MEDGENOME | Prima Cancer Genetics

ThyroTrack

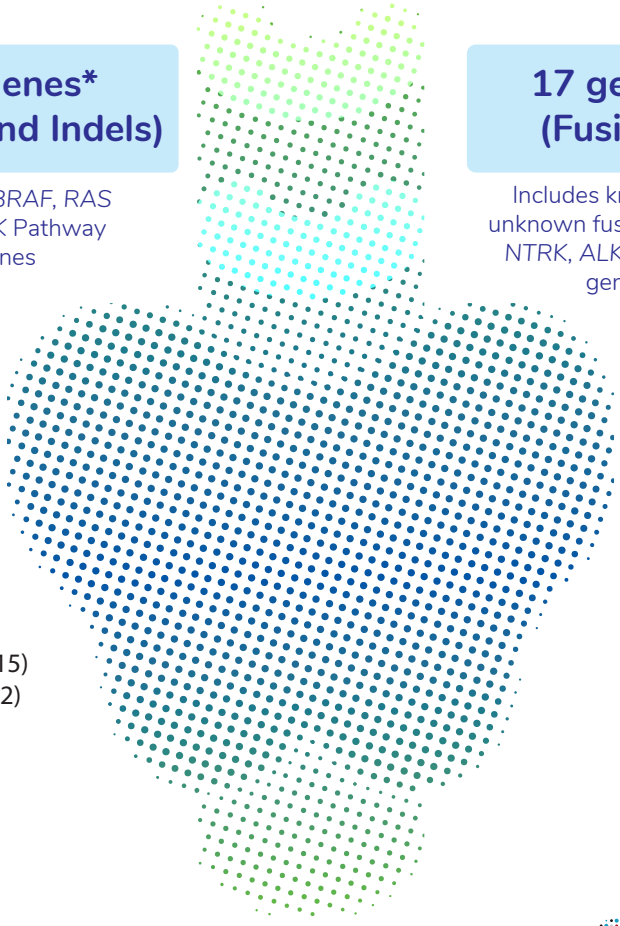
Next generation sequencing based test to detect genomic biomarkers in thyroid nodules

37 genes* (SNVs and Indels)

Includes *BRAF*, *RAS* and *P13K* Pathway genes

17 genes* (Fusions)

Includes known and unknown fusions in *RET*, *NTRK*, *ALK* and other genes



*As per ATA (2015) and NCCN (2022) Guidelines

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What is a thyroid nodule?

Thyroid nodules are solid or fluid-filled lumps that form within the thyroid, a small gland located at the base of your neck, just above the breastbone. Most thyroid nodules aren't serious and don't cause symptoms. Only a small percentage of thyroid nodules are cancerous.

Are all thyroid nodules cancerous?

FNA biopsy of thyroid nodules is the gold standard to identify diagnosis, prognosis, and treatment. Bethesda system for reporting thyroid cytopathology classifies 55% - 74% of thyroid nodules as definite benign and 2%-5% as definitive malignant. However, irrespective of the size, for 30% of nodules FNA cytology results are indeterminate (Bethesda III to IV). These nodules have challenges with regard to ideal diagnostic and therapeutic management [PMID: 29091573]. Bethasda I and II category nodules can also be cytologically insufficient or sonographically suspicious. All such nodule categories would benefit from molecular testing.

How molecular testing helps in clinical management decisions?

Molecular testing in the nodules can help to identify genetic mutations which provide an accurate diagnosis, prognosis, and treatment recommendations. Certain genomic alterations if found to be present in the thyroid nodule indicates that there is a high risk of the nodule being cancerous eg. *BRAF V600E* etc. Conversely, if certain gene mutations are absent, the nodule is most likely benign. The information about genetic alterations determines cancer probability in thyroid nodules with indeterminate cytology, informing the most appropriate management of these patients.

