AUSTRALIAN Clinicallabs

GENETICS
MBS UPDATE
Special Edition

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PATHOLOGY *focus*

Medical Newsletter

GENETIC CARRIER SCREENING

MBS update

Navigating genetic carrier screening in general practice

By Associate Professor Mirette Saad

Genetic Carrier Screening, available at Australian Clinical Labs, provides patients with information regarding their chances of having a child with a genetic condition such as cystic fibrosis (CF), spinal muscular atrophy (SMA), or fragile X syndrome (FXS). If the patient or the partner has a family history of any of these conditions, the chance of being a carrier may be higher.

CARRIER SCREENING for CF, SMA & FXS: *Medicare-rebatable* from 1st November 2023

Article continues over page

Genetic Carrier Screening should be offered to every woman or couple

Australian clinical guidelines (RANZCOG & RACGP)[1,2] recommend offering genetic carrier screening for common genetic conditions, such as cystic fibrosis, spinal muscular atrophy, and fragile X syndrome, to every woman or couple who are either planning or in the first stage of pregnancy, regardless of their probability of having these conditions.

Ideally, screening is performed prior to conception to offer greater reproductive choice. Early detection is paramount as it allows more time for counselling and provides greater reproductive options for those at risk.

With carrier screening for CF, SMA, and FXS being Medicare-rebatable, testing can be offered earlier during routine appointments, alongside other prenatal screening tests.

References

1. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) Guidelines.
2. The Royal Australian College of General Practitioners (RACGP) Guidelines.

Genetic Carrier Screening – Now Medicare-Rebatable

From 1st November 2023, carrier screening for cystic fibrosis (CF), spinal muscular atrophy (SMA), and fragile X syndrome (FXS) will be fully Medicare-rebatable. These Medicare items now make genetic carrier screening accessible to the wider Australian population; the test is covered once in an individual's lifetime.

"These Medicare items now make genetic carrier screening accessible to the wider Australian population."

CARRIER SCREENING for CF, SMA & FXS: *Medicare-rebatable* from 1st November 2023

Extended Carrier Screening Options Available at Clinical Labs

Clinical Labs is pleased to offer patients two expanded carrier screening options at an additional out-of-pocket cost.

For information about our Comprehensive and Ashkenazi Jewish Carrier Screening tests, including the conditions tested for, please visit antenatal.clinicallabs.com.au/doctor/carrier-screening.

	 3 gene access carrier screening	 100+ COMPREHENSIVE carrier screening	 8 *Ashkenazi Jewish* carrier screening
Genetic conditions	CF, SMA & FXS	100+ inherited conditions	Eight genetic conditions common among individuals from the Ashkenazi Jewish community
Cost	Fully Medicare-rebatable once in the patient's lifetime	$595	$330
Turnaround time	5–7 business days	3–6 weeks	7–10 business days
Request form	Request forms for our Genetic Carrier Screening tests can be found at: antenatal.clinicallabs.com.au/doctor/carrier-screening. **Please include any family history of relevant genetic conditions.**		

A Cystic Fibrosis, Spinal Muscular Atrophy, and Fragile X Syndrome screening test

Genetic Carrier Screening gives patients information regarding the chances of their child having cystic fibrosis (CF), spinal muscular atrophy (SMA), or fragile X syndrome (FXS).

- One in 20 individuals are carriers of at least one of these conditions;
- 90% of carriers do not have a family history;
- One in 160 couples will be found to be at risk of having an affected child.

Cystic fibrosis (CF)

Approximately one in 25 individuals are carriers of CF, and CF genetic testing covers more than 75 common mutations in the CFTR gene. CF affects about 1 in 2,500 individuals and is a severe genetic condition that causes lung and gastrointestinal problems.

Spinal muscular atrophy (SMA)

SMA is an inherited neuromuscular disease historically associated with high morbidity and mortality. Approximately one in 35 individuals are carriers of SMA, and the SMA test identifies deletions of the SMN1 gene. SMA affects about 1 in 6,000 people.

Fragile X syndrome (FXS)

FXS is the most common cause of inherited mental retardation, affecting approximately 1 in 3,600 men and 1 in 6,000 women.

FXS carrier screening is recommended for females, as it is inherited in a different way to CF and SMA, and it only requires that the female has the gene change (number of repeats) in the FMR1 gene for there to be a risk of having a child affected by FXS.

