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syzygy

New Insight Into **Oesophageal** cancer

An important step towards understanding how oesophageal cancer develops has been made as a result of new research by SNP Surgical Pathologist, Dr Ian Brown.

His investigation of malignant tissue samples removed during surgery has identified as common certain cell changes seen in oesophageal cancer that were previously thought to be rare. This is the first time this has been reported.

The study, and a separate study of a rare process, collagenous gastritis, were presented last month at the pre-eminent international pathology conference, the United States and Canadian Academy of Pathology (USCAP) annual meeting in Boston.

As well as setting new directions for world research, Dr Brown's findings have important implications for future monitoring and treatment of, and intervention into, the precursor of the condition known as Barrett's oesophagus. It is well known that having this condition puts people at high risk of developing cancer of the oesophagus. In the western world, rates of oesophageal cancer are rising faster than those of almost any other cancer – each year, about 1000 Australians are diagnosed.

The lining of the oesophagus is normally squamous epithelium, but when the oesophagus is continually washed with stomach acids and digestive enzymes during acid reflux, the squamous tissue may be replaced by mucus-producing epithelium, which can better withstand acidic conditions. This gastric and intestinal metaplasia constitute Barrett's oesophagus. The metaplastic epithelium may progress to dysplasia, and finally to adenocarcinoma.

The clinical significance of the different forms of Barrett's dysplasia remains uncertain. In the stomach where this dysplasia classification has recently been applied, gastric-type dysplasia appears to be a more biologically aggressive lesion, with a higher likelihood of progression to invasive (usually poorly differentiated) adenocarcinoma.

Dr Brown explained, "Broadly speaking, our study showed that there are two types of dysplasia – intestinal-like (adenomatous), and gastric-like (foveolar). Previously, it was thought that the vast majority of dysplasia was intestinal-like, and that gastric-type dysplasia was rare. Our study showed that gastric-type dysplasia is actually a little more common than dysplasia of the intestinal type."

This research is an offshoot of work Dr Brown had previously undertaken as part of the four-year Australian Cancer Study for Esophageal Carcinoma, one of the world's biggest studies of its kind, conducted in Brisbane by Dr David Whiteman at the Queensland Institute of Medical Research (QIMR).

Dr Brown has been working in collaboration with his friend and colleague, Professor Greg Lauwers, a world authority on adenocarcinoma, dysplasia and abnormalities of the oesophagus, who holds the post of Chief of Surgical Pathology at the Massachusetts General Hospital.

"Greg came to Australia at the start of last year to work on this project with me. He had long wondered whether gastric-type dysplasia existed in Barrett's oesophagus. Our large database of cases, and access to innovative new stains and molecular techniques, gave us the perfect opportunity to investigate this."

The Australian part of the project was funded by SNP, with the American costs being met by the Massachusetts General Hospital.

The tissue samples analysed were taken from 81 oesophago-gastrectomy cases received between June 2001 and December 2006, which were reported by SNP as part of its normal workload, and entered into the QIMR study. The results were cross-referenced with the extensive lifestyle information collected from patients as part of the epidemiological study in the QIMR project.

Various possible causes have been proposed as increasing the risk of oesophageal cancer. These include smoking, alcohol, obesity, exposure to heavy metals, and diesel or petrol fumes. Even drinking carbonated water, opium smoking, and chewing seal fat among Eskimos, have been suggested.

In the present study, no differences were observed between dysplasia types with regard to obesity, proton pump inhibitor medication or tobacco use.

Dr Brown and colleagues are currently working on the next stage of the project, which is to examine 106 tissue samples collected from biopsies. Again, he will be searching for the presence of gastric-like dysplasia.

Sullivan Nicolaides PATHOLOGY

Answers to Doctor's challenge

Q.1 How is Giardiasis spread?

A.1 Millions of germs can be released in a bowel movement from an infected person or animal. The parasite can be found in soil, food, water, or the surfaces of objects. It can be spread by swallowing contaminated water (e.g. from swimming pools, fountains, lakes, streams), eating uncooked contaminated food, and accidentally swallowed from contaminated surfaces such as toys, bathroom fixtures, changing tables, nappy buckets.

Q.2 How can you be sure *Blastocystis hominis* is the cause of symptoms?

A.2 It is unknown whether *Blastocystis hominis* is the primary cause of your symptoms. The presence of the organism in stool samples does not mean it is the cause of your symptoms and the finding should be accompanied by a careful search for other possible causes (e.g. other parasitic organisms, bacteria, or viruses). Often *Blastocystis hominis* is found along with other organisms that are a more likely cause of your symptoms. Sometimes the symptoms are not caused by an infection at all, but may be due to antibiotics, some cancer drugs, or medications used to control high blood pressure. Hormone and endocrine diseases, Crohn's disease, colitis, and hereditary factors may produce similar symptoms. Food additives and food allergies may also cause abdominal discomfort.