Genomic alterations in different thyroid cancer types

Gene	Papiliary carcinoma	Follicular carcinoma	Poorly differentiated carcinoma	Anaplastic carcinoma
RET/PTC	10-20%			
TRK	<5%			
BRAF	40-45%		10-20%	10-20%
RAS	10-20%	40-50%	20-40%	20-40%
TERT			40-50%	40-50%
PAX8/PPARγ		12-35%		
PTEN		<10%		5-15%
TP53			20-30%	50-80%
CTNNB1				5-60%
PIK3CA		<10%	5-10%	10-20%
AKT1			5-10%	5-10%
EIF1AX			11%	9%
MED12			15%	
RBM10			12%	

Reference: Dettmer, M.S., Schmitt, A., Komminoth, P. et al. Poorly differentiated thyroid carcinoma. Pathologe 41, 1–8 (2020). https://doi.org/10.1007/s00292-019-0600-9

MedGenome Thyrotrack Test

NGS based panel test to determine the mutational profile of thyroid nodules for proactive and accurate diagnosis, prognosis and treatment decision.

Simultaneous high throughput sequencing analysis of 40 unique genes for SNVs, InDels and fusions

Provides comprehensive understanding of thyroid nodule/tumour biology

Helps in predicting accurate diagnosis or prognosis of thyroid nodules with indeterminate cytology

Determines informed decisions for surgery plans

Identifies actionable variants in advanced cancer types for informed treatment decisions

Interpretation and Reporting is done according to NCCN (2022) and ATA guidelines (2015)

Who can be tested?

1. Thyroid FNA with indeterminate cytology (Bethesda categories III and IV)
2. Malignant thyroid cytology (Bethesda category V and VI), when results of the NGS are expected to affect the decision for extent of oncological surgery/treatment
3. Benign thyroid cytology (Bethesda category II), when strong suspicion exists on clinical grounds such as presence of a highly suspicious sonographic pattern
4. Bethesda category I nodules which are cytologically insufficient and suspicious on sonographic findings
5. When the diagnosis of thyroid cancer is established cytologically or histologically and molecular profiling will affect decision regarding radioactive iodine therapy, intensity of follow up, or for selection of targeted therapies in patients with advanced cancer

Clinical Utility

Diagnostic Importance

Accurate diagnosis of benign category nodules with a clinical suspicion for malignancy

Stratification of indeterminate nodules into likely benign/ likely malignant category

Pre-Operative Prognostication

Informed decisions on the surgery plans and extent of surgery

Therapeutic Targets

Detection of therapeutic targets for approved drugs or enrolment into a clinical trial.

Assay Specifications

Sample Requirements*	FNAC Fluid in RNA later; Tissue in RNA later ; FFPE tissue block
FFPE block requirement*	Cross-sectional tumor area of 25mm^2 containing at least 40 µm of tumor
Tumor Purity Minimum	20%
DNA or RNA input required	70-100 ng
Limit of detection	5% VAF for SNV and INDELs >10 spanning reads for fusions
Panel size	40 unique genes (Complete coding regions are covered) 37 genes analysed for SNVs and InDels; 17 genes analysed for fusions (All partners can be identified)
Depth of sequencing	Average >250X
Analytical Sensitivity	98%
Analytical Specificity	>99.9%

VAF-Variant allele frequency; SNV-Single nucleotide variation; INDELs - Short insertions & deletions

