

QML PATHOLOGY

newsletter september 06

>> Molecular Pathology in Daily Practice

Dr Nigel Brown, Head of Molecular Pathology

Where can I use Molecular Pathology?

Doctors in all fields are finding more areas where Molecular Pathology testing can help in patient management.

Modern pathology now has in its armamentarium an expanding array of tests based on direct analysis of genetic information by the examination of nucleic acids or chromosomes. Not only is human genetic testing used but also an increasing number of microbiological tests rely on the analysis of bacterial or viral genetic material.

> cont page 2

>> Molecular Pathology in Daily Practice

Dr Nigel Brown, Head of Molecular Pathology

QML Pathology is at the forefront of nucleic acid testing in pathology, with applications available across a wide range of practice interests – for example Oncology, Infectious Diseases, Paediatrics, Neurology, Obstetrics & Gynaecology, Coagulation Disorders, Gastroenterology, Hyperlipidaemias and Immunology. Additionally, referral of testing not performed by QML Pathology is provided as a supplementary service.

A selection of the nucleic acid tests performed by QML Pathology and others commonly referred are presented in Table 1.

Molecular Pathology at QML Pathology

A purpose built Molecular Pathology suite was created when QML Pathology moved to its new Central Brisbane Laboratory. This suite is where the more manually intensive procedures are performed. Automated molecular pathology testing is located where best receipt-to-report turn-around times are achieved. Cytogenetic analysis is provided by a highly trained team using both conventional microscopy and molecular cytogenetic methods.

Testing that is not performed locally can be referred to specialist centres by QML Pathology, including handling the referral process from specimen collection through to reporting. Provision of Molecular Pathology services is under the overview of pathologist Dr Nigel Brown, with Discipline Pathologists providing clinical oversight, interpretation and consultation in their respective areas of expertise.

Dr Stephen Withers is available as a consultant Clinical Geneticist to discuss counselling aspects of genetic testing as well as investigational strategies for cytogenetics and family studies (including family cancer genetics).

Medicare Rebates

Medicare rebates exist for some Molecular Pathology tests, sometimes requiring medical criteria to be met in order to qualify for a rebate. A patient's history relating to the rebate must be provided in writing. Where testing lies outside the Medicare Schedule, QML Pathology's own charges are usually made on a cost-recovery basis. Costing for a referred test is at the discretion of the testing laboratory. If you are unsure what charging arrangements apply to the required testing, please do not hesitate to contact our laboratory.

Test	Rebate Status
HFE mutations (Haemochromatosis)	Rebate if at least two demonstrated abnormal ferritins or saturations or a first-degree relative has clinical haemochromatosis or two mutations
Factor V (Leiden) & other relevant mutations	Rebate if patient has Venous Thromboembolism (VTE, PE or DVT) or 1st degree relative has proven presence of a relevant mutation
Gene rearrangement studies	Rebates for specific leukaemias to a maximum of 4 tests in a 12 month period
Cystic Fibrosis mutations	No rebate available
Infectious agents - microbial detection tests	Rebated
Chromosome Studies - constitutional abnormalities	Rebated
Fluorescent in-situ hybridization (FISH) studies	No rebate available

Table 1: Molecular Pathology Testing at QML Pathology

Clinical Area	Molecular Pathology Tests at QML Pathology
Infectious Diseases	Herpes simplex and Varicella zoster, Chlamydia trachomatis, Neisseria gonorrhoeae, Hepatitis C virus (HCV) qualitative, quantitative & genotyping, Hepatitis B virus quantitative, Trichomonas vaginalis, CMV, Bordetella pertussis, HIV viral load, Adenovirus & Respiratory virus multitest (Influenza A, B; RSV; Parainfluenza 1, 2, 3), Pneumocystis carinii (jiroveci), Neisseria meningitidis, Legionella, Clostridium difficile toxin A & B, Mycoplasma pneumoniae, Malaria speciation, Bartonella henselae
Oncology	Cytogenetics, FISH (fluorescent in-situ hybridization) on paraffin sections, BCL-1, BCL-2, BCR-ABL quantitative, T & B cell gene rearrangement studies, Her2 (Breast Cancer), JAK2 (in development)
Reproductive & Chromosomal	Cytogenetics, FISH studies, DAZ/SRY Infertility studies, Fragile X PCR, Metaphase CGH
Metabolic Disorders	Haemochromatosis (HFE), APO-E
Thrombotic Disorders	Factor V (Leiden), Prothrombin mutations, Methylenetetrahydrofolate reductase (MTHFR) mutation
	Commonly Referred Testing
Various	Cystic Fibrosis, Muscular Dystrophies, Autosomal recessive deafness (Connexin 26), Huntington Disease, Spino-Cerebellar Ataxias, paternity studies, HLA-DQ (coeliac disease related)

