleagues presented a numerical model for Tg kinetics, RAI therapy choice, and grouping patients into responders and non-responders (40). A new way to examine cancer genetics in the blood has recently been developed in the form of a fluid biopsy. Specific thyroid disease detection and anticipation methods deliberate over fluid biopsy (41).One of the main innovations in the field of novel diagnoses is the circulation of cell-free DNA (cfDNA).In addition to blood, additional organic liquids like urine, pleural, cerebrospinal, or cytology sample may be used to assess residual flow (48). Previous studies found that cfDNA fixation is associated with lung cell disintegration, which is correlated with a worse outcome (19). The presence of cfDNA levels can be associated with many pathological diseases, including as cancer, sepsis, and various other situations including maternity and activity. It is necessary to examine the dynamic limits of a biomarker in order to determine whether or not it is useful as an analytical instrument. Plasmatic cDNA introduces new ways in medical applications since it has a changing rate that provides valuable data for a biomarker. (47).

## FUTURE POSSIBILITIES

Personalized cancer therapy has opened up a new horizon in the fight against cancer. The field of fundamental sciences, as well as pharmacogenetics and drug design, will need to progress further in order to make functional applications of this research possible. Analysts are constantly in search for innovative approaches to disease detection and treatment that are more efficient while also reducing costs and adverse effects in patients. Over the past several years, there have been several approaches to cancer therapy, which has allowed several treatment options.

## CONCLUSION

Personalized medication is a number of diagnostics, predictive, and targeted therapies performed according to individual patient's characteristics. As the population of developed and emerging nations grows in the future, the prevalence of diseases such as cancer among the general public will increase as a result of future expansion. Thyroid cancer is the most aggressive, lethal, and incurable type of cancer and it affects both men and women. Unfortunately, existing medicines are not targetable, and as a result, they can only play a limited role in the treatment of thyroid cancer patients.cfDNA is considered as one of the advances in the diagnostic area. Consequently, mortality from this type of cancer growth presents a significant challenge to appropriate detection and treatment.The nature of personalized medicine requires an increased focus on pharmacogenetics investigations. cfDNA is regarded as one of the most significant advancements in the field of inventive and it is used as a fluid biopsy in many cases.Interestingly, the application of personalized medication is still in its infancy, and future randomized clinical trials will be the basis for its further expansion (42). To achieve these goals, a collaborative effort between scientists and physicians is essential in order to advance targeted therapy and personalized medicine for thyroid cancer growth.

## ABBREVIATIONS

**FTC**: Follicular thyroid carcinoma

**ATC**: Anaplastic thyroid carcinoma

**HGP**: Human Genome Project

**PDC**: Differentiated carcinoma

**MTC**: Medullary thyroid carcinoma

**MAPK**: Map kinase

**RAS**: Renin angiotensin system

**PTEN**: Phosphatase and tensin homolog

**PDTC**: Poorly developed thyroid carcinoma

**cfDNA**: Circulating cell-free DNA

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