Gene List

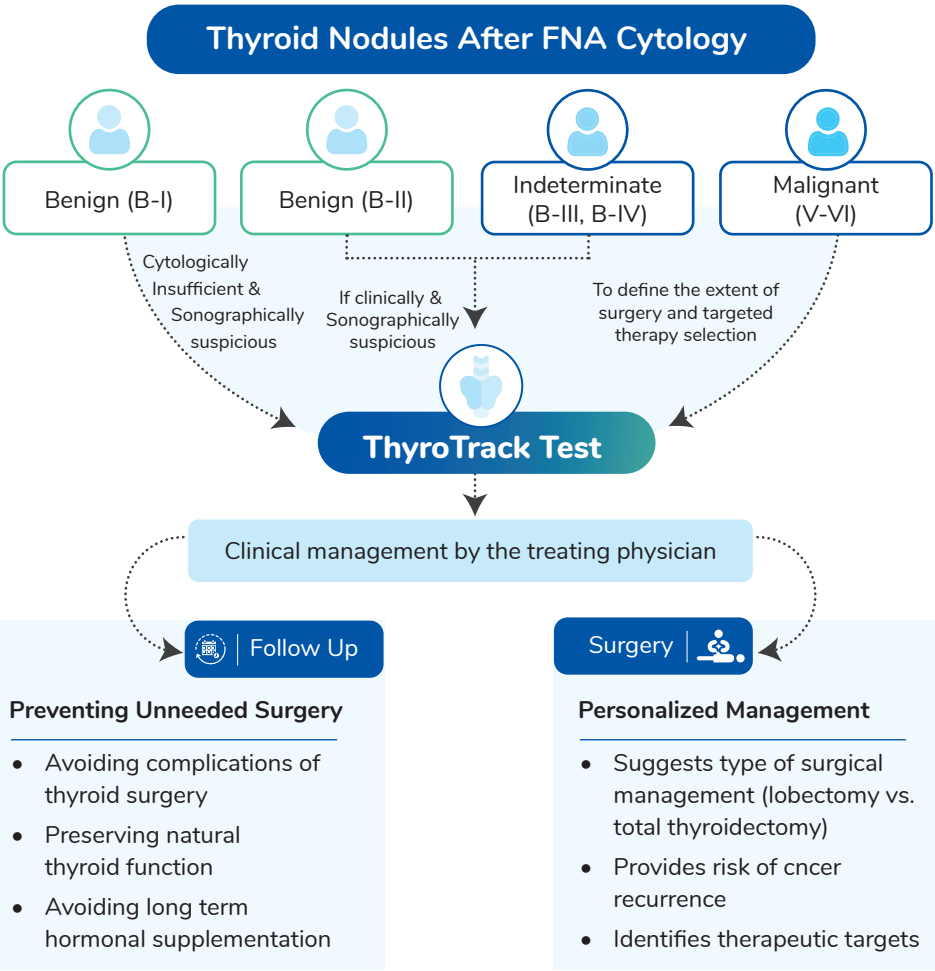
SNV's and Short Indels									
AKT1	*CHEK2*	*ERBB4*	*FGFR4*	*IDH2*	*NF2*	*NTRK3*	*RAF1*	*TERT*	*TSHR*
ALK	*CTNNB1*	*FGFR1*	*GNAS*	*KDM6A*	*NRAS*	*PIK3CA*	*RET*	*TG*	*VHL*
APC	*EIF1AX*	*FGFR2*	*HRAS*	*KRAS*	*NTRK1*	*PPARG*	*ROS1*	*TP53*	
BRAF	*EP300*	*FGFR3*	*IDH1*	*MET*	*NTRK2*	*PTEN*	*STK11*	*TSC2*	
Fusions									
ALK	*EML4*	*FGFR2*	*FGFR4*	*MET*	*NTRK2*	*PPARG*	*RET*	*SS18*	
BRAF	*FGFR1*	*FGFR3*	*KIF5B*	*NTRK1*	*NTRK3*	*RAF1*	*ROS1*		

Test Details

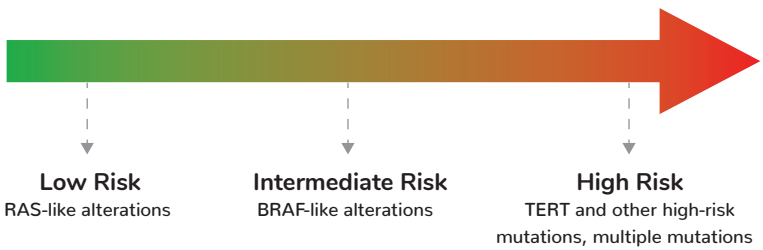
Test Code	Name	TAT	Sample Type	Storage Condition
MGM2538	**Thyroid Prognostication NGS Panel (Thyrotrack)**	3 weeks	FNAC fluid in RNA Tissue in RNA later	Shipped at 2-4 degree Celsius
			FFPE Tissue Block FFPE Cell Block	Room Temperature

Ultrasound findings/ Cytology report is mandatory with the sample.