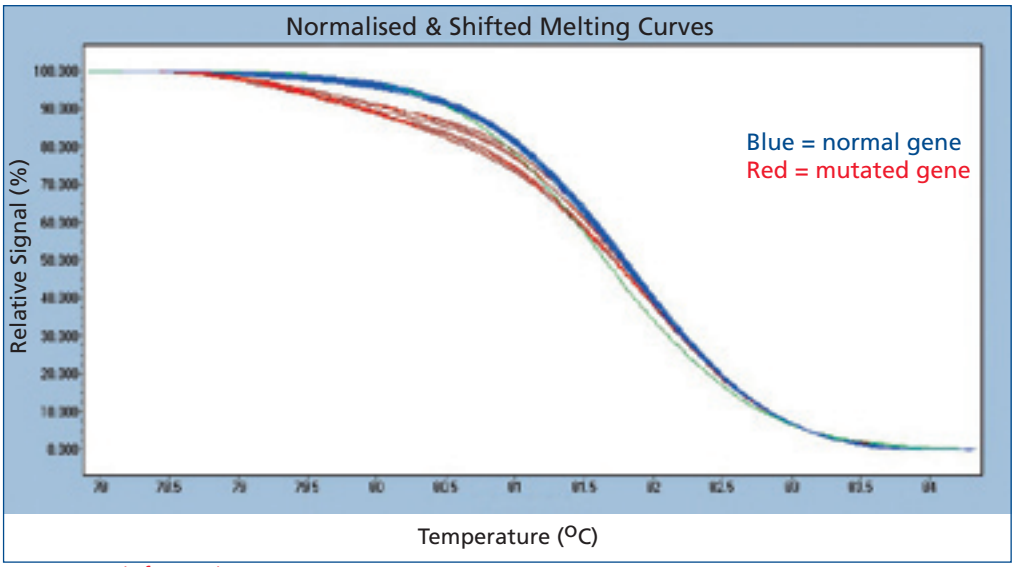
KRAS mutation screening NOW available at SNP

The epidermal growth factor receptor (EGFR) mediates molecular events critical to cellular growth and survival. This receptor is up-regulated in the majority of colo-rectal cancers (CRCs) and contributes to cancer progression via proliferation, adhesion and angiogenesis.

Monoclonal antibody treatments, such as cetuximab, have been developed that target the extracellular binding domain of EGFR to combat the effects of the up-regulation. However, a significant proportion of cases remain resistant to this therapy. One of the reasons for resistance is that the same pathway may also be activated due to mutation of the KRAS oncogene. KRAS mutation occurs in approximately 30-40% of CRCs. The overall survival benefit in patients with stage IV CRC following treatment with anti-EGFR therapies is modest. However, the overall and progression-free survival rates are significantly improved for patients with wild type KRAS.

SNP, with assistance from Vicki Whitehall and Aarti Umapathy at the QIMR Conjoint Gastroenterology Laboratory, have established a High Resolution Melting assay for screening the KRAS gene for the presence or absence of mutations to indicate possible therapeutic benefits from anti-EGFR treatment.

Testing is available on request from formalin fixed tissue containing 20% or more tumour cell component. Test cost is $250 which may be paid by Merck-Serono for patients meeting the interim access criteria for Erbitux®.



For more information contact:

Dr Ian Brown
Surgical Pathologist
email: ian_brown@snp.com.au
Phone: (07) 3377 8433

Shane Byrne
Molecular Pathology
email: shane_byrne@snp.com.au
Phone (07) 3377 8349

Collection Centre updates

Brisbane Opened

Teneriffe
9a Teneriffe Hill Apartments
29-83 Florence Street
Mon – Fri 7 am – 7 pm
Phone (07) 3377 8747

Walloon
Shop 1/11 Queen Street
Mon – Fri 7 am – 3 pm
Phone (07) 3377 8747

Regional – now open

Lismore
Shop 8
Wyrallah Road Shopping Centre
Mon – Fri 7 am – 5.30 pm
Sat 8.00am – 1.00 pm
Phone (02) 6622 4571

Maroochydore – open early
Saltwater,1st Avenue
Mon – Fri 6 am – 5 pm
Ph (07) 5459 1400

F.Y.I.

Our Minyama Collection Centre on the Sunshine Coast has sessional rooms available. Please contact Tjitske Bunnag on (07) 5459 1400 for more information.

Syzygy – now on 100% recycled paper

Sullivan Nicolaides Pathology recognises our corporate responsibility to respect and improve the environment in which we work and live. As part of our commitment to continually improve environmental performance and prevent pollution, *Syzygy* is now printed on 100% recycled paper.

Environmental savings per issue of Syzygy compared to using non-recycled paper:
3.7 trees saved
720 kg carbon dioxide emissions
55% less water used
60% less energy used.