>> Molecular Pathology in Daily Practice

Dr Nigel Brown, Head of Molecular Pathology

Clinical Examples – how we do the tests

Haemochromatosis (HFE Gene Mutations)

Haemochromatosis is an autosomal recessive disorder (you need two mutations to be affected) that results in iron accumulation, potentially leading to liver damage, diabetes mellitus and arthritis. Blood specimens are tested for the mutations C282Y, H63D and S65C by automated PCR (polymerase chain reaction) with melting curve analysis of tagged fragments. Figure 1 shows the LightCycler™ instrument used and its result output.

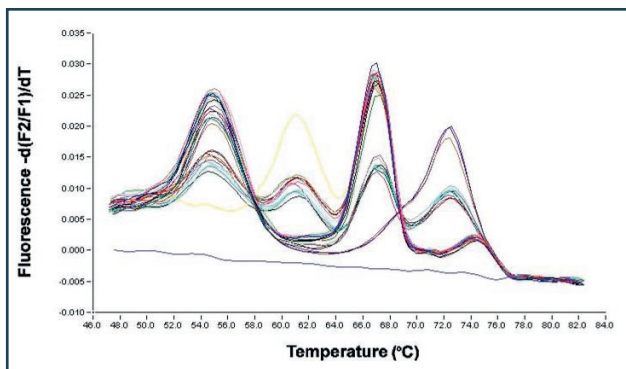


Figure 1

a) Lightcycler™ instrument
b) HFE mutation raw results

Chlamydia trachomatis and *Neisseria gonorrhoeae* Testing

These pathogens are detected by targeting the ribosomal RNA (rRNA) characteristic of each organism. This rRNA is captured then amplified by Transcription



Figure 2. APTIMA instrumentation

Mediated Amplification and detected with chemiluminescent DNA probes. Figure 2 shows the APTIMA instrumentation used for this analysis.

Cytogenetic and Related Studies.

The characterisation of chromosomal abnormalities is performed using both traditional conventional microscopy (Figure 3) and newer molecular pathology techniques. Gene rearrangement studies exemplify newer molecular analytical methods, expanding the range of detection of what were first recognised as abnormalities by conventional microscopy. This also allows new applications such as residual disease determinations and clonality studies. These studies (Figure 4) are performed by multiplex PCR, with detection using traditional gel electrophoresis or quantitative real-time PCR.

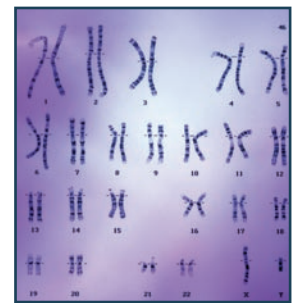
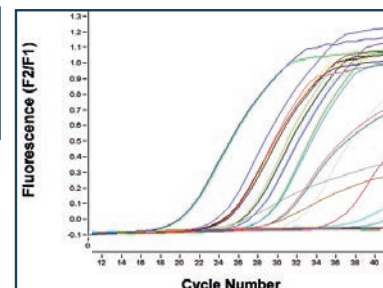
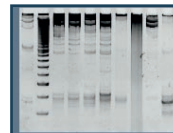


Figure 3: Normal Male Karyotype by conventional microscopy

Figure 4 Detection of Gene Rearrangements by a) gel electrophoresis and b) quantitative real-time PCR



Dr Nigel Brown
DipRACOG FRCPA

Head of Molecular Pathology

Ph: (07) 3121 4428

Email: nigel.brown@qml.com.au

Dr Nigel Brown is a medical graduate from the University of Queensland. He completed his training in Chemical Pathology (FRCPA) at the Royal Brisbane Hospital (RBH), followed by Specialist and Senior Specialist positions at the RBH. In addition to his involvement in general Chemical Pathology, Dr Brown supervised a range of Molecular Pathology genetic testing with a special interest in Cystic Fibrosis and Mitochondrial disorders.

Since joining the QML Chemical Pathology team in 1999, Dr Brown has continued his interest in genetic testing. In 2006 he was appointed the Head of Molecular Pathology, overseeing molecular pathology testing within QML Pathology.

>> Measurement of Serum Mast Cell Tryptase

Dr Heyworth-Smith, Consultant Clinical Immunologist

Tryptase is a protease of uncertain physiological role. It is released from activated mast cells and basophils. Measurement of serum tryptase is a specific marker of mast cell degranulation, since basophils contribute minimally to tryptase levels and there is no other source of tryptase.

