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