Histology Group of Victoria Inc.

Org. No. A003523F
ABN 49 725 623 468

http://www.hgv.org.au

PARAFFINALIA

Volume 17 Number 5

October 2012

Contents:

Editor: Elizabeth Baranyai

"The HGV aims to provide a dynamic continuing education program in which all persons with an interest in Histology and Histotechnology are freely invited to participate."

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Blurb from the Bush

Cape Schanck – we cannot wait to do it again. It was great to see so many Histologists and Haematologists being part of some stimulating education and mingling together socially. The venue delivered a relaxing setting for a wonderful variety of talks many pertinent to both disciplines, but even those that were only haematology centred brought back stored information from 2nd year undergraduate studies that I had not accessed for years. The social events saw some good wine and cider tasted, some golf played amongst exciting buggy driving, all culminating in a Saturday evening dinner which saw good food, plenty of drink and ended with dancing (Note the Russian leg dance can result in new suit pants splitting). It was universally agreed that revisiting this concept in the future was definitely worthwhile.

Registrations for the National meeting next year are open. The early bird registrations close at the end of January, so now is the time to start thinking about setting aside the weekend for some quality national and international education. The committee have made every effort to put together a diverse range of topics and workshops in a world class venue.

Our September scientific meeting at the Royal Children's Hospital saw record numbers appear out of the woodwork to get a glimpse of the RCH new facilities and to hear some quality presentations. Our last scientific meeting this year in combination with our AGM is on Thursday 15th November at Peter MacCallum. Nomination forms are now available for next year's committee. We are always welcoming of anyone who would like to contribute to the operations of the HGV.

If any members have suggestions as to any operational component of the HGV, please feel free to contact a committee member or alternately send an email to membership@hgv.org,au

Adrian Warmington
HGV President

Meeting Report:

The Royal Children's Hospital – Presentation and Tours

Hosted by: **Bronwyn Christiansen - Senior Scientist, Anatomical Pathology, The Royal Children's Hospital**
Presenters: **Megan De Koning, Histology Scientist, RCH – *Hirschprung's Disease***
Danka Mijatovic, Histology Scientist, RCH - *Medulloblastoma*
Maheema Langsakara, final year RMIT student – *Ewing's Sarcoma*

It was raining histologists at the most recent scientific meeting held at The Royal Children's Hospital (RCH). A crowd of fifty-nine packed the function room adjacent to the Ella Latham Auditorium. They were greeted with an array of food and sat patiently through a series of fascinating presentations, jumping off their seats to head off and explore the amazing surroundings of the newly built hospital.

Senior scientist of Anatomical Pathology at RCH, Bronwyn Christiansen hosted the night, welcoming everyone and introducing our first speaker, Megan De Koning. Megan's cleverly titled presentation, "Why does my bum AChE", detailed Hirschprung's disease and RCH's crucial role in the diagnosis of children suffering from this condition.

Hirschprung's disease is a congenital disorder of the large intestine in which certain nerve cells, known as ganglion cells, are absent causing constipation. The GIT is a long tube of muscles which contract and relax, but only if innervated. During foetal growth, the ganglion cells migrate through the proximal end of the GIT, right through to the distal end. In some cases, the ganglion cells do not always travel the entire way down to the rectum. In these cases, the bowel cannot contract, the passing stool gets stuck at the point where the innervation ceases, and the baby/child becomes constipated. The presentation and severity of symptoms depend on where the innervation ceases.

Treatment of Hirschprung's disease is through a "pull-through" operation, in which the diseased, aganglionic portion of the bowel is removed and the healthy portion is attached to the rectum, returning normal bowel function.

So where does anatomical pathology fit into this disease? Well, it's a histopathologist's job to determine whether ganglion cells are present or absent in bowel tissue, and if they are absent, where in the bowel do they finish? Hirschprung's disease traditionally used to be diagnosed through the review of a large series of at least 60 serial H&E sections, looking very hard for the absence of ganglion cells. This was an extremely difficult task, and so to make life a little easier a positive test for the disease utilising acetylcholinesterase (AChE) staining is now used. Histologically, the absence of ganglion cells leads to the hypertrophy of cholinergic nerve fibres. A normal bowel contains less than three nerve fibres per x10 microscopic field. In the diagnosis of Hirschprung's disease, greater than ten nerve fibres are seen per x10 microscopic field. The enzyme histochemical AChE stain is able to highlight these nerve fibres, staining them brown. The AChE stain is a direct colouring technique: cholinesterase activity produces thiocholine → reduces ferricyanide to ferrocyanide → precipitates copper ferrocyanide (brown) directly at the site of enzyme activity.

A fresh intestinal biopsy is received by the histology laboratory. Preliminary frozen sections are cut and stained with a rapid Toluidine Blue stain to ensure that all three layers of the intestinal wall are present. Nine serial sections are cut onto coverslips: H&E, AChE x7, H&E. AChE sections are incubated in AChE solutions for one hour at 37°C. The sections are washed, counterstained with haematoxylin, and mounted onto glass slides for interpretation.

It is very important that the tissue is **"big"** enough - the muscularis mucosal layer must span the width of a x10 microscopic field. It must be **"high"** enough – glandular epithelium must be seen and not squamous epithelium. And it must be **"deep"** enough – mucosa must be present.

Rectal biopsies to be sent to RCH must follow a few prerequisites. **IMPORTANT**: **the biopsy must BE FRESH**. Formalin vapour alone is enough to deactivate the enzymes which results in absolutely no staining. The best method of transport is fresh (not frozen), wrapped in some damp gauze (and not swimming in saline) in a specimen container and packed on ice packs. It is helpful to call in advance before sending the biopsy, so that the scientists at RCH can plan their day around the timely staining process. If in doubt, please contact the RCH scientists for proper delivery instructions.