The main mediator of the allergic response is histamine. Why then, measure tryptase? Serum histamine measurement is hampered by the very short half life of histamine. Tryptase in contrast, has kinetics that allows its measurement. After anaphylaxis, tryptase is detectable in serum by 30-60 minutes, has peak levels at 60-120 minutes, and is usually eliminated by 6-12 hours. The optimum time to measure tryptase after a suspected allergic reaction is 1-2 hours after the event.

The principle indication for the measurement of tryptase is to establish if an adverse reaction, after the administration of a drug, was allergic in nature. For example after the administration of drugs to induce or maintain anaesthesia. It may be difficult to determine on the basis of clinical signs alone whether stigmata, such as hypotension, bradycardia, or flushing, are due to exaggerated physiological effects of the anaesthetic drugs or due to drug allergy. In contrast, there is little value in the measurement of tryptase; whereas measurement of peanut specific IgE (RAST or skin prick test) is indicated.

Other less common indications for measurement of tryptase are:

- Diagnosis of mastocytosis (a rare illness due to mast cell proliferation). In mastocytosis, serum tryptase levels may be raised continuously
- Post-mortem assessment of anaphylaxis as a possible cause of sudden death
- Some authorities recommend the measurement of tryptase in all patients with insect venom allergy, because this group may have a higher incidence of unsuspected mastocytosis, but this recommendation is not universally accepted



UniCAP® Instrument performing measurement of Serum Mast Cell Tryptase

QML Pathology has recently introduced the measurement of serum tryptase to its repertoire of tests. Unfortunately there is no Medicare rebate for the measurement of tryptase and QML Pathology charges on a cost-recovery basis. For further information please do not hesitate to contact one of our Immunologists on (07) 3121 4444.

Abnormal Cytology: New Guidelines

Dear Colleagues

Recently, QML Pathology's Pap smear reports have been reformatted in order to comply with the new NPAAC guidelines. With these changes there has been a difference in information being sent. It is not my intention to increase the cost of the test, but to provide a concise and useful overview of the changes that will assist with your reporting practice.

Below I have briefly outlined the modifications you will notice in your Pap smear reports, followed by a slightly more detailed explanation of the guideline changes. In addition to this, I have provided a quick reference sheet that gives you a summary of the new terminology along with two simple flowcharts outlining the management of patients with LGSIL and HGSIL.

If you would like further clarification or wish to discuss your patients' results, please don't hesitate to call one of our cytologists on (07) 3121 4009.

Kind regards
James Duhig
James Duhig, Head of Cytology Department

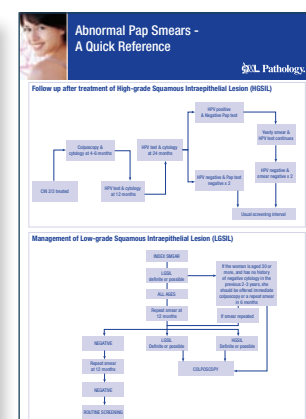
Dr James Duhig, Head of Cytology Department
A graduate of the University of Queensland (1985), Dr Duhig trained in pathology at the Royal Brisbane Hospital and Prince of Wales Hospital before returning to Queensland in 1988. He received his postgraduate training in cytology at the University of Queensland (1990-1992), receiving a Fellowship Award of the Royal Society of Pathology. He has been in the private sector since 1992.

Dr Duhig joined QML Pathology in January 1997 as Pathologist in Charge of the Cytology Laboratory. He subsequently joined the Queensland Government in the central Brisbane Laboratory in 2005, assuming Head of Cytology in 2006.

Telephone: (07) 3121 4009 Email: james.duhig@qml.com.au

Pap Smear Report changes...at a glance

- Cyt terminology will continue to be used in the Specific Diagnosis.
- You will no longer get a specific statement of adequacy. An unsatisfactory smear will be reported in the UNSATISFACTORY category.
- An endocervical component will be reported in the Specific Diagnosis.
- New reporting categories will be incorporated.



Recently, QML Pathology's Pap smear reports have been reformatted to comply with the new NPAAC guidelines. In order to inform you of these changes we distributed some documentation to General Practitioners and Gynaecologists across Queensland and Northern New South Wales.

These documents briefly outlined the modifications you will notice in your Pap smear reports, followed by a slightly more detailed explanation of the guideline changes. In addition to this we provided a quick reference sheet that gives you a summary of the new terminology along with two simple flowcharts outlining the management of patients with LGSIL and HGSIL.

If you did not receive the information please contact your local Medical Liaison Officer for a copy. If you wish to discuss these changes further, please do not hesitate to call one of our Cytologists on (07) 3121 4009.