Tumour cellularity will not be determined in samples in RNA later solution.



Risk of Developing Malignancy in Thyroid Nodules



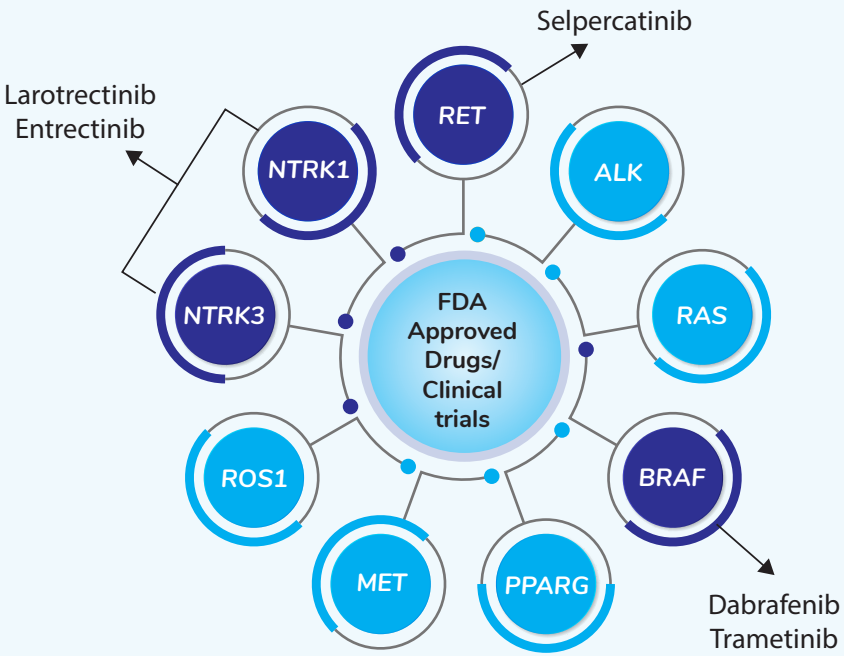
Clinical Evidences

Positive testing for BRAF, RET/PTC or PAX8/PPARγ was specific for a malignant outcome in 100% of cases, whereas RAS mutations had an 84% risk of cancer and a 16% chance of benign follicular adenoma [PMID: 24811481].

462 thyroid nodules with AUS/FLUS cytology were assessed using mutation profiling ; 31 were positive on mutational analysis (6.7%). 98 of the cases (21%) had a definitive diagnosis by either surgical (n=96) or non-surgical (n=2) methods [PMID: 26356635].

In the largest prospective study of nodules with indeterminate cytology (n=653) ; detection of mutations was reported to convey an 88% risk of cancer among nodules with surgical follow-up; 63% of cancers on final histopathology were identified with a positive mutation preoperatively and 94% of nodules that were negative on mutation analysis had a benign final histopathology [PMID: 21880806].

Therapeutic targets



About MedGenome

MedGenome is a Global Leader in Genetic Testing services, Genomics Research and drug discovery solutions. MedGenome is committed to deliver world class genomic solutions with greater precision and accuracy to empower every human being for better management of their health.

MedGenome is the only CAP accredited Genetic testing lab in India that offers 1300+ genetic tests backed by the best and the latest testing technologies available across the world.

MedGenome is dedicated to bring the best precision testing solutions for quicker and smarter diagnosis of the complex diseases. We are working towards democratizing the access of quality and affordable genetic solutions to serve over 4 billion people for their healthcare needs through the power of genetic testing.

We are MedGenome.

