Hereditary Thyroid Cancer

Precision Panel

Overview

Thyroid malignancies are divided into papillary carcinomas (80%), follicular carcinomas (10%), medullary thyroid carcinomas (5-10%), anaplastic carcinomas (1-2%), primary thyroid lymphomas and primary thyroid sarcomas. Hereditary thyroid cancer can arise from either follicular cells, known as familial non-medullary thyroid cancer (FNMTC), or from calcitonin-producing C cells, known as familial medullary thyroid cancer (FMTC). The latter may be related to multiple endocrine neoplasia (MEN) IIA or IIB or pure FMTC syndromes. Advances in molecular genetics have helped identify the presence of several familial cancer syndromes with FNMTC, usually papillary and follicular cancers.

Hereditary cancer syndromes are encountered in all medical specialties. Although they account for about 5% of all malignancies. Most hereditary cancers are associated with a "germline mutation" that will be present in every cell of the human body. Identification of patients at risk of inherited cancer susceptibility is dependent upon the ability to characterize genes and alterations associated with increased cancer risk as well as gathering a detailed personal and family history aiding in the identification of the mode of inheritance as well as other family members at risk of suffering from this susceptibility. Most of these genes are inherited in an autosomal dominant fashion.

The Igenomix Hereditary Thyroid Cancer Precision Panel can be used as a screening and diagnostic tool ultimately leading to a better management and prognosis of the disease. It provides a comprehensive analysis of the genes involved in this disease using next-generation sequencing (NGS) to fully understand the spectrum of relevant genes involved, and their high or intermediate penetrance.

Indications

The Igenomix Hereditary Thyroid Cancer Precision Panel is indicated in those cases where there is a clinical suspicion of thyroid cancer alongside family history, presenting with the following manifestations:

- Painless, palpable, solitary thyroid nodule
- Hoarseness
- Parathyroid tumors
- Pancreatic tumors: gastrinoma, insulinoma, glucagonoma etc
    - Diarrhea
    - Abdominal pain
    - Hypoglycemia
    - Hyperglycemia
- Anterior pituitary tumors: prolactinoma, somatotropinoma

  - Headaches
  - Visual field defects
- Pheochromocytoma
  - Recurrent hypertension
  - Sweating
  - Palpitations
- Marfanoid phenotype: slender body, long thin extremities, abnormal laxity in joints, pectus excavatum etc

Clinical Utility

The clinical utility of this panel is:

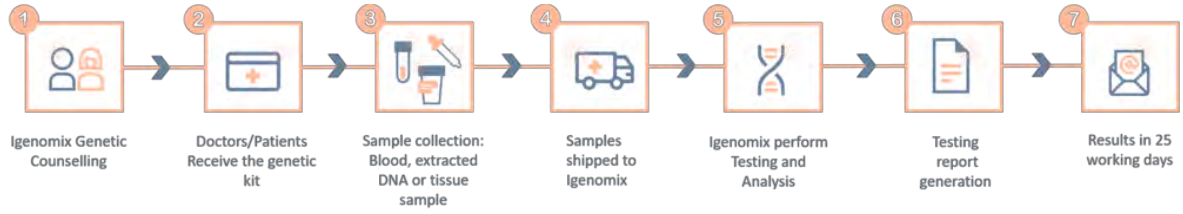
- The genetic and molecular diagnosis for an accurate clinical diagnosis of a patient with personal or family history suggestive of hereditary thyroid cancer.
- Early initiation of treatment with a multidisciplinary team for appropriate surveillance, surgery, radiation therapy or ablation.
- Risk assessment of asymptomatic family members according to the mode of inheritance
- Reduce morbidity related to thyroid cancer or morbidity secondary to complications of surveillance and treatment.
- Improved pathways from diagnosis to treatment in susceptible populations.