**Dr James Duhig
Head of Cytology Department**



QML updates sept 06

Time Efficient Pathology Communication via Technology

With heavy time constraints on your working week, QML Pathology is committed to introducing more time-effective methods for you to contact our staff. In line with this we have a range of requests that can be submitted online, sent via email or alternatively by fax. These include requests for added tests, historical results and home visits. By offering you a variety of alternatives, QML Pathology hopes to provide a time efficient means of dealing with your patient follow-up.

Added Tests:

To request added tests you can fax the information or submit it online. A fax form is available on our website or by contacting your local Medical Liaison Officer. Alternatively you can submit an online request by visiting www.qml.com.au and using the For Doctors and Added Test Service links. (Please note: when an online request is submitted it is a Medicare Australia (HIC) requirement that we send you a confirmation request form for your signature).

Due to the time-critical nature of testing and limits to storage capabilities, most samples are only stored for seven days after completion of testing; although some specimens do not comply with this timeline. Serological testing may be stored for extended periods to assist assessment of seroconversion, however the instability of some analytes may mean a sample that is several days old will be unsuitable for analysis.

Historical Results:

To request historical results you can fax or email us the relevant information. A fax form is available on our website at www.qml.com.au (see For Doctors and Receiving Results links) or can be obtained by contacting your local Medical Liaison Officer. Alternatively you can email your request to results@qml.com.au. When making a request via email it is important you include the following details:

- Your contact details including name, address and QML Doctor Code
- Patient's Full Name
- Patient's Date of Birth
- Patient's QML Lab Number (if available)
- Date of Pathology Service
- Tests Requested

Please note that historical test results will be sent as per your usual method of result delivery. If you require historical results urgently please call us directly on (07) 3121 4555.

Home Visits:

To request a home visit you can send us a fax with all the relevant information. A fax form is available by contacting your local Medical Liaison Officer. **Please note that if you require an urgent home visit it is essential you call us directly on (07) 3121 4450.**

For any queries regarding the above contact methods please speak with your local Medical Liaison Officer.

Doctor's Noticeboard

- Dr Terence Casey, Dermatologist, has recommenced consulting on a sessional basis at:

Aspley Specialist Centre
1st Floor, 825 Zillmere Road (cnr Gympie Road), Aspley

Dr Casey continues to consult at his city rooms on the:
4th Floor, 113 Wickham Terrace, Brisbane

For appointments please phone Wickham Terrace on (07) 3831 3755 or Aspley on (07) 3263 5844.

- Dr Neroli Ngenda would like to advise that she has sessional rooms available at:

Suite 5, McCullough Centre, 259 McCullough St, Sunnybank

Sessions are available at the following times: Tuesday PM, Wednesday AM/PM and Friday AM. Please call (07) 3344 1233 for further information.

- Dr Phillip Bushell-Guthrie, Oral and Maxillo-Facial Surgeon, has commenced consulting on a sessional basis at:

The Specialist Centre, Suite 2, Level 5
Pacific Private Clinic, Southport

For appointments please phone (07) 3839 6394.

- Dr Andrew Field and Dr Stephen O'Hagan wish to advise that Dr Brian Todd, Surgical Ophthalmologist and sub-specialist in Glaucoma, has commenced practice at:

Cairns Eye & Laser Clinic, 92 – 94 Pease Street, Manooora

Dr Todd can be contacted on - phone (07) 4053 7577, fax (07) 4053 7145 or email admin@cealc.com.au.

- Dr Blair Bowden, General Surgeon, would like to advise that he has commenced consulting at:

Sandford Jackson Building, Suite 93, Level 5
30 Chasely Street, Auchenflower

Dr Bowden has VMO status at Wesley, Greenslopes and the RBH. His special interests include all forms of laparoscopic, gastrointestinal surgery and hernia surgery, with a particular focus in hepato biliary, anti reflux and weight loss surgery (predominately lap band surgery). For appointments please phone (07) 3371 4333.

- Dr Bruce Hansen, General Practitioner, would like to announce his impending retirement at the end of September 2006. Dr Hansen has consulted in the Petrie district for over 30 years, working at the Petrie Medical Centre. Dr Shams Mughal will be taking over the care of Dr Hansen's patients. Dr Hansen would like to thank his staff and colleagues for their continued support over this time.

- Dr Frank Carmody, Obstetrician & Gynaecologist, would like to advise that he has medical suites available for sessional or permanent lease at Sunnybank. Consulting rooms are situated opposite Sunnybank Private Hospital (on second floor) and include an adjacent procedure room, wiring for internet access and a range of nearby support services with undercover parking available. Please direct any enquiries to Jenny on (07) 3371 4933.