Genetic Carrier Screening in General Practice

By Dr Caroline Rogers

Dr Caroline Rogers has been a GP on Sydney's Northern Beaches for the last 20 years and has been working at South Steyne Medical Centre in Manly since 2021. Her practice focuses on women's health and chronic disease, with a special interest in proactive, preventative care.

As GPs, we are ideally placed to discuss genetic carrier screening with patients. Over the last few years, I have started offering this test as part of my routine pre-conceptual and pregnancy planning consultations. When discussing carrier screening with patients, I often use the analogy of rhesus status. Just like rhesus testing, the screening is done once and has implications for pregnancy care. Knowing about it sooner rather than later allows us to put plans in place to manage and prevent pregnancy complications. It is only necessary to test the partner if the patient tests positive.

The advantage of obtaining the results of genetic carrier screening before a pregnancy begins is that it reduces the stress and anxiety which can be associated with waiting for results while pregnant. If the test is positive for one or more genetic mutations and the partner also needs to be tested, the wait can be weeks. If this process is only initiated at the initial antenatal visit, we are often well into the second trimester before the patient knows for certain what the outcome is. This can significantly impact the joy and well-being many couples hope and expect to experience during this time.

Pre-pregnancy testing allows this to happen in a much less time-sensitive and emotionally charged environment. The patient and their partner can be referred to a genetic counsellor to discuss the nature of the conditions being screened for, if necessary, and their options in terms of pregnancy planning. This includes discussing preimplantation testing if a positive result is found for both parties.

As this is a once-in-a-lifetime test, and once cost is no longer a barrier, I anticipate it being raised more often during pill checks and cervical screening appointments with younger women who are not actively considering a pregnancy but would like to have this information to help them plan future fertility choices.

Interpretation of results

CF and SMA

There are two possible outcomes when being tested for CF or SMA. Screening results may indicate your patient is either:

A CARRIER: This means the test has identified that the patient carries a change in a copy of the CF or SMA gene. If this occurs, then testing of the patient's partner for this condition(s) is recommended to further clarify the risk of having a child affected by that condition.

A NON-CARRIER: This means that the patient was not found to carry any of the common gene changes tested for. Negative results can significantly reduce the risk of having an affected child with those conditions.

FXS

The table below shows the four different types of test results from FXS carrier screening based on the number of CGG repeats detected.

Possible FXS test results	Number of CGG repeats identified
Normal Range	5-44 repeats
Intermediate Range	45-54 repeats
Premutation Range	55-200 repeats
Full Mutation Range	>200 repeats

Women with repeats within the normal range are not at increased risk of having a child affected with FXS. Women in the intermediate or premutation range are not affected by FXS (although they may present with clinical disorders), and they may pass on the risk to future generations or be at increased risk of having children affected by FXS. Women with repeats in the full mutation range are at increased risk of having children affected with FXS and should be offered a referral to a clinical geneticist or genetic counsellor for expert advice.