Genes & Diseases

GENE	OMIM DISEASES	INHERITANCE*	% GENE COVERAGE (20X)	HGMD**
CDKN1A	Multiple Endocrine Neoplasia Type 1	-	100%	2 of 2
CDKN1B	Multiple Endocrine Neoplasia Type 1, Multiple Endocrine Neoplasia Type 4	AD	99.99%	19 of 20
CDKN2B	Familial Melanoma, Multiple Endocrine Neoplasia Type 1	-	100%	7 of 7
CDKN2C	Multiple Endocrine Neoplasia Type 1	-	99.83%	2 of 2
FOXE1	Athyreosis, Bamforth-Lazarus Syndrome, Familial Papillary Or Follicular Thyroid Carcinoma, Hypothyroidism, Nonmedullary Thyroid Cancer	AD,AR	84.65%	14 of 22
HABP2	Familial Papillary Or Follicular Thyroid Carcinoma, Venous Thromboembolism, Nonmedullary Thyroid Cancer, Nonmedullary	AD	100%	2 of 2
HRAS	Bladder Cancer, Costello Syndrome, Epidermal Nevus, Linear Nevus Sebaceus Syndrome, Schimmelpenning-Feuerstein-Mims Syndrome, Nonmedullary Thyroid Cancer	AD	100%	34 of 34
MEN1	Familial Isolated Hyperparathyroidism, Insulinoma, Multiple Endocrine Neoplasia Type 1, Pituitary Gigantism, Prolactinoma	AD	99.90%	871 of 876
MINPP1	Familial Papillary Or Follicular Thyroid Carcinoma, Nonmedullary Thyroid Cancer	AD	100%	2 of 2
NRAS	Colorectal Cancer, Epidermal Nevus, Large Congenital Melanocytic Nevus, linear Nevus Sebaceus Syndrome, Neurocutaneous Melanosis, Noonan Syndrome, RAS-associated Autoimmune Lymphoproliferative Syndrome Type 4, Schimmelpenning-Feuerstein-Mims Syndrome, Nonmedullary Thyroid Cancer	AD	100%	15 of 15
RET	Congenital Failure of Autonomic Control, Haddad Syndrome, Hereditary Pheochromocytoma-Paraganglioma, Multiple Endocrine Neoplasia Type 2A, Multiple Endocrine Neoplasia Type 2B, Pheochromocytoma, Renal Agenesis, Sporadic Pheochromocytoma/Secreting Paraganglioma, Familial Medullary Thyroid Carcinoma	AD	100%	453 of 454
SRGAP1	Nonmedullary Thyroid Cancer	AD	99.92%	5 of 5

*Inheritance: AD: Autosomal Dominant; AR: Autosomal Recessive; X: X linked; XLR: X linked Recessive; Mi: Mitochondrial; Mu: Multifactorial.
**Number of clinically relevant mutations according to HGMD

Methodology



Contact us

Call +34 963 905 310 or send an email to supportspain@igenomix.com for any of the following objectives:

- Get more information about the test.
- Request your kit.
- Request a pick up of the kit after collecting the sample.

References

1. Dralle, H., Machens, A., & Lorenz, K. (2008). Hereditäre Schilddrüsenkarzinome [Hereditary thyroid cancer]. *Der Chirurg; Zeitschrift fur alle Gebiete der operativen Medizen*, *79*(11), 1017–1028. https://doi.org/10.1007/s00104-008-1558-y
2. Guilmette, J., & Nosé, V. (2017). Hereditary and familial thyroid tumours. *Histopathology*, *72*(1), 70-81. doi: 10.1111/his.13373
3. Accardo, G., Conzo, G., Esposito, D., Gambardella, C., Mazzella, M., Castaldo, F., Di Donna, C., Polistena, A., Avenia, N., Colantuoni, V., Giugliano, D., & Pasquali, D. (2017). Genetics of medullary thyroid cancer: An overview. *International journal of surgery (London, England)*, *41 Suppl 1*, S2–S6. https://doi.org/10.1016/j.ijsu.2017.02.064
4. Haugen, B., Alexander, E., Bible, K., Doherty, G., Mandel, S., & Nikiforov, Y. et al. (2016). 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid*, *26*(1), 1-133. doi: 10.1089/thy.2015.0020
5. NCCN Clinical Practice Guidelines in Oncology: Thyroid Carcinoma. Version I.2016. National Comprehensive Cancer Network. (2021). Retrieved 18 February 2021, from https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf.