



Australasian Division of the
International Academy of Pathology Limited

Newsletters - 2002

Number Two

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Novartis Lecturer

Dr Chris Corless will deliver a lecture entitled "The Role of KIT Tyrosinase Kinase in the Diagnosis and Treatment of Gastrointestinal Stromal Tumours".

Dr Corless is a Staff Pathologist and Associate Professor of Pathology at Oregon Health and Science University and its associated hospital. He has a long-standing interest in gastrointestinal, urological and transplantation pathology.

He has recently been closely involved with developments in the understanding of gastrointestinal stromal tumours (GISTs) and C-KIT, and the relevance of this to treatment with Glivec (STI-571).

His lecture will be delivered on Saturday June 1, at 4.45pm His visit is being sponsored by Novartis.

Other invited speakers are Dr Robert Petras on Saturday and Dr David Owen on Sunday.

Special Visitor: Professor Shinichiro Ushigome, President of the I.A.P. for Congress 2004.

INTERNATIONAL SOCIETY OF GYNAECOLOGICAL PATHOLOGISTS

Convenor: *Dr Richard Jaworski*

Main Auditorium : 8.55 - 10.40 am

Lecture: "Smooth Muscle Tumours of the Uterus: A Selected Review and Recent Advances" *Dr. Richard Jaworski, I.C.P.M.R., Westmead Hospital, Westmead, N.S.W.*

This will be followed by 5 interesting gynaecological pathology cases.

Presenters:

Dr Jonathan Allin, North West Pathology, Tasmania.

Dr Sandra Biankin, I.C.P.M.R., Westmead Hospital, Westmead, N.S.W.

Dr Catherine Camaris, Royal Hospital for Women, Randwick, N.S.W.

Dr Richard Jaworski, I.C.P.M.R., Westmead Hospital, Westmead, N.S.W.

Dr Veli Marjoniemi, St George Hospital, Kogarah, N.S.W.

NEUROPATHOLOGY

Convenor: *Dr Victor J Ojeda*

Meeting Room 2 : 8.55 - 10.40 am

1. Lecture: Frozen Sections and Neurosurgical Biopsies *Victor J. Ojeda, Central Coast, NSW*

2. Slide Seminar

Case 1: Peter D Robbins, Perth, WA

Case 2: Judith A Fryer, North Shore, Sydney, NSW

Case 3: Michael F Gonzales, Melbourne, VIC

Case 4: Catriona A McLean, Melbourne, VIC

DERMATOPATHOLOGY

Convenor: *Dominic Wood*

Chairperson: *Geoffrey Strutton*

8:55 - 9:20 : Post-transplant lymphoproliferative disorders and the skin. A review and presentation of an interesting case. *Geoffrey Strutton, Princess Alexandra Hospital, Brisbane*

9:20 - 9:40 : Spitz naevus vs. Spitzoid melanoma. *Richard Scolyer, Royal Prince Alfred Hospital, Sydney*

9:40 - 10:40 : Case presentations :

A nodule on the ear - Carcinosarcoma. *Bish Dutta, Dutta Pathology, Sydney*

A nodule on the scalp - Superficial Angiomyxoma. *Bish Dutta, Dutta Pathology, Sydney*

Mycobacterium marinum infection masquerading as a vasculitis. *Adrian Cachia, Skin and Cancer Foundation, Sydney*

Cryoglobulinaemia: Are monoclonal and mixed types distinct histologically? *Peta Fairweather, Princess Alexandra Hospital, Brisbane*

Cutaneous calciphylaxis. *Maya Cherian, Canberra Hospital, Canberra*
Congenital self-healing histiocytosis. *Anna Simpson, Flinders Medical Center, Adelaide*

Unusual nodules on the lower limbs - Phlebitic tuberculid. *Richard Williamson, Royal Brisbane Hospital.*

FACULTY OF ORAL PATHOLOGY

Convenor: *Dr Michael Aldred*

8:55 - 10:40 am
Meeting Room 5

8.55 : An approach to the diagnosis of pigmented lesions of the oro-facial region. *Invited lecturer, Dr Stan McCarthy Dept of Anatomical Pathology, Royal Prince Alfred Hospital, Sydney*

9.30 : Neuroendocrine Tumour presenting in the Maxillary Sinus. *Dr Anastasia Georgiou and Professor Murray Walker, Institute of Clinical Pathology and Medical Research, Westmead Hospital, Sydney*