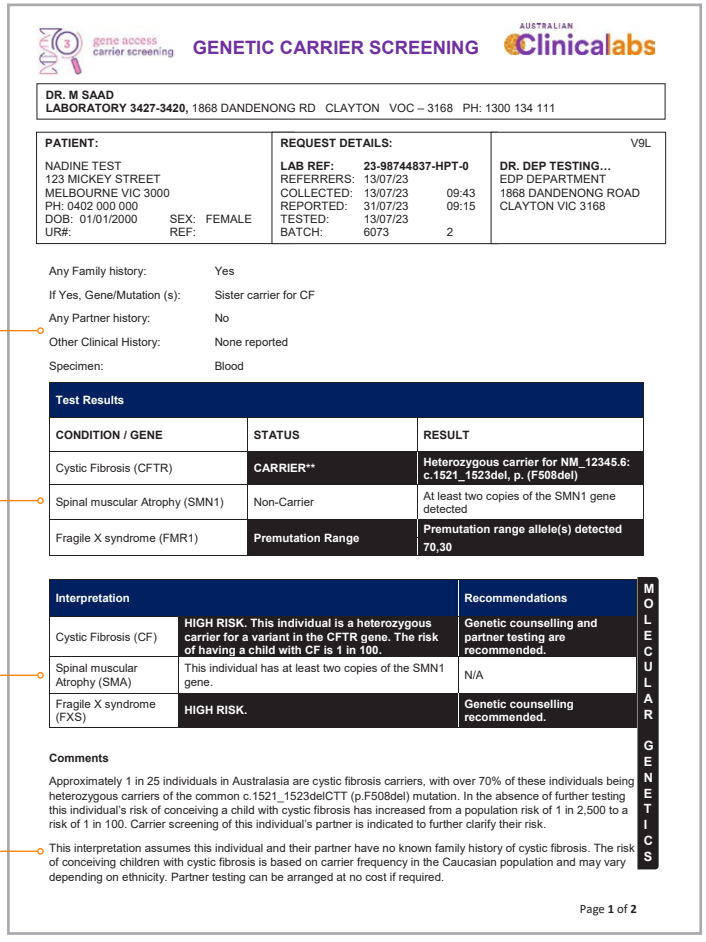
Genetic counselling

Positive cases are offered one genetic counselling session at no cost. Any follow-up consultations, if necessary, will incur an out-of-pocket fee.

- Clinical Labs will notify the referring clinician and provide contact details for the genetic counselling service.
- The referring doctor can either contact the genetic counsellor to schedule the appointment, or the consultation can be organised through the lab.
- Appointments are conducted over the phone and are generally available within 48 hours of referral. During the call, which lasts 15-20 minutes, the genetic counsellor will discuss the risk of having a child carrying this condition with the patient and their partner. It is also optional for the referring clinician to be on the call.

Please note: The genetic counselling request must be made within two weeks of receiving the partner's CARRIER test results.

Gene Access Carrier Screening Report



gene access carrier screening — GENETIC CARRIER SCREENING — Australian Clinicalabs

DR. M SAAD
LABORATORY 3427-3420, 1868 DANDENONG RD CLAYTON VOC – 3168 PH: 1300 134 111

PATIENT:	REQUEST DETAILS:	V9L
NADINE TEST 123 MICKEY STREET MELBOURNE VIC 3000 PH: 0402 000 000 DOB: 01/01/2000 SEX: FEMALE UR#: REF:	**LAB REF: 23-98744837-HPT-0** REFERRERS: 13/07/23 COLLECTED: 13/07/23 09:43 REPORTED: 31/07/23 09:15 TESTED: 13/07/23 BATCH: 6073 2	**DR. DEP TESTING...** EDP DEPARTMENT 1868 DANDENONG ROAD CLAYTON VIC 3168

Any Family history: Yes
If Yes, Gene/Mutation (s): Sister carrier for CF
Any Partner history: No
Other Clinical History: None reported
Specimen: Blood

Test Results

CONDITION / GENE	STATUS	RESULT
Cystic Fibrosis (CFTR)	**CARRIER****	**Heterozygous carrier for NM_12345.6: c.1521_1523del, p. (F508del)**
Spinal muscular Atrophy (SMN1)	Non-Carrier	At least two copies of the SMN1 gene detected
Fragile X syndrome (FMR1)	**Premutation Range**	**Premutation range allele(s) detected 70,30**

Interpretation		Recommendations
Cystic Fibrosis (CF)	**HIGH RISK. This individual is a heterozygous carrier for a variant in the CFTR gene. The risk of having a child with CF is 1 in 100.**	**Genetic counselling and partner testing are recommended.**
Spinal muscular Atrophy (SMA)	This individual has at least two copies of the SMN1 gene.	N/A
Fragile X syndrome (FXS)	**HIGH RISK.**	**Genetic counselling recommended.**

MOLECULAR GENETICS

Comments

Approximately 1 in 25 individuals in Australasia are cystic fibrosis carriers, with over 70% of these individuals being heterozygous carriers of the common c.1521_1523delCTT (p.F508del) mutation. In the absence of further testing this individual's risk of conceiving a child with cystic fibrosis has increased from a population risk of 1 in 2,500 to a risk of 1 in 100. Carrier screening of this individual's partner is indicated to further clarify their risk.

This interpretation assumes this individual and their partner have no known family history of cystic fibrosis. The risk of conceiving children with cystic fibrosis is based on carrier frequency in the Caucasian population and may vary depending on ethnicity. Partner testing can be arranged at no cost if required.

Page **1** of **2**

Clinical History: includes family/partner history.

Status: includes genes detected for CF, SMA & FXS.

Interpretation: includes clinical recommendations.

Comments: includes pathologist's comments in relation to the findings of the report.

Ordering Genetic Carrier Screening with Clinical Labs

How to order

For Gene Access (CF, SMA & FXS) testing, please complete the Clinical Labs Genetic Carrier Screening Request Form located at antenatal.clinicallabs.com.au/doctor/carrier-screening. **Please provide any relevant family or partner history of CF, SMA, or FXS.**

Testing locations

Your patients can visit any of our 1,300 collection centres for their carrier screening blood test. Locations can be found at clinicallabs.com.au/location.

Turnaround time

Results for Gene Access (CF, SMA & FXS) testing will be available within 5-7 business days from the time we receive the sample at our laboratory.

Test cost

From 1st November 2023, genetic carrier screening for CF, SMA, and FXS will be fully Medicare-rebatable. The test is covered once in an individual's lifetime.

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EndoPredict®: Precision medicine for breast cancer treatment strategies

By Associate Professor Mirette Saad

Partially MEDICARE-REBATABLE from 1st November 2023

EndoPredict is an in vitro multi-gene prognostic test that provides highly important and clear information for different stages of treatment planning for patients with estrogen receptor-positive (ER+), human epidermal growth factor receptor 2-negative (HER2-) primary breast cancer.

Who to test

Target Group

- Invasive primary breast cancer
- ER-positive
- HER2-negative
- 0-3 pos. lymph nodes
- G1-3
- Size: pT1-3

> *"EndoPredict is the only prognostic test that can help in deciding whether your patient can safely avoid chemotherapy, how beneficial chemotherapy would be, and whether your patient can avoid extended endocrine therapy."*

When to use

EndoPredict is performed on FFPE tumour tissue from biopsy or surgical specimens from patients who have not received systemic endocrine therapy and/or chemotherapy.

Screening	Clinical Diagnosis	Pathological Diagnosis	Surgery	Adjuvant Therapy Decision
Palpatory findings	Biopsy	ER, PR, and HER2 status	Tumour size	Endocrine therapy
Mammography	Imaging	Other parameters	Nodal status	Chemotherapy if necassary

PATIENT JOURNEY

EndoPredict

> *"EndoPredict provides clinicians with highly important and clear information for different stages of treatment planning."*

Information is summarised by treatment planning stage

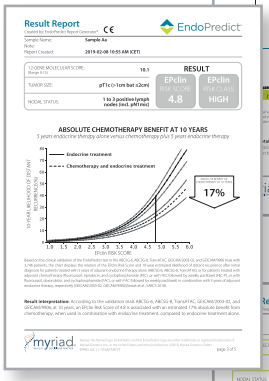
Initial treatment plan

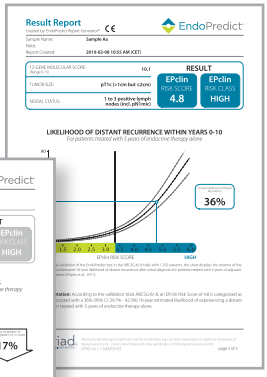
Risk of recurrence within 0-10 years after diagnosis - Can chemotherapy be avoided?

Each patient's report will show a graphic curve illustrating their risk of recurrence within years 0-10 after diagnosis. This information helps you to identify patients with a low risk of recurrence who may safely avoid chemotherapy.

Chemotherapy benefit - What is the absolute benefit from chemotherapy?

The second graph in the report illustrates the absolute chemotherapy benefit based on whether the patient receives endocrine therapy alone or endocrine plus chemotherapy. This helps your patient to make a confident decision about chemotherapy treatment.





Long-term treatment planning

Risk within 5 to 15 years after diagnosis - Can the extension of endocrine therapy be avoided?

The third graph in the report illustrates your patient's risk of recurrence within years 5-15 after diagnosis.* This information guides treatment decisions regarding endocrine therapy beyond 5 years.

**5-15 year risk is based on treatment with 5 years of endocrine therapy only – no chemotherapy. The result assumes the patient has not experienced recurrence by 5 years.*

Comparison with other prognostic tests

When compared to other gene expression tests, EndoPredict was the most prognostic signature for distant recurrence, both in years 0-10 and in years 5-10, in all patients[1]. EndoPredict identified the largest group of women with breast cancer, both in node-negative and node-positive disease:

- at low risk (<10% chance in 10 years) of distant recurrence, who might safely avoid chemotherapy.
- at low risk of late distant recurrence, for whom an extended endocrine therapy might not be justified.

Breast cancer patients and their treating doctors must make complex, highly personalised treatment decisions. Prognostic tools, such as EndoPredict, can play a vital role in determining the type of treatment and prognosis for the patient by assisting with adjuvant therapy decision-making in ER-positive breast cancer. High-quality pathology is a vital part of breast cancer diagnosis and management, and molecular assays such as EndoPredict can provide important additional information to support complex decision-making about the use of chemotherapy in ER-positive breast cancer.