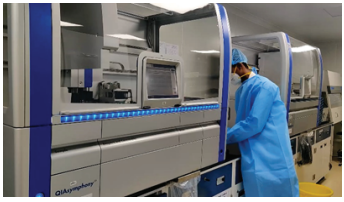
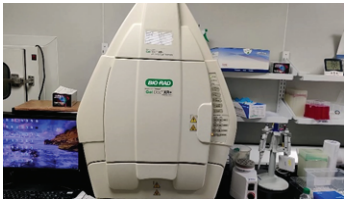
- Science is our DNA
- Innovation is our Focus
- Precision is our Expertise
- Human Impact is our Vision

Our Expertise

Largest CAP-accredited and NABL-certified Genomics sequencing lab in South Asia	2,50,000+ Exomes and Genomes sequenced	First and only Lab with CAP accreditation for Whole Genome and Whole Exome Testing	1300+ Genetic tests across various diseases categories
700+ Clinical Geneticists, Genome Analysts, Bioinformatics Engineers	Founded GenomeAsia 100K, an initiative to sequence 100K individuals of Asian descent	Successfully tested about 30,000 NIPT samples with no false-negative	First Lab to offer Whole-genome sequencing SPIT-SEQ through NGS for MDR TB.
First Validated Liquid Biopsy (OncoTrack) in India	First in India to introduce Tumour mutation burden (Cancer Agnostic Marker), Clinical Exome & Whole Exome testing.		

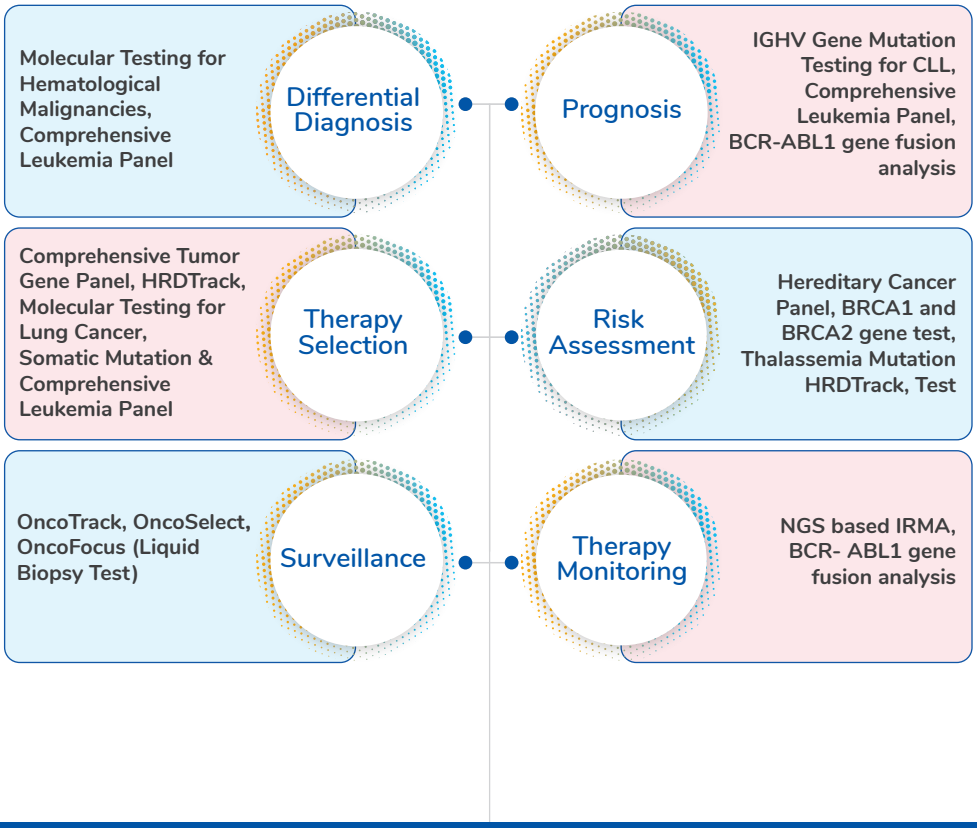
MedGenome is dedicated to bring the power of Genetics and Genomics to empower every human being for better health and improved quality of life.



MedGenome Prima

offers precision genetic testing for a wide range of Oncology and Haematology tests :



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Talk to the Experts

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