Danka Mijatovic was next to present, exploring a case study on medulloblastoma. The case study involved a two year-old boy who presented to his clinician with a tumour in the posterior fossa of his brain. The boy had been vomiting and feeling lethargic. Three specimens were received by the laboratory: cerebrospinal fluid for cytological evaluation, and fresh and formalin-fixed brain tissue. Danka discussed the microscopic findings of the patient's brain tumour, which was diagnosed as medulloblastoma, through a variety of histology and cytology images.

Medulloblastomas are small blue cell tumours. They are one of the more common neuroepithelial tumours in paediatric patients. Medulloblastomas arise in the posterior fossa of the brain, and occur mostly in young children between the ages of five and six, with a predominance seen in boys. The tumour starts primarily in the cerebellum, which is the part of the brain that controls balance, movement and coordination. Increased intracranial pressure results from tumour growth. The cause of this tumour is unknown. It is not genetically inherited, however, several studies suggest that chromosomal abnormalities can occur at any point in the affected child's development, even while still a foetus.

The immunohistochemical stains which are positive for this tumour are glial fibrillary acidic protein (GFAP) and synaptophysin, however, staining can be variable. GFAP stains positive mostly in the desmoplastic variant of medulloblastoma. GFAP measures the astrocytic differentiation of tumour cells and distinguishes medulloblastoma from reactive gliosis. Synaptophysin is an integral membrane glycoprotein that arises from neurons or neuroendocrine proteins, and is also present mostly in the desmoplastic variant. The main differential diagnosis of medulloblastoma is ependymoma which has an almost identical gross appearance.

The treatment of medulloblastoma is dependent of several factors: the age of patient, tumour size, and the tumour's ability to spread and metastasize. Treatment is usually through the surgical removal of as much of the tumour as possible, without causing impairment to the normal brain tissue. After surgery, chemotherapy follows to prolong the survival of the patient. The five year survival rate of paediatric patients post-chemotherapy is around 85%.

The final presentation of the evening was by Maheema Langsakara who reported on a case of Ewing's sarcoma. The case study involved a fifteen year-old boy who presented with a right ileal mass and localised pain. A core biopsy was taken from the mass and the microscopic findings showed a largely viable round blue cell tumour admixed with mitoses, apoptotic debris and coagulative necrosis. At this point, the differential diagnosis included Ewing's sarcoma, lymphoma and rhabdomyosarcoma. Special stains and immunohistochemical stains were performed. The tumour cells were positive for PAS, negative for PAS-D, strongly positive for CD99 (MIC-2), and negative for CD45, desmin and cytokeratin. These results, together with the morphology of the tumour cells, all steered towards the diagnosis of Ewing's sarcoma.

Ewing's sarcoma is a relatively uncommon tumour, only accounting for 6-8% of primary malignant bone tumours. However, it is the second most common sarcoma in bone and soft tissue in children, with a median age of onset of 14 years, and a male predominance. The pelvis is the most common primary site of the tumour. Ewing's sarcoma clinically presents with pain and a mass in the involved area, remittent fever and anaemia. Common sites of metastases include the lung, bone and bone marrow. A core biopsy is the recommended tissue for diagnosis as there is less local contamination compared to an open biopsy.

85-90% of Ewing's sarcoma patients have a translocation between chromosomes 11 and 22 – t(11;22) (q 24;12). The remaining 5-10% of tumours have a translocation between chromosomes 21 and 22 – t(21;22) (q21;12). Treatment includes local therapy, surgery, and radiation therapy. The prognosis of a patient is dependent on the presence/absence of metastases, the size, and the extent and location of the primary tumour.

After the series of informative presentations, Bronwyn spoke about the RCH move, showing a slide show of photographs from their previous residence. Everyone was then separated into three groups. Bronwyn, Megan and Tania Marsden each took a group to tour around the hospital's atrium, Main Street, and the fourth floor laboratories where the histopathology laboratory is located.

On Main Street, we encountered Mali, a life-sized sculpture of Melbourne Zoo's baby elephant, a tapestry by the Victorian Tapestry Workshop, a two-story coral reef aquarium and a 14 metre tall sculpture by artist Alexander Know called "Creature". Everyone ogled in jealously at the hospital food outlets, including ice creamery Trampoline, and McDonalds.

With eyes wide open in awe, everyone was escorted up to the histopathology laboratory where they got to witness the laboratory's transformation from "old" to "new".

In summary, the Royal Children's Hospital impressed histologists from all around at this scientific meeting, covertly bringing out the child in everyone.

Michelle Zammit
The Alfred Hospital

Review of the 2nd International Conference in Diagnostic Immunohistochemistry Part 2

Day 2 It's going to be a long one! The first speaker was **Xavier Matias-Guiu**, whose topic was **"IHC as a tool to assess molecular alterations in cancer".** In the case of endometrial cancer both types 1 and 11, morphology is very important, so is IHC the most appropriate technique to address the issue? Considerations include tumour heterogeneity and specificity of the antibodies. Micro satellite instability can be associated with endometrial carcinoma, either in familial tumours involving a hereditary mutation, or sporadic tumours with random methylation errors. One of the features of many types of malignancy is EMT (epithelial to mesenchymal transition), transient moving to permanent. Epithelial cells "change" to fibroblasts, myometrial cells become sarcomatoid, and invasion indicates carcinoma. The current treatment for endometrial carcinoma is surgery and radiation, 80% of patients do well, but 20% are resistant to radiation. Some tumours develop an adaptation to hypoxia which confers a resistance to radiation and leads to post-radiation recurrence. It would be useful to be able to identify a predictive marker for drug response, and to be able to evaluate the patient's likely response to treatment.

Young Kwun was the next presenter, discussing **Proteomic analysis of colorectal cancer using iTRAQ mass spectrometry with IHC validation.** Proteins consist of amino acids and peptide bonds, and are expressed by a genome. PROTEins genOME. Proteomics is the study of the global changes of proteomes in cells and tissues in response to both internal and external stimuli. The emphasis is on identification by database matching.