For more detailed information on EndoPredict, please visit our website: clinicallabs.com.au/endopredict.

EndoPredict®
One Test – Three Clinical Answers

Only available from Australian Clinical Labs

EndoPredict®

TARGET GROUP

- Invasive primary breast cancer
- ER-positive
- HER2-negative
- 0-3 pos. lymph nodes
- G1-3
- Size: pT1-3

1. Sestak I. et al. Comparison of the Performance of 6 Prognostic Signatures for Estrogen Receptor- Positive Breast Cancer. A Secondary Analysis of a Randomized Clinical Trial. JAM Oncology Published online February 15, 2018

Ordering EndoPredict with Clinical Labs

How to order

Please download the EndoPredict request form, which can be found at clinicallabs.com.au/endopredict. Fill in patient details and clinical history, and select "EndoPredict". Ensure that referring clinician details are complete, and if known, provide specimen details. If you would like a copy of the report to be sent to another clinician, please provide the necessary details. The payment process can be found on the request form.

Specimens required

EndoPredict is performed on FFPE tumour tissue from biopsy or surgical specimens.

Turnaround time

4–5 business days from the sample receipt date.

Test cost

From 1st November 2023, EndoPredict will be partially Medicare-rebatable.

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Somatic Mutation Testing in Solid Tumours at Clinical Labs

By Associate Professor Mirette Saad

3 NEW pathology MBS items for NSCLC from 1st November 2023

Australian Clinical Labs offers Solid Tumour Somatic Mutation Gene Panels for cancer patients that support treatment decisions and improve patients' outcomes.

Precision or Personalised Medicine harnesses genomic knowledge banks to tailor individualised treatments based on patients' or their tumours' genetic signatures. Analysis of tumour-associated genetic alterations is increasingly used for diagnostic, prognostic, and treatment purposes.

Somatic Mutation and Targeted Therapy in Cancer

The advent of molecular profiling overcame the limitations of morphological solid tumour classification methods. The presence or absence of activated therapeutic driver mutations or gene targets (e.g., *BRAF* in melanoma, *KRAS* in colorectal cancer, and *EGFR* mutation, or *ALK/RET/ROS1* rearrangements in non-small cell lung cancers [NSCLC]) is currently employed to guide treatment decisions.

An increasing number of therapies are approved to treat cancers harbouring specific genomic biomarkers. However, not all alterations (variants, copy-number changes, or fusions) in actionable genes confer sensitivity to available drugs.

> ***"Precision or Personalised Medicine harnesses genomic knowledge banks to tailor individualised treatments based on patients' or their tumours' genetic signatures."***

Genetic profiling in tumours can identify resistant mutations in response to therapy (i.e., *BRAF K601E* mutation is resistant to the known RAF inhibitors vemurafenib or dabrafenib). Some genetic variants, such as *KRAS* and *TP53* gene mutations, may predict a poor prognosis in cancer.

Next Generation Sequencing at Clinical Labs

Clinical Labs uses a high-quality genomic analysis, such as Next Generation Sequencing (NGS) testing panels designed to investigate multiple relevant actionable mutations in formalin-fixed paraffin-embedded (FFPE) tumour samples.

The efficiency of NGS of DNA and RNA has led to an increasing number of large, targeted multi-gene somatic mutation panels that provide a more efficient, cost- and tissue-saving tumour analysis. They confer greater depth of coverage in selected areas of interest (e.g., hotspot regions with known actionable mutations, rarer mutations and tumour sub-clones), faster turnaround, and more clinically relevant data. However, despite the high sensitivity of NGS, there are limitations and caveats to consider for each test type that vary by biomarker and tumour type.

What Do We Test?

An FFPE sample of 5-10 µm thickness from the tumour tissue. NGS can detect variants using inputs of ~20ng of FFPE-extracted DNA/RNA and from specimens with a tumour cell content less than 50%, for which, when possible, we recommend micro-dissection.

Options of Somatic Mutation Testing Panels:

Comprehensive Oncomine Precision Assay (OPA) Gene Panel (ThermoFisher Scientific)

Local and International Guidelines (NCCN & ASCO) strongly recommend comprehensive multi-gene panel–based genomic sequencing for cancer patients with the goal of identifying rare driver mutations for which effective drugs may already be available. Comprehensive tumour profiling aids clinicians in selecting the most appropriate treatment for their cancer patients, avoiding unnecessary toxic therapy, resistance, or overtreatment, or in suggesting potential synergistic drug combinations (e.g., combination of *BRAF* and *MEK* inhibitors in *BRAF* mutant melanoma)[25]. This approach is also of valuable use if the tumour is poorly differentiated or of unknown origin.

Lung Cancer (New Medicare Items)

Mutation in *EGFR* occurs in ~35% of NSCLC patients of East Asian origin and ~16% in Western populations[8,9,10]. Studies have confirmed *EGFR* mutations as a predictive biomarker of treatment response to tyrosine kinase inhibitors (TKIs), Gefitinib, and Erlotinib[11,12]. A third-generation *EGFR* TKI is approved in Australia and is effective in patients with tumours harbouring the resistance *p.T790M EGFR* mutation (~50-60% of lung cancer patients[13,14,15]) following progression on *EGFR* TKIs[16,17]. Detection of *KRAS* or *BRAF* mutations (observed in 2-4% of NSCLC patients) is considered a negative predictor of response to anti-*EGFR* treatment and is associated with poorer survival[20;22,24].

From November 2022, testing for *MET* exon 14 skipping mutation (3-4%) should be performed for patients with all types of NSCLC to determine the eligibility for *MET* inhibitors capmatinib and tepotinib[25].

RNA Fusion Test Panel in Solid Tumours

RNA-based fusion testing is recommended for patients with no other oncogenic driver detected by DNA. Approximately 5% of NSCLC patients display a rearrangement in *ALK* (2-5%), while *ROS* proto-oncogene 1 (*ROS1*) and *RET* proto-oncogene (*RET*) rearrangements are observed in 1-2% of patients. With variable prevalence, the presence of neurotrophic tyrosine receptor kinase (*NTRK*) fusions provides a rationale for genomic testing for all solid tumours for patients who may be candidates for *TRK*-inhibitor therapy. *NTRK1-3* fusion is described in 90-100% of secretory salivary gland carcinomas (also known as MASC). They may also be present in 2-15% of papillary thyroid carcinomas and in less than 1% of other head and neck tumours[25].

Colorectal Cancer (CRC)

Mutations in proto-oncogene *KRAS* are detected in up to 40% of CRC[5], which can confer resistance to treatment with *EGFR* antibodies, and only patients with wild-type *KRAS* tumours obtain benefit from these agents[6,7]. It is, therefore, vital that the *KRAS* mutation status of a patient's colorectal tumour can be detected to allow patients access to treatment.

Melanoma

Targeted therapy with Anti-*BRAF* (vemurafenib or dabrafenib) remains the first-line treatment for melanoma tumours which harbour a *BRAF* mutation, particularly in Australia[18]. In cutaneous melanoma, the *BRAF* gene is mutated in ~60% of cases and p.*V600E (c.1799TA)* accounts for more than 90% of *BRAF* mutations[19]. Detection of c*KIT* mutations may guide the selection of *KIT* TKIs (imatinib and sunitinib) for melanoma treatment[21, 23] and may lead to better outcomes compared to *BRAF* melanoma patients treated with *BRAF* inhibitors[23].

Breast Cancer

In breast cancer, oncogenic mutations in *PIK3CA* or *ERBB2* amplification (along with *TP53* mutations) occur in ~25% of cases[1,2]. As such, mutated *PI3K* has become an attractive therapeutic target in breast cancer therapy, and a number of agents targeting the *PI3K* pathway are currently in clinical development[25].

Thyroid Cancer

In anaplastic thyroid cancer (ATC), *BRAF p.V600E* mutation occurs in ~40% of patients with papillary thyroid carcinoma (PTC) and is associated with a more aggressive disease[3,4]. Medullary thyroid cancer (MTC) is associated with oncogenic mutations in *RET* (40-60%) that can be targeted by therapeutic treatments[25].