9.45 : Oncocytic adenocarcinoma arising in a Warthin's tumour. *Dr Ajiravudh Subarnbhesaj and Professor Murray Walker, Institute of Clinical Pathology and Medical Research, Westmead Hospital, Sydney*

10.00 : Odontodysplasia or amelogenesis imperfecta - a diagnostic dilemma. *Dr Yeo Jinn Fei, Dr Winston Tan Kwong Shen and Dr Juliet Tay, National University of Singapore, Singapore*

10.15 : Oral focal mucinosis - report of 12 cases and review of the literature. *Dr Michael Aldred and Dr Anna Talacko, Mayne Health Dorevitch Pathology, Melbourne*

SOFT TISSUE TUMOURS

Convenor: *Dr Richard Jaworski*

11 am - 12.45 am, Main Auditorium

Lecture : "Smooth Muscle Tumours of the Soft Tissues"

Speaker: *Dr. Gelareh Farshid, Senior Consultant Pathologist, Division of Tissue Pathology, Institute of Medical and Veterinary Science, Adelaide, South Australia.*

This will be followed by 5 interesting Soft Tissue Tumour cases

Presenters:

Dr. Christopher Henderson, Liverpool Hospital. N.S.W.

Dr. Penelope McKelvie, St Vincent's Hospital, Melbourne, Victoria.

Dr. Bish Dutta. Epping. N.S.W.

Dr. Caroline Fung, I.C.P.M.R., Westmead Hospital, Westmead. N.S.W.

Dr. Richard Jaworski, I.C.P.M.R., Westmead Hospital, Westmead. N.S.W.

LIVER

Convenor: *Dr David Cohn*

Meeting Room 2 : 11am - 12.45pm
"A Tribute to Dr Dorothy Painter"

11:00 - 11:20 am

Lecture: Update on Clinical Issues and Role of Liver Biopsy in Transplantation

Speaker: *Professor Geoff McCaughan, A.W. Morrow Gastroenterology and Liver Centre, Royal Prince Alfred Hospital, Sydney, NSW.*

(5 minutes question time).

11:25 - 12:05pm

Lecture: Basics of Liver Transplantation Pathology

Speaker: *Dr Bastiaan De Boer, Pathcentre, QEII Medical Centre, Perth, WA.*

(5 minutes question time).

12:10 - 12:40 pm

Lecture: Histological Evaluation of the Patient with Cholestatic Liver Function Tests

Speaker: *Professor Prithi Bhathal, Department of Pathology, University of Melbourne, VIC.*

(5 minutes question time).

LUNG

Convenor: *Dr Jenny Ma Wyatt*

Meeting Room 4 : 11:00 - 12:45

Case Presentations:

1. An unusual spindle cell tumour of the lung. *Dr Richard Scolyer, Royal Prince Alfred Hospital, NSW*
2. Desquamative interstitial pneumonia. *Dr Jeanette Philips, Royal North Shore Hospital, NSW*
3. Miliary pulmonary clear cell tumours and lymphangiomyomatosis in a patient with tuberous sclerosis. *Dr Tatiana Jelihovsky, Royal Prince Alfred Hospital, NSW*
4. Pleomorphic mesothelioma. *Professor Doug Henderson, Flinders Medical Centre, SA*
5. Cavitated rheumatoid nodule of the lung. *Dr Edwina Duhig, The Prince Charles Hospital, Qld*
6. Pulmonary blastoma. *Dr John Ireton, Austin & Repatriation Medical Centre, VIC*

BREAST

Convenor: *Dr Gelareh Farshid*

Main Auditorium

2:00 - 3:34 pm

1. The clinical significance of hormone receptor status of breast cancer for patient management. **Associate Professor Michael Freidlander, Oncologist.**
2. Australian Quality Assurance data on the reporting of immunohistochemical assessment of hormone receptor status of breast cancer. **Dr Bridget Cooke.**
3. Review of various systems of reporting the results of immunohistochemical testing of hormone receptor status of breast cancer. Minimum requirements for the pathology report. **Dr Jane Dhalstrom.**
4. Update on Her2 testing in Australia. **Associate Professor Michael Bilous.**

ORELL FNA

Convenors: **Dr Judy Bligh and Dr Ann Finney**

2.00 - 3.45pm, Meeting Room 2

1. Lecture: FNA of the Liver

Speaker: **Dr Bastiaan De Boer, Pathcentre, Perth.**

2. Lecture: FNA of the Pancreas

Speaker: **Dr Merle Greenberg, Medical Diagnostic Australia, Sydney**

3. Lecture: Bile Duct Brushings, an overview

Speaker: **Dr Greg Sterrett, Pathcentre, Perth.**

4. Lecture: A Practical approach to Bile Duct Brushings

Speaker: **Dr Felicity Frost, Pathcentre, Perth**

5. Case presentations:

Speakers:

Dr Stephen Allpress, Western Diagnostics Pathology, Perth.

Dr James Kench, Westmead Hospital, Sydney.

Dr Lloyd McGuire, Queensland Medical Laboratory, Gold Coast.

Images from the three case presentations can be viewed prior to the meeting in the Members Section of the Australasian IAP web site.

PAEDIATRIC

Convenor: **A/Professor T. Yee Khong**

Meeting Room 4

2:00 - 3.45 pm

Lecture: Clinical Aspects of the Diagnosis of Liver Diseases in Childhood

Speaker: **SFA Dorney, The Childrens Hospital at Westmead, Sydney.**

Lecture: The Laboratory Investigation of Genetic Metabolic Disorders Presenting with Liver Disease

Speaker: **John Christodoulou, Director, Western Sydney Genetics Program, Childrens Hospital at Westmead, Dept of Paediatrics & Child Health, University of Sydney**

Lecture: Paediatric Liver Diseases and the Anatomical Pathologist

Speaker: **C W Chow, Royal Children's Hospital, Melbourne**

RENAL

Convenor: Dr John Dowling Meeting

Room 5 : 2:00 - 3:45 pm

6 cases for diagnosis on CD.

Speakers include *Drs. Claire Cooke-Yarborough, Moira Finlay, Prue Hill, Jeffrey Searle and John Dowling.*

GASTROENTEROLOGY

Convenor: Dr John Pedersen

Main Auditorium : 5:15 - 7:00 pm

Carditis - *Professor P Bhathal*

Gastric Observations - *Dr John Pedersen*

Intra-epithelial lymphocytosis in architecturally normal small intestinal biopsy specimens - *Ian Brown*

Inflammatory Bowel Disease: Uncommon Patterns and diagnostic pitfalls - *Andrew Clouston*

LYMPHOMA

Unfortunately there will be no Lymphoma Club Meeting this year.

UROLOGY

Convenor: Dr Geoff Watson

Meeting Room 4 : 5:15 - 7:00 pm

There will be a short presentation from *Dr Hema Samaratunga* discussing work she did with Jonathon Epstein on low-grade urothelial neoplasms and which she then presented at the Chicago IAP. This will be followed by a series of 7 slides.

Lecture:

"Comparison of WHO/ISUP and 1973 WHO classification of non-invasive papillary urothelial neoplasms for risk of progression". *Dr Hema Samaratunga*

Slide Presentations:

Dr Hema Samaratunga, Sullivan and Nicolaidis, Queensland

Prof Brett Delahunt, University of Wellington, NZ

Dr Cate Higgins, Princess Alexandra Hospital, Brisbane

Dr Leo Francis, Royal Brisbane Hospital

Dr Chris Douglas, HistoPath, Burwood, Sydney

*Dr Tony Watt, Princess Alexandra Hospital Brisbane.
Dr Sue Fredericks, Royal Prince Alfred Hospital, Sydney*

Visit of IAP President Elect Professor Shinichiro Ushigome, Emeritus Professor, Jikei University, Tokyo, and Past President of the Japanese Division will be attending our ASM.

Professor Ushigome will be President of the I.A.P. for our Congress in 2004. This visit will allow him to meet members of the Division and to inspect the Congress facilities in Brisbane.

Website Update Our Division's website can be accessed at: <http://www.iap-aus.org.au> or <http://iap-aus.org.au>

Within the site you will find information about the Division, this year's Annual Scientific Meeting and information about registering on-line, newsletters, information about other important pathology meetings, links to other sites of pathological interest, information about contacting the secretariat and information about becoming a member.

I am developing a Member's section on the website. In this area you will find interesting educational cases. To access the Member's site section you will need to know the username and password.

The Division's website is constantly being updated so remember to REFRESH the page in your browser. I would like to hear from members as to what they would like to see put on the website and how I can improve it. You can contact me at :

Email: richardj@icpmr.wsahs.nsw.gov.au

Phone: (02) 9845 6222

Richard Jaworski , Website Co-ordinator

Subscriptions Reminder Kindly check you records as to whether your subscriptions for Membership of the IAP are up to date. As a financial member you are entitled to discount attending the Annual Scientific Meeting.