DNA	→	GENOME
↓		Regulatory genes
mRNA		
↓		↓
Polypeptide		
↓		Regulatory proteins
Protein	→	PROTEOME

The proteome consistently changes in response to the needs of the body. Proteins are closest to the actual disease that the parent genes, and are the ultimate cell marker. The development of colorectal carcinoma:

Normal colon	→	Proliferation of epithelium	→	Adenoma	→	Colorectal ca
↑		↑		↑		
Hereditary abnormalities		methylation abnormalities		Mutations, deletions		More genetic abnormalities

The aim is analyse and compare the proteomes of normal and tumour tissues and evaluate potential proteins as predictive markers. Proteins found to be differentially expressed in adenoma are Galactin-1 and S100A9. Galactin-1 showed strong expression in tumour. S100A8/9 was expressed in histiocytes and neutrophils while tumour cells were negative. Other antibodies investigated include CEA, CK20, Caldesmon, Maspin and β-catenin. In short, the findings of the study included the confirmation of some previously published protein alterations in CRC, the identification of alterations previously observed in other tumours but not CRC, the identification of novel and specific alterations in protein expression and some understanding of the influence of differentially expressed proteins on such functions as cell proliferation, vascular proliferation and cell survival.

The last speaker before morning tea (what! Only morning tea time??) was **Kieran Sheehan** discussing **Prognostic markers in colorectal cancers, morphology, IHC or molecular?** Morphology is crucial, and with the intelligent use of IHC, screening will improve CRC mortality more than biologics, but can we improve on the use of traditional markers such as CDX-2,CK7 and CK20? Can we introduce new reproducible markers? Some stages of cancer are more important than others (Tumour, Node, Metastases is the current form of staging). With CRC there is variable prognosis in Stage 11, with 30% mortality which can create the dilemma of whether to treat a patient aggressively or not. Some prognostic markers are stage independent. The retrieval of lymph nodes is important, there can be a gain in survival if up to 19 negative nodes are found which requires mesocolon to be present in the resection specimen. The microscopic prognostic markers to be examined include peritoneal involvement, lymphovascular invasion, perineural invasion, extent of extramural spread and tumour budding. The presence of any of these indicate the need to treat aggressive disease. Venous invasion can be investigated using an elastin stain, D2-40 can be used to evaluate lymphatic invasion and CAM 5.2 to evaluate tumour budding, but neither are better than an H & E! Extramural spread is recorded as the maximum distance of tumour spread beyond the bowel wall, measured and recorded in millimetres, from the outer margin of the muscularis propria. Excellent gross and microscopic pathology is essential!

Tumour budding is a strong and reproducible prognostic marker in T3N0 CRC, it is the mechanism by which peritoneal invasion occurs. Tumour budding is the detachment of tumour cells singly or in small groups (<5), beyond the edge of the tumour and is an adverse prognostic marker. All slides are examined so there is an inbuilt control for tumour heterogeneity, rapid assessment is incorporated into routine pathological examination, it is simple, rapid and cost effective. H&E is specific and cheap, IHC (for cytokeratins) is more sensitive, perhaps less specific and is more expensive, and molecular techniques are more complex, there are at least 50 genes associated with epithelial-mesenchymal transition.

Mismatch repair gene IHC is commonly requested for CRC. This is relevant for 1:10 patients, is a good prognostic indicator as well as predictive for treatment, and offers personal and familial surveillance for CRC. In this case morphology isn't relevant, IHC is inexpensive, can be performed in a routine laboratory with a satisfactory turnaround time, compared to molecular studies for microsatellite instability which are more costly, performed in a molecular laboratory and are less relevant clinically. In general all techniques and criteria should be standardised, excellent gross and microscopic pathology is essential, and prognostic parameters need to be evaluated by substage and by molecular classification.

After a well-deserved morning tea, **Stephen Fox** from Peter McCallum Cancer Centre spoke about **Her-2 testing in breast and gastric cancers**. Predictive markers are essential for targeted therapies. Her-2 in breast predicts the likelihood of relapse and over-all survival, the response to chemotherapy either positive or negative. 90% of Her-2 over-expression is due to amplification, which is an early event during the course of a tumour's development. The Her-2 status can change during the progression of cancer. A measurement of Her-2 status at diagnosis requires accurate and standardised testing to facilitate the

correct classification. Fixation is critical for any tissue undergoing testing for Her-2, particularly for ISH, 10%NBF is the fixative of choice, avoid decalcification fluids, chloroform (in Carnoy's). For a laboratory to be accredited for SISH testing each pathologist needs to report a minimum of 50 cases per year, and 150 cases per laboratory. A TAT of 7 days is expected.

Her-2 status in gastric/ gastro-oesophageal carcinomas: 10-25% are Her-2 positive. The staining pattern is basolateral, not circumferential as in breast, because the gastric cells are polarised. 50% of cases are heterogeneous, so multiple biopsies should be taken (6-8) and at least 5 clustered cells are required, more in surgical specimens.