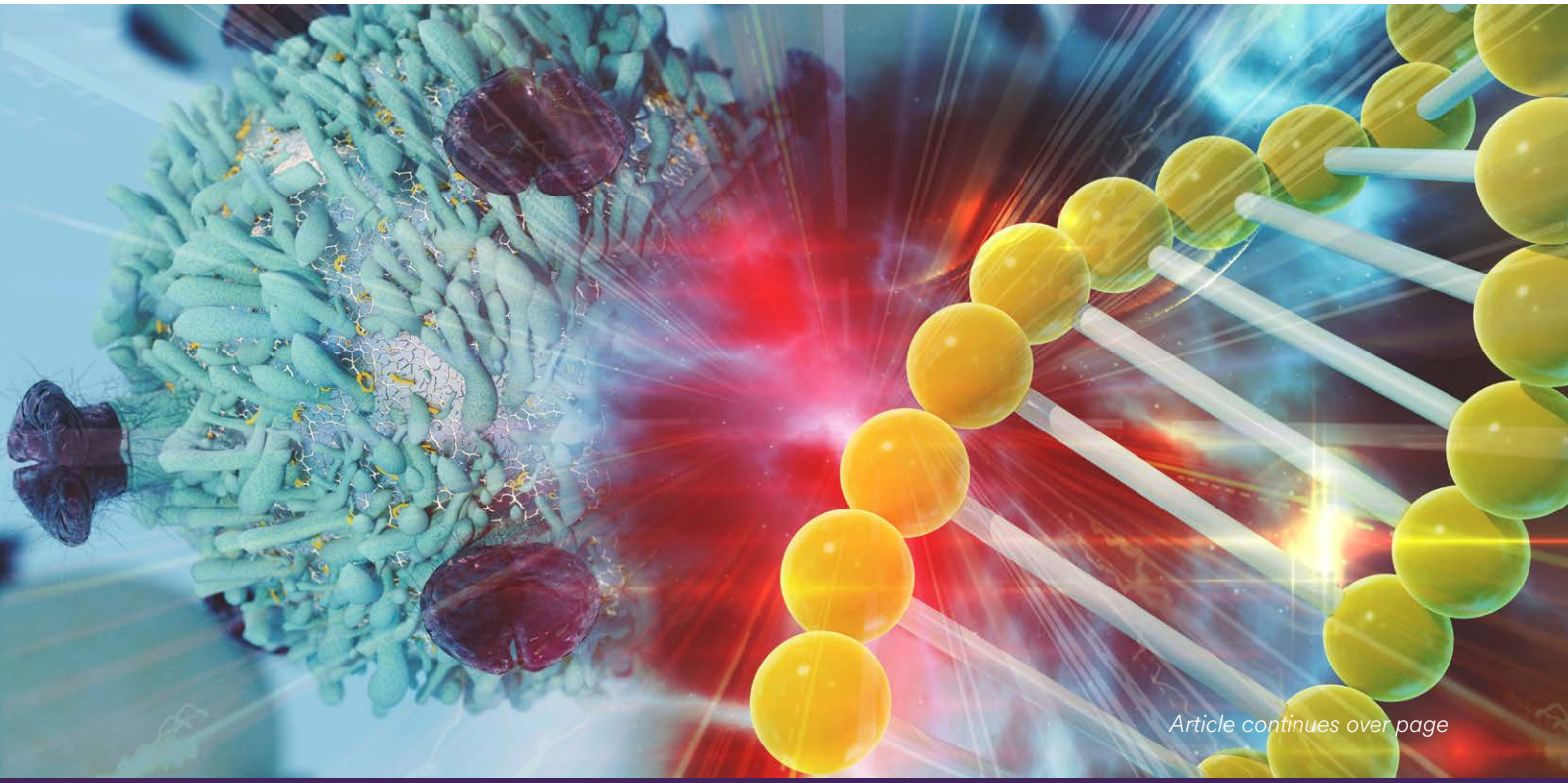
Conclusion

Precision medicine has already transformed cancer care: both common and rare malignancies can be targeted by specific therapies to improve clinical outcomes in patients.

Ordering Somatic Mutation with Clinical Labs

How to order

1. Fill out our Somatic Mutation Testing Request Form.
2. Tick the Somatic Mutation test panel required.
3. Send to our lab along with Fresh FFPE (of 5-10 µm thickness from the tumour tissue).
4. Results will be available 5-7 business days after the receipt of the patient's sample.



Article continues over page

For further information about Somatic Mutation testing available at Clinical Labs, including gene panels, pricing, and request forms, please visit clinicallabs.com.au/molecularcancerservices.

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MBS Update

From 1 November 2023, three new pathology items will be included in the MBS to test for genetic variants in patients with non-squamous (or histology not otherwise specified) non-small cell lung cancer. MBS items will include broader actionable gene variants along with fusion genes to access specific therapies relevant to these variants listed on the PBS.