Payments should be sent direct to the IAP office at 207 Albion Street, Surry Hills NSW 2010. (Not enclosed with payment for the ASM to Hoteliers International).

Memories of the 2001 Meeting



Noel Gordon-Glassford (Auckland), Myfanwy Plunkett (Perth), Kerry Knapp (Perth)



Dianne Payton (Brisbane) and Suzanne Arbuckle (Sydney)



Frances Petrey (Melbourne), Alison Skene (Melbourne), Leonard Wu (Melbourne)

ASM Accomodation

Hoteliers International have generously offered to process registrations for the ASM this year along with taking hotel bookings. Please utilise Hoteliers service and forward booking form as included in the registration brochure.

Sponsorship Donations for Congress 2004

Government:
Queensland Health

Companies:
QML Pathology
S&N Pathology
Mater Laboratory Services
Cytoc Thin Prep
PKF Accountants

Individuals:
Dr Ann Warrell

The Third Annual Asia-Pacific Meeting

The Third I.A.P. Asia Pacific Meeting is to be held in Bangkok January 21 - 23, 2003.

Delegates and speakers are required.

This is a combined meeting of all the Divisions in the Asia Pacific Region.

These include Thailand, India, Japan, Korea, Hong Kong, Indonesia and Australia and New Zealand.

For more information contact:
Dr Rangdaeng, (Email: srangdae@mail.med.cmu.ac.th)

Experience of an Australian
HER-2 Fish Reference
Laboratory: Correlation of
HER-2 Immuno-
histochemistry and Tumour
Type & Grade with HER-2
Fish Status.

**A.L. Morey,
A.S. Field
Anatomical
Pathology,
St Vincent's
Hospital,
Darlinghurst,
Sydney NSW
2010
Australia.**

INTRODUCTION

Since December 2001, Australian women with metastatic breast carcinoma have had access to government-funded Herceptin therapy if their tumour has been demonstrated to score 3+ on HER-2 immunohistochemistry (IHC) (regardless of antibody used) or is positive for HER-2 gene amplification by FISH. A centralised laboratory for HER-2 FISH testing funded by Roche on a per-test basis has been established in our University teaching hospital Anatomical Pathology department for assessment of cases with equivocal IHC. We have previously correlated tumour type and grade with IHC and FISH results on 30 cases from our laboratory (1), and here extend this analysis to the first 263 cases (the majority with 2+ IHC) referred from elsewhere in Australia.

Considerable variation in hybridisation efficacy has been noted between paraffin-embedded tissue blocks from different laboratories, most likely due to different fixation and processing protocols. This has resulted in an 18.6% repeat rate and a 14.4% non-diagnostic rate. As many of the blocks are archival, and a retrospective analysis of processing variables difficult, we took surplus fresh material from two breast tumours (Grade 3 ductal carcinomas, subsequently shown to be IHC 3+ and FISH positive), and assessed a variety of fixation strategies with the aim of detecting procedures deleterious to FISH analysis.

METHOD

i) Analysis of referred specimens

The 263 referred cases came from over 40 different laboratories. Tumour type and grade was independently reviewed (A.S.F) on H&E stained sections then compared with IHC and FISH results. 219 cases were primary tumours and 44 were nodal deposits or distant metastases. Outside IHC staining had been performed using several different primary antibodies and various protocols including the HercepTest (Dako). If IHC had not been performed prior to referral, in 64 cases this was performed using an in-house assay employing Dako polyclonal antibody A0485 (diluted 1:1000) on a Dako Autostainer after antigen retrieval in citrate buffer (pH6) for 40 mins at 95C. In preliminary experiments using antibody dilutions from 1:200 to 1:1600 on 19 tumours we found that this 1:1000 dilution most closely mimicked the result of the more expensive HercepTest (Dako). Detection was via the Vecta ABC Elite system. Staining was scored from 0 to 3+ according to HercepTest criteria.

FISH was performed on 4 micron paraffin sections using the Vysis Paraffin Pretreatment Reagent Kit and dual probe PathVysion HER-2 DNA Probe Kit, according to the manufacturer's instructions. A positive control section was included in each batch. Signal was analysed using a Zeiss Axioscope II microscope with attached AxioCam digital camera and Axiovision software. Gene amplification was defined as a HER-2/chromosome 17 ratio greater than 2.

ii) Mock fixation experiments

Small samples of fresh breast carcinoma tissue were exposed to a range of fixation procedures; the first experiment involved comparison of HER-2 IHC and FISH results

on tissue fixed in 10% neutral buffered formalin for 2 hr, 18 hr or 6 days. The second experiment involved comparison of IHC and FISH results on tissue samples exposed to: 4hr formalin fixation; freezing followed by 4hr formalin; microwave-aided (30mins at 60C) formalin fixation; delayed (by 2hr) formalin fixation; warm formalin fixation (60C, 18hr); and 2hr Carnoy's fixation followed by 2hr formalin. Similar variables have been represented among the cases referred to us, sometimes in combination. All results were digitally photographed at the same exposure under identical illumination. A subset of results is shown in Figure 1.

RESULTS

Table 1 : FISH results on 146 cases with "Scored" Outside IHC vs 64 Cases with In-House IHC (Dako A0458, 1:1000)

IHC Score	Number	FISHneg	FISHpos	Non-diagnostic	% Amplified
0	2 (12)	2 (5)	0 (0)	0 (7)	0% (0%)
1+ *	21 (16)	17 (12)	2 (0)	2 (4)	10% (0%)
2+	102 (17)	55 (10)	37 (6)	10 (1)	40% (38%)
3+ **	21 (19)	4 (0)	15 (16)	2 (3)	79% (100%)

* includes borderline 1+/2+ cases

** includes borderline 2+/3+ cases ; 2 outside 3+ IHC cases were also 0 or 1+ with a second antibody

Table 2 : FISH results by tumour grade

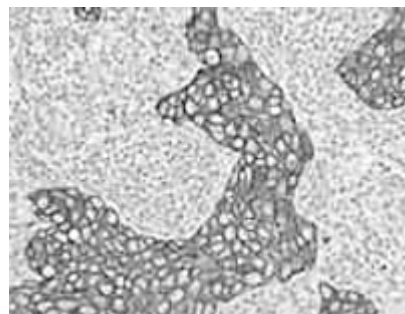
Tumour Type	Number	FISHneg	FISHpos	Non-diagnostic	% Amplified
Ductal grade I *	n = 12	9	0	3	0%
Ductal grade II	n = 65	37	15	13	29%
Ductal grade III	n = 157	79	62	16	44%
Classical lobular	n = 6	5	0	1	0%
Other tumours	n = 9	6	2 **	1	
Unclassifiable ***	n = 14	8	2	4	

* includes 2 tubular carcinomas

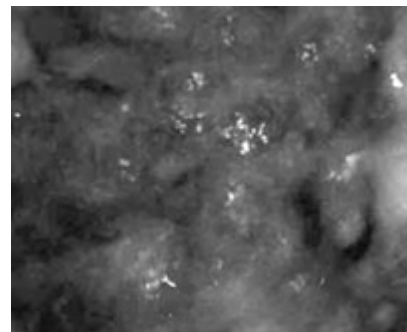
** the amplified cases were an invasive papillary tumour, grade 2, and one of 3 pleomorphic lobular carcinomas, grade 2.

*** unclassifiable due to limited material or crush artefact

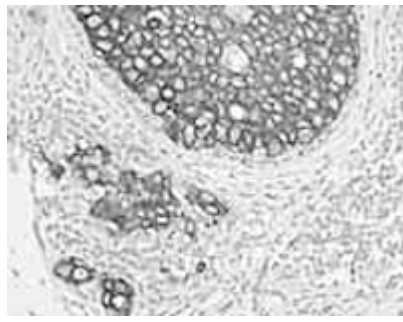
Figure 1 : Subset of Results of Mock Fixation Experiments