Piero Nelva (scientist) and **Beena Kumar** (pathologist) from Monash Medical Centre together delivered an entertaining and informative presentation focussing on the team-work required within a laboratory to achieve the right result! Pre-analytical: **Fixation cannot be overstated and cannot be underdone!** Piero showed examples of how under-fixation can significantly alter the staining result. Other factors which can influence the final result include the presence of crush artefact, the adequacy of tissue processing, the thickness of the section, the integrity of the slides used, the age of the section (time lag between cutting the section and staining), there is a noticeable difference in staining intensity after 24 hours! Analytical: pathologists require a clear understanding of: expected staining patterns, established protocols for scoring, the expectations of the treating clinicians, the subjectivity associated with the assessment of IHC stains. Post-analytical: a clear expression of the results in a pathology report which avoids the use of equivocal terminologies. IHC has a significant role in breast pathology. Predictive markers are ER,PR,Her-2; prognostic markers p53,Ki-67; diagnostic markers p63,CD 10, Smooth muscle actin(SMA), Smooth muscle myosin heavy chain (SMMHc) and E-Cadherin. Good ER and PR staining should show a crisp nuclear stain that facilitates the evaluation of the percentage of nuclei stained and the staining intensity. Several examples of good and poor were shown. Choosing the best antibody clone is important as well as being able to trouble-shoot false results. There will always be differences in staining results between cores and excision specimens, for several reasons including fixation, particularly penetration, and tumour heterogeneity. There is an established protocol for the interpretation of Her-2 staining: 0-no staining; 1+faint, incomplete membrane staining of <30% of tumour cells; 2-(equivocal) weak to moderate complete membrane staining in at least 10% of tumour cells; 3+(positive) strong complete membrane staining in at least 30% of tumour cells. Good and poor examples were demonstrated, the key to acceptable results is appropriate retrieval and the use of a multi-tissue control block. Trouble-shooting tips for resolving unacceptable performance include assessing antibody concentration, incubation time and investigate amplification techniques or blocking techniques. Optimal staining results were also discussed for p63, Ki-67 and E-Cadherin, as well as the role these antibodies play in breast pathology. The take home message was to carefully monitor daily testing results, participate in appropriate external Quality assurance programs and take the results seriously!

The final speaker before lunch was **Louise Alldridge** who presented a report on her project **Validation of Protein Biomarkers for Proteome changes in Human Breast Carcinoma.** Recent advances in breast cancer have relied on the detection of specific target molecules, and more are needed. The aim is to apply proteomics to human tissue to systematically identify and characterise proteins for structure, function, activity, quantity and interaction, because cancer drugs act on or via proteins and need to be individualised as not one fits all. A great deal of data was displayed throughout the presentation. The conclusions reached were that IHC was successfully and extensively used to validate and investigate the potential of a sub-group of proteins as markers for tumour genesis, invasiveness and lymph node metastasis.

After a sensational lunch in the only revolving restaurant on the Gold Coast (atop the Crowne Plaza), the afternoon sessions were off to a flying start. **Dr Rose Miller** from Wellington New Zealand delivered presentation which brilliantly covered **Immunohistochemistry in the Diagnosis of Bladder and Prostate Neoplasms.** Prostatic neoplasia is most commonly of epithelial cell origin, adenosis being the benign form, and malignancy either acinar or ductal adenocarcinoma. The risk factors include age, race, family history, hormone levels and environmental influences. The condition is often asymptomatic with only a raised serum PSA and an abnormal digital rectal examination (the male equivalent of a mammogram in terms of dignity and discomfort??), urinary symptoms occur late in the progression of the disease to metastasis. The approach for diagnosis is serum PSA, digital rectal examination, TRUS biopsy, transurethral resection of the prostate or radical prostatectomy +/- lymph node dissection. Bladder neoplasia is most commonly epithelial, papilloma being the benign form and urothelial carcinoma either non-invasive or invasive. Risk factors include being a male cigarette smoker and exposure to aromatic amines. Symptoms include haematuria, lower urinary tract irritation, hydronephrosis and systemic symptoms of malignancy. The approach to diagnosis involves urine cytology, cystoscopy and biopsy and cystectomy.

The IHC panel is as follows:

Prostate	Bladder
Epithelial -AE1/AE3	34βE12 CK 7 CK 20 P63
Basal cells -34βE12 - p63 -CK5/6	
Prostate carcinoma associated marker –p504S	
Prostate differentiation – PSA - PSAP	

Other markers include Uroplakin, Thrombomodulin, Prostein, ERG and cocktails such as p504s/p63/34βE12; p504s/p63/CK5/6; p504s/p6s; and PIN-4 (CK 5/CK 14/p63/p504s.

Two superbly-illustrated case studies demonstrated the use of some of the antibodies discussed, and the relevance of the staining results particularly in relation to the Gleeson Score. Some key points to note are that not all prostate cancers are positive for p504s and not all benign lesions are negative. Basal cells are specialised epithelial cells located in the basal layer, and are lost in carcinoma, however, morphologically their appearance can be mimicked by prostatic stromal cells, endothelial cells and neoplastic cells tangentially sectioned, hence the need for true basal cell markers. Two cases involving bladder neoplasia and the differentiation between bladder and prostate neoplasia again superbly illustrated demonstrated the need for differentiation and the appropriate antibodies to employ. The treatment for bladder and prostate neoplasia is different, as is their morphology, however both may be present at the same time. The take home message is that IHC is critical for determining prostate pathology, helpful in bladder pathology, don't discount morphology, know the expected results for the IHC stains employed and be vigilant for the appearance of new markers.

The final presentation before afternoon tea: **IHC prognostic and predictive markers in lung cancer- Dr Edwina Duhig** (Director of Anatomical Pathology, The Prince Charles Hospital, Chermside, QLD). The 10 most common cancers diagnosed in Australia, according to "Cancer in Australia, an overview 2010" are as follows:

Male	Number	Female	Number
Prostate	19403	**Breast**	12567
Bowel	7804	**Bowel**	6430
Melanoma of skin	5980	**Melanoma of skin**	4362
Lung	*5948*	***Lung***	*3755*
Lymphoid cancers	4116	**Lymphoid cancers**	3160
Myeloid cancers	1859	**Uterus**	1942
Kidney	1716	**Unknown primary**	1401
Bladder	1644	**Thyroid**	1331
Unknown primary	1496	**Ovary**	1266
Pancreas	1352	**Myeloid cancers**	1232

Also from "Cancer in Australia, an overview 2010", the 10 most common causes of death from cancer are as follows:

Male	Number	Female	Number
Lung	*4715*	***Lung***	*2911*
Prostate	2938	**Breast**	2680
Bowel	2191	**Bowel**	1856
Lymphoid cancers	1423	**Lymphoid cancers**	1129
Unknown primary	1247	**Unknown primary**	1097
Pancreas	1233	**Pancreas**	1015
Myeloid cancers	867	**Ovary**	848
Melanoma of skin	864	**Myeloid cancers**	592
Oesophagus	790	**Brain**	457
Liver	717	**Other digestive**	441

It can be seen that although lung cancer is the fourth most commonly diagnosed cancer in Australia it is the most common cause of death from cancer for men and women. Lung cancers present late, with most patients already having metastatic disease at the time of diagnosis. The primary aim of histology and cytology is to determine the cell-type. Only small cell carcinoma is responsive to irradiation and chemotherapy, whereas the treatment for all other malignant lung cancers is surgery. IHC facilitates the determination of cell type and better sub-typing of lung tumours, and identifies markers for specific genetic abnormalities and also new prognostic and predictive markers.

Metastatic cancers occurring in the lung can be identified using the following antibodies: Breast carcinoma ER and CK7 +, colorectal carcinoma CK20 and CDX2 +, urothelial carcinoma CK7,CK20 and thrombomodulin +, prostatic carcinoma CK7, CK 20-, PSA +, thyroid carcinoma TTF-1 and thyroglobulin +, there are no reliable markers for metastatic SCC. Pathologists are asked to subtype lung cancers, and rely on classification and ancillary tests to do so. They need to be able to identify the different types of lung cancer such as SCC, adenocarcinomas, non small cell carcinomas, non squamous carcinomas and large cell carcinomas. The WHO classification 2004 lists 8 specific and a 9th "other" category of tumour. The first 5 are

carcinomas with specific identifying criteria, in conjunction with IHC results, the following algorithm for primary lung cancers has been proposed.(Mukhopadhyay et al. Am J Surg Pathol 2011; 35: 15-25)

DIAGNOSIS	TTF-1	Napsin	p 63	CK 5/6
Adenocarcinoma	+	+/-	+/-	-
Squamous cell carcinoma	-	-	+	+
Squamous cell carcinoma	-	-	Diffusely +	-
Poorly differentiated NSCLC NOS	-	-	Focally +	_
Poorly differentiated NSCLC NOS	-	-	-	-

TTF-1 and p63 are the most useful and reliable markers, Napsin and CK 5/6 and mucin stains are also valuable.

With the aim of improving the accuracy of predictive and prognostic markers, testing beyond IHC is moving into the realm of molecular and biomarkers. The role of the EGFR signalling pathway in carcinogenesis was highlighted. It comprises proliferation, angiogenesis, invasion, metastasis and resistance to apoptosis. Molecular testing for EGFR-activating mutations, EML4-ALK mutations, KRAS, ERCC1, RRM1, BRCA1 and SerpinB3 were mentioned, with EGFR mutation being further discussed. IHC for EGFR mutation involves the use of mutation-specific monoclonal antibodies. The results have been compared with direct DNA sequencing and revealed 92% sensitivity and 99% specificity. However a review in 2011 on the use of biomarkers in the treatment of NSCLC suggested that there is insufficient evidence to support testing for KRAS, chemosensitivity markers such as ERCC1, BRCA, RRM1, p53,Ki-67, and p16, to name a few.

Apologies to the speakers after afternoon tea, but the lure of the swimming pool was too great, it was after all the Gold Coast in the height of summer!

Sunday morning's presentations had a strong research flavour, commencing with **Mark Slevin** discussing **IHC and fluorescent identification of immature dysfunctional vessels.** The ability to identify dysfunctional vessels is important in such conditions as stroke and even Alzheimers. Markers discussed included CDK5 and actin.

Sharon Mason shared her experiences using **IHC as a tool for neuroscience research.** The use of vibratome sections for IHC was discussed. Thicker sections enable axon tract phenotypes to be examined, 3D morphology of dendrites can be determined and confocal imaging and stereology is better. Sections are stained as free-floating section, technical advantages include no need to dehydrate before embedding, no deparaffinisation and rehydration before IHC, no retrieval required, reduced artefacts and tissue autofluorescence. Disadvantages include no ribbons so delicate single sections must be handled, sections are thicker so antibody penetration time is longer and attaching vibratome sections to glass slides can initially be difficult. Examples of work with mouse embryos were described, including trouble shooting for unexpected results (fixation again!!!), and methods for counting cells. The final words of wisdom are worth remembering *" Immunohistochemistry is like cooking. There are many recipes out there, but some of them do not work out well. However, when they do, they are great! You need the right ingredients, a dose of experience, a few tricks from old cooks, and a grain of common sense"* (or should that read "old chooks" ?)

Again, apologies to those speakers whose presentations I missed, the call of the beach was too strong! The next session I attended was delivered by **Greg Rice** who discussed **New approaches in Biomarker Discovery.** The first example discussed was ovarian cancer, of which there are 230,000 new cases per year,

90% of which occur in women with no identifiable risk factors, 70% present with disseminated disease, the 5 year survival is 50% and there are 110,000 ovarian cancer-related deaths per year. Sobering statistics. Currently CA125 screening is part of an algorithm leading to further investigation for patient management. Trials are being done to investigate the possibility of developing tests involving" multi-markers" Premature birth was also discussed, more children under 5 die due to pre-term birth than from AIDS, malaria or TB. 130 million babies are born each year. 2.7 million die before their first birthday due to prematurity, in 50% of cases the cause of prematurity is unknown, and there is no effective antenatal treatment. A biomarker than can be detected in vaginal fluid to predict prematurity would impact on the majority of paediatric and obstetric morbidities and mortalities associated with prematurity.

Xavier Matias-Guiu discussed **New IHC markers: PTEN** Phosphatase and tensin homolog (PTEN) is also known as MMAC1 (mutated in multiple advanced cancers 1) is a tumour suppressor gene. In the nucleus it controls double strand repair and in the cytoplasm it increase apoptosis. Cowden syndrome, caused by PTEN mutations is a rare, autosomal dominant disorder characterised by multiple benign hamartomas and an increased risk of developing certain malignancies such as breast, thyroid and endometrium. Non-inherited (somatic) mutations of the PTEN gene are among the most common genetic abnormalities found in human cancers, but unlike Cowden syndrome these mutations are only present in tumour cells. PTEN may be the most frequently mutated gene in prostate cancer and endometrial cancer, is frequently seen in glioblastoma, melanoma and triple negative (ER ,PR, Her-2) breast cancers and colon cancer. PTEN is a potential marker of response or resistance to targeted therapy.

Given that Jetstar waits for no-one, I was reluctantly obliged to depart before the final sessions. The next International Workshop in Diagnostic Immunohistochemistry will be held in Sydney on 30th May 2013, prior to the IAP meeting which starts on 31st May.

Judy Brincat

Focus Pathology

Under the Microscope : Bernadette Middleton

Anatomical Pathology
Scientist 2IC
St John of God-PathCare Geelong

Reported by: Kellie Vukovic and Rebecca Forrester

1. What was your first job?
Trainee Medical Laboratory Technologist at The Victorian Cytology Service/Prince Henry's Hospital

2. How long have you worked in histology?
I have been in pathology 41 years, mostly in Anatomical Pathology, both histology and cytology. Hard to estimate how many years in histology, but I first worked in histology in 1973!!!!

3. When people ask, "So, what do you do?" How do you explain Histology?
We prepare tissue for examination by a pathologist so they can diagnose what disease a patient may be suffering from…..but if I want to scare the children, we 'chop up bits of people'

4. Who would you most like to have dinner with and why?
Mick Jagger, what can I say, I'm a child of the sixties, saw him first when I was about 14!!! Sure neither of us has changed much in the interim.

5. What is your all-time favourite movie?
The Innocents, a very old movie based on a P D James novel, saw it as a teenager, and it started my love of psychological thrillers!

6. What is your favourite stain?
PAS – Silver, on a renal biopsy. The way it shows the structure of the kidney is unbelievable

7. What is your favourite food/Restaurant?
I love food as can be seen from my girth. Toss up between chocolate or seafood….but definitely not together.

8. What is the best conference you have ever attended?
Combined ASC and NZSC conference in Auckland. Great conference and those New Zealanders know how to party!

9. What is your dream holiday destination and why?
Europe and by the time you read this I will be there. I promised myself not to die before I saw the Sistine Chapel.

10. How has the move to a new home been?
Less enjoyable than sticking pins in my eyes! I promise myself never again, but once settled it does have some very good points…

National Meeting Provisional program 2013

Workshops

Speaker	Topic
Dr Thomas Haas	(Basic) – Tissue identification for the Histologist
Dr Guy Orchard	(Advanced) – MOHS technique
Dr Thomas Haas	(Advanced) – Stalking the Big Four: New developments in the diagnosis of breast, prostate, colon and lung carcinomas
Various Jason Kelly Alex Laslowski Mark Bromley	(Basic) - Basic Immunohistochemistry: Focus on stain identification and recognition of some popular antibody markers Prostate markers. Lymphoma markers Skin markers.

Provisional Program (Confirmed speakers to date)

Dr.Keith Byron	Introduction to Molecular Techniques
Dr. Guy Orchard	IHC Diagnosis of Malignant Melanoma
Dr Beena Kumar & Piero Nelva	Technical aspects related to Breast cancer diagnosis
Dr Thomas Haas	Sentinal Lymph Nodes: A look at the significance from a histotech's perspective.
Professor Peter Choong	Targeted therapies in Osteosarcoma.
Soeun Kinh Mom	Male infertility : Testicular biopsies
Natalie Kvaleheim	Abalone virus ISH
David Gan	Making the most of your specimen in IHC
Greg Jenkins	Histology disasters
Anne Prins & Alana Treasure	Interesting Histology
Andrew Griffin	NATA: Aspects of the standard in reference to laboratory accreditation.
Naomi McCallum	TBA (Diagnostic Electron microscopy group)
Dr Nina Fotinatos	Career Paths/ research opportunities post the Medical Laboratory Science course
Sarah Morabito	TBC
Anthony Van Galen	Prostate cancer
Suzanne Svobodova	Companion diagnostic molecular testing for BRAF, KRAS and EGFR.
MyHoa Huynh	GVHD: An Introduction
Lynne Hartley	Ovarian cancer (research)

AUSTRALIA

NATIONAL HISTOLOGY CONFERENCE 2013

Registration Form

26-28 April 2013

Crown Conference Centre, Melbourne

HGV

Histology Group of Victoria Inc.

NATIONAL HISTOLOGY CONFERENCE 2013

HGV Histology Group of Victoria Inc.

Venue
The National Histology Conference 2013 will be held at the Crown Conference Centre which is located at 8 Whiteman Street, Southbank, Victoria.

Car Parking
Free car parking will be available at Crown Conference Centre should you require this please advise InFront Events Australia, as spaces must be booked in advance to receive complimentary parking.

Registration Payments and Inclusions
All prices are listed in Australian dollars (AUD), and are GST inclusive.

Full package registrations include
- Attendance to all sessions of the conference
- All conference documentation
- Conference satchel
- Catering as per program
- Welcome Reception on Friday 26th of April
- Conference Gala Dinner on Saturday 27th of April
- Does not include attendance to workshops on Friday 26th of April, these must be purchased separately

Conference only registrations include
- Attendance to all sessions of the conference
- All conference documentation
- Conference satchel
- Catering as per program
- Welcome Reception on Friday 26th of April
- Does not include attendance to Conference Gala Dinner, tickets must be purchased separately for this
- Does not include attendance to workshops on Friday 26th of April, these must be purchased separately

Day Registrations Include
- Attendance to all sessions on nominated day
- Conference satchel
- Catering as per program on nominated day
- Does not include attendance to social events, tickets must be purchased separately for this

Conference Fees Do Not Include
- Travel to and from conference venue
- Insurance of any kind
- Hotel and other personal expenses (competitive room rates are available through InFront Events Australia)

Early Bird
Early Bird is available until the 31st of January, full registration fees will be applicable from the 1st of February, 2013.

Welcome Function
The Welcome Function is a great way for delegates to talk to exhibitors and manufacturer's in a relaxed and casual environment, there will be nibbles and drinks provided.

Conference Gala Dinner
The Conference Gala Dinner will be held in the River View Room in the Crown Casino, watch the iconic Melbourne flames on the Promenade from the balcony, enjoy a three course meal and some great entertainment with industry fellows.

Payment Policy
Full payment **must** accompany the registration form, for your registration to be confirmed.

Cancellation policy
All cancellations must be notified in writing to Conference Managers, InFront Events Australia. Cancellations prior to December 1, 2012 will receive a 50% refund of total registration fees. Refunds for cancellations made after December 1, 2012 will only be made in exceptional circumstances. Accommodation refunds are subject to the terms and conditions of each hotel, please contact InFront Events Australia if you wish to find out more about these terms and conditions.

Liability Disclaimer
In the event of industrial disruption or other unforseen circumstance, the Conference Organisers accept no responsibility for loss of money incurred by delegates, exhibitors or sponsors.

Further Information
For further information on terms of registration and up to date information on speakers, sponsor and conference program, please refer to the conference website:
www.nationalhistologyconference.com.au

Registration Desk
All exhibitors, delegates and participants will be required to visit the registration desk prior to entering the conference areas and functions, on your first day only. The registration desk will be located in the ground foyer of the Crown Conference Centre on Whiteman Street.

Accommodation
Melbourne ShortStay Apartments – Southbank Deluxe
The Melbourne ShortStay Apartments at Southbank Deluxe have a fully equipped kitchen with a gas cook top and dishwasher. Broadband is available in the room and each room has 26 Foxtel channels. The hotel has a stunning garden terrace with a heated indoor pool, with a gymnasium for those who like to keep fit.

Crown Promenade Hotel
Set in the heart of South Wharf, conveniently located within the building of the conference venue. Each of their modern guest rooms and suites have been innovatively designed, and includes internet access for one device.

Holiday Inn
The Holiday Inn is conveniently located a "stone's throw" away from the trendy Southbank area. Swim a few laps in their heated pool or steam away stress in their sauna.

Travel Lodge
The Hotel is within easy walking distance to great restaurants and cafés (chargeback facilities available with some restaurants in Southbank), impressive shopping, renowned art galleries and the Crown Casino.

Melbourne
Just when you think you've got Melbourne figured out, you'll uncover one more pocket of the CBD with a particular vibe that makes it feel so right to lose another three hours or so.

While fairly compact in size, Melbourne's CBD is split into distinct areas, each with its own fortes and flavours. Bourke Street Mall offers no-strings-attached retail therapy, Chinatown is all dumplings and heritage, Collins Street knows how posh you really are, Flinders quarter squeezes your creative juices, and the sports precinct's fever is contagious. The alleys and laneways, conventional and vertical, make their own rules, and encourage you to break them.

Go on, just look around one more corner, so it might be a good idea to extend your stay!

NATIONAL HISTOLOGY CONFERENCE 2013

Histology Group of Victoria Inc.

Personal Details

Title: Dr / Prof / Mr / Mrs / Ms / Miss / Other

First Name | Surname

Position

Organisation

Address

Suburb / City

State | Postcode

Country (If other than Australia)

Email | Mobile

Phone | Fax

Other Requirements (e.g Dietary, Wheelchair access, Hearing Loop, etc)

Will you require onsite car parking at Crown Conference Centre | Yes ☐ No ☐ | Number Plate

☐ I authorise Histology Group of Victoria to keep me informed about future events and promotions (Please Tick)

☐ I authorise my contact details to be provided to registered Exhibitors and Sponsors of the Histology Conference 2013 (Please Tick)

☐ I authorise for my name and contact details to be published in the conference brochure (Please Tick)

Registration Details

Registration Type:

☐ Early Bird Delegate – Full Package Available until 31st of January, 2012	$570.00
☐ Early Bird Delegate – Conference Only Available until 31st of January, 2012	$450.00
☐ Delegate – Full Package Applicable from 1st of February, 2012	$720.00
☐ Delegate – Conference Only Applicable from 1st of February, 2012	$600.00
☐ Student Delegate	$100.00

Day Registration:

☐ Early Bird Saturday Only Registration Available until 31st of January, 2012	$270.00
☐ Early Bird Sunday Only Registration Available until 31st of January, 2012	$180.00
☐ Saturday Only Registration Applicable from 1st of February, 2012	$360.00
☐ Sunday Only Registration Applicable from 1st of February, 2012	$240.00
☐ Student Day Registration (Please Circle) Saturday Sunday	$50.00

Friday Workshop:

All Workshops are $95 each

☐ Workshop 1 – MOHS - Guy Orchard PhD (Advanced)

☐ Workshop 2 – Stalking the Big Four: New developments in the diagnosis of breast, prostate, colon and lung carcinomas -Thomas Haas DO (Advanced)

☐ Workshop 3 – Tissue Identification - Thomas Haas DO (Basic)

☐ Workshop 4 – Immunohistochemistry Stain Identification - Various (Basic)

Social Program:

Welcome Function:
If you have purchased a Full Package or Conference Only registration please indicate by ticking the box below should you wish to attend the Welcome Function, which is included in the registration cost. A non-marked box will be listed as a non-attendee.

☐ Welcome Function

If you have purchased a Day or Student Registration or wish to purchase additional tickets for non-delegates to the Welcome Function please indicate below:

☐ Welcome Function additional tickets _____ $80.00

Please outline the number of tickets required

Conference Gala Dinner:
If you have purchased a Full Package Registration, the Conference Gala Dinner is included in the registration cost. All other delegates wishing to attend the Conference Gala Dinner or for additional tickets for partners or colleagues please indicate below:

☐ Conference Gala Dinner Tickets _____ $120.00

Please outline the number tickets required

NATIONAL HISTOLOGY CONFERENCE 2013

Histology Group of Victoria Inc.