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Choosing Between Vitamin B12 and Active B12 Testing: Considerations for Clinical Practice

By Associate Professor Chris Barnes

Introduction

Vitamin B12, also known as cobalamin, plays a critical role in various physiological processes, such as DNA synthesis, red blood cell production, and neurological function. Deficiency in vitamin B12 can lead to megaloblastic anaemia and neurological disorders. Accurate assessment of vitamin B12 status is crucial for timely intervention and appropriate management. Recently, the introduction of Active B12 testing has raised questions about its utility compared to conventional B12 testing. This article aims to explore the factors influencing the choice between vitamin B12 and Active B12 testing, including prevalence rates, risk factors, and the potential impact of B12 deficiency on fatigue.

Prevalence of vitamin B12 deficiency

Vitamin B12 deficiency is a significant global health concern. Studies have reported varying prevalence rates depending on the population and geographical location. Suboptimal B12 levels have been observed in up to 15% of the general population, while clinical deficiency affects approximately 2-3% of adults[1]. Certain subgroups, such as the elderly, vegetarians, and individuals with gastrointestinal disorders, are at higher risk for deficiency. Adequate testing strategies are necessary to identify those at risk and ensure early detection of deficiency.

Risk factors and indications for testing

Several risk factors contribute to the development of vitamin B12 deficiency. Inadequate dietary intake, malabsorption conditions (e.g., pernicious anaemia, Crohn's disease), gastrointestinal surgeries, and the use of certain medications (e.g., proton pump inhibitors, metformin) are known contributors to deficiency[2]. Healthcare providers should consider testing for B12 deficiency in individuals with anaemia, neurological symptoms, macrocytosis, unexplained cognitive decline, or other clinical signs suggestive of deficiency.

> ***"Healthcare providers should consider testing for B12 deficiency in individuals with anaemia, neurological symptoms, macrocytosis, unexplained cognitive decline, or other clinical signs suggestive of deficiency."***

Vitamin B12 testing and Active B12

Conventional vitamin B12 testing involves measuring total serum B12 levels. This method is widely available, cost-effective, and serves as the current standard for assessing B12 status. A low B12 level indicates deficiency, prompting further evaluation to determine the underlying cause. However, it is important to note that B12 levels alone may not provide a comprehensive assessment of tissue B12 status or functional deficiency[3].

Active B12 testing, also known as holotranscobalamin (holoTC) testing, measures the biologically active form of B12 available for cellular uptake. HoloTC represents a fraction of total B12 but reflects the metabolically active fraction. Active B12 testing offers potential advantages in detecting early or functional B12 deficiency, as it provides insights into the availability of B12 at the cellular level[4]. However, the clinical significance of Active B12 as a standalone test is still under investigation, and more research is needed to establish its role in clinical practice.

Conclusion

Vitamin B12 deficiency is a prevalent condition with significant health implications. The choice between vitamin B12 and Active B12 testing depends on the clinical context, including the presence of specific risk factors and the need for a comprehensive assessment. While conventional B12 testing remains the current standard, Active B12 testing may offer additional insights, particularly in cases of suspected functional deficiency. Healthcare providers should remain vigilant in evaluating patients presenting with risk factors and clinical manifestations of B12 deficiency, ensuring appropriate testing and management strategies are implemented.

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When ordering vitamin B12 tests, the following MBS guidelines apply:

VITAMIN B12 TESTING
MBS Guidelines

- If the B12 level is low, an Active B12 test will be automatically performed.
- If the B12 level is not low, only the B12 test will be conducted.
- If both B12 and Active B12 are requested, both tests will be performed.
- There is a restriction on the B12 item, limiting it to once within a 12-month period. The first occurrence may be bulk billed if requested. Additional B12 tests within the same 12-month period are privately billed to the patient at a cost of $23.60.
- Active B12 tests can be bulk billed anytime they are ordered, as there are no restrictions under the Medicare Benefits Schedule (MBS).
- If both B12 and serum folate tests are ordered, the first occurrence may be bulk billed if eligible, and subsequent B12 tests are privately billed. Folate testing (66840) is typically bulk billed if eligible.
- For patients not covered by Medicare or DVA, private billing applies. In such cases, the patient will receive an invoice. If both B12 and Active B12 tests are conducted, the approximate cost of the invoice would be around $155.00.

These guidelines ensure correct billing practices and accurate reimbursement for vitamin B12 testing based on MBS regulations.

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