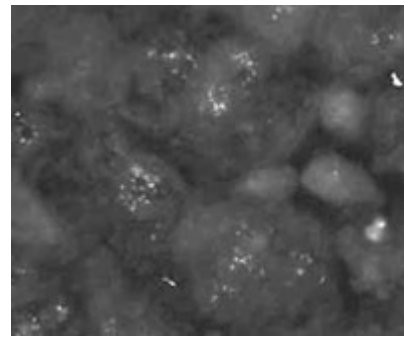
1 a) 18 HR FIXATION IH



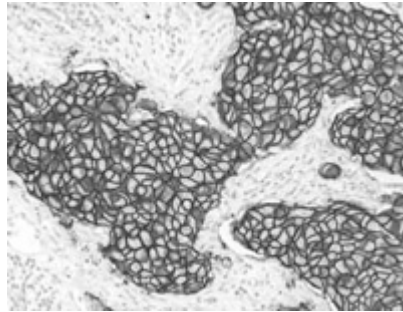
HER2 FISH



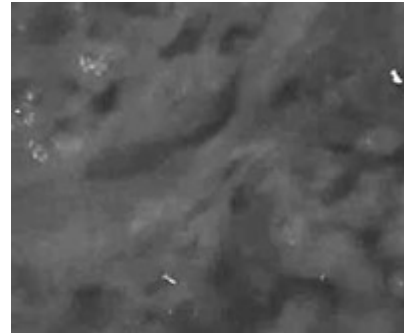
1 b) 6 DAY FIXATION IHC



HER2 FISH



1 c) CARNOYS FIXATION IHC



HER2 FISH

Discussions of results :

These data reinforce our previous suggestion:

(1) that triaging of cancers by type and grade could be used to focus HER-2 testing on tumours that are potentially amplified. Of the 141 assessable grade 3 ductal carcinomas referred with equivocal IHC, 44% were FISH+, whereas only 29% of the 52 assessable grade 2 ductal carcinomas and none of the 9 assessable grade 1 ductal/tubular carcinomas were FISH+. None of the 6 classical lobular carcinomas was positive, although one of three "pleiomorphic" lobular carcinomas showed low-level amplification. There was excellent correlation between in-house IHC 3+ and FISH+ (100% of assessable cases), although "external" 3+ IHC results showed slightly lower specificity (79%). All but two of the 37 IHC 1+ were FISH-negative (IHC slides were not reviewed); one of these showed borderline low-level amplification. The overall proportion of IHC 2+ cases found to be amplified (40%) is similar to recent reports

(2). Mock fixation studies demonstrated a surprising resistance of 3+ IHC and amplified HER-2 hybridisation signal to a range of "abusive" fixation regimens. Despite the fact that Vysis only guarantee successful FISH results for tissues fixed in 10% neutral buffered formalin for between 24 and 48 hours, in reality we have to deal with archival tissues fixed and processed in a variety of ways, often aimed at speeding up turn-around times. There is little available literature on the effects of such procedures on FISH efficacy. In general, FISH was more resilient to fixation variables than IHC, with most of the variables examined having minimal effect on FISH signal strength, however we noted a small diminution in hybridisation signal with prolonged fixation (Fig. 1b), and a marked loss of signal and increase in background autofluorescence in tissues exposed to Carnoy's fixative (containing chloroform and acetic acid) (Fig. 1c). Further questioning of referring laboratories supports the thesis that this "defatting" fixative may be responsible for a substantial proportion of our non-diagnostic cases. It is suggested that consideration be given to setting aside a small portion of each breast carcinoma at the time of receipt for "optimal" 24 hr formalin

fixation and potential subsequent HER-2 IHC/FISH, regardless of the fixation and processing regimen pursued for the remainder of the specimen.

References :

- 1). Field AS, Chamberlain N, Tran D, Morey A (2001) Suggestions for HER2/neu testing in breast carcinoma based on a comparison of immunohistochemistry and fluorescence in situ hybridization. *Pathology*, 33: 278-282.
- 2). Mass RD, Sanders C, Kasian C, et al. The concordance between the clinical trials assay and fluorescence in situ hybridization in the Herceptin pivotal trials. ASCO 36th Annual Meeting, May 2000, New Orleans. Abstract 291.

Note : Referral of material for HER-2 FISH testing

FISH analysis for HER-2 gene amplification is recommended in patients with equivocal immunohistochemical staining for HER-2. Roche have undertaken to fund HER-2 FISH on tumour tissue specimens from patients with metastatic (Stage 4) breast carcinoma and equivocal (2+) immunohistochemistry.

Please arrange for a paraffin block containing tumour tissue and a copy of the pathology report to be forwarded to:

FISH Laboratory Anatomical Pathology, L16 O'Brien Bldg St.Vincent's Hospital
Victoria St., Darlinghurst NSW 2010

If a patient does not fulfill the above criteria, FISH will not normally be funded by Roche, but may still be arranged through the laboratory. Enquiries about this, or other aspects of the test should be directed to Dr Adrienne Morey or Dr Andrew Field on (02) 8382 2319.