Accommodation Details

Arrival Date

Departure Date

Length of Stay

Name of Person/s Sharing Room (if applicable)

All locations have been selected as they are all within walking distance to the conference venue

Holiday Inn Melbourne on Flinders

575 Flinders Lane, Melbourne

☐ $220.00 Standard Room

Room Type	Bedding Configuration	Bathroom	Max people
Standard	1 x Queen Bed	1	2

Crown Promenade Hotel

8 Whiteman Street, Southbank Melbourne

☐ $250.00 Standard Room

Room Type	Bedding Configuration	Bathroom	Max people
Standard King	1 x King Bed	1	2
Standard Queen	2 x Queen Bed	1	3

Melbourne ShortStay Apartments – Deluxe

63 Whiteman Street , Southbank, Melbourne

☐ $235.00 Condo Room

☐ $349.00 Executive Room

☐ $462.00 Superior Room

Room configuration (please tick)

☐ Queen ☐ Twin

Room Type	Bedding Configuration	Bathroom	Max people
Condo	1 x Queen Bed	1	2
Executive	2 x Queen Bed	2	4
Superior	2 x Queen Beds and 2 x Single Beds	2	6

Travelodge Southbank

9 Riverside Quay, Southbank

☐ $140.00 Standard Room

Room Type	Bedding Configuration	Bathroom	Max people
Standard	1 x Queen Bed 1 x Double Sofa Bed	1	2

Payment Summary

Registration Sub Total $

Social Program Sub Total $

Accommodation Sub Total $

Total Amount Payable $

Payment Details

I would like to make payment by (Please Tick)

☐ Cheque Made payable to InFront Events Australia Pty Ltd

☐ E.F.T.

Account Name : In Front Events Australia

BSB: 085-458

Account Number: 823167020

A remittance advice must be provided for your payment to be credited and please ensure you reference payment with your full name

☐ Credit Card (4% Merchant fee applicable)

Card Type Visa / MasterCard

Credit Card Number

Expiry Date

Card Holders Name

Signature

Return and Further Details

Please return this form with payment to:

National Histology Conference 2013 C/- In Front Events Australia

108 Magill Road Norwood, SA, 5067

Phone: (08) 83629844 / Fax: (08) 83624377 / Email: events@infront.com.au

Agreement to Terms and Conditions

I wish to register for the 2013 National Histology Conference and I acknowledge the registration terms and conditions including the cancellation policy

Signature_____

Histology Group of Victoria Inc.
Org. No. A0035235F

Nomination Form for Election to the Committee of Management of the Histology Group of Victoria Inc.

Thursday 15th November, 2012 Peter MacCallum Cancer Centre

Nominated Person.....

Institution.....

Email Address.....

Position Nominated For (Please tick box)	President	□
	Treasurer	□
	Secretary	□
	Committee Member	□

All nominations must be signed by two HGV members
(If you receive Paraffinalia you are a member)

Name of Member.....Signature.....

Name of Member.....Signature.....

Nominations must have the consent of the nominee

Signature of Nominee.....

Nominations must be returned no later than Thursday 8th November, 2012.

Please send nomination form to:
The Secretary
Histology Group of Victoria
PO Box 1461
Collingwood,VIC 3166

Scanned and emailed to
secretary@hgv.org.au

Histology Group of Victoria Inc.
Org. No. A0035235F

AGENDA

Histology Group of Victoria Incorporated
Committee Meeting

Thursday 15th November 2012
Peter MacCallum Cancer Centre
7 St Andrews Place, East Melbourne

6:45pm

Opened:

1. **Minutes AGM 2011**

2. **President's Report**

3. **Treasurer's Report**

4. **Life Membership**

In accordance with the Rules of the Histology Group of Victoria, the committee recommend the following members be bestowed the honour of Life Membership for meritorious commitment to the HGV

- Judy Brincat
- Neil O'Callaghan
- Adrian Warmington

5. **Election of office bearers and committee**

6. **General Business**

Meeting Closed:

Histology Group of Victoria Inc.
Org. No. A0035235F

HGV SCIENTIFIC MEETING/AGM

Speakers: Paul Kennedy/ Veronika Gazdik (VNLS)

Date: Thursday 15th November, 2012

Time: 6:00 – 6:45 Refreshments
6.45 – 7:30 Presentations & AGM

Venue: Peter MacCallum Cancer Centre
St. Andrew's Place, East Melbourne
Brockhoff Lecture Theatre
Level 3, Smorgan Family Building

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ABACUS ALS

Attendance at this meeting contributes to APACE points.

Histology Group of Victoria Inc.
Org. No. A0035235F

Future Scientific Meetings:

2012

~~**22nd March**~~
~~HGV/ASC Scientific Meeting – Student Presentations~~
~~Venue – Peter Mac~~

~~**3rd May**~~
~~HGV Scientific Meeting – Julian Richardson (Cabrini) – Renal Failure to Transplant~~
~~Venue – PeterMac~~

~~**28th June**~~
~~HGV Scientific Meeting – Dr. Peter Crowley FRCPA (Austin Health) "Why the Community needs public hospital Anatomical Pathology – Lessons from the Liver" Venue Peter Mac~~

~~**27nd July**~~
~~Social Event – Trivia Night~~
~~Venue – Mount Erica Hotel, 420 High St. Prahran~~

~~**18-19th August**~~
~~HGV/HDV Joint Meeting - Mornington Penninsula~~

~~**6th September**~~
~~HGV Scientific Meeting and Tour of the new RCH Facility~~
~~Venue: The Royal Children's Hospital~~

~~**24th – 27th September**~~
~~AIMS Conference – Darwin~~

~~**28th September – 3rd October**~~
~~NSH Conference~~

15th November
HGV Scientific Meeting/AGM – Paul Kennedy/ Veronika Gazdik (VNLS)
Venue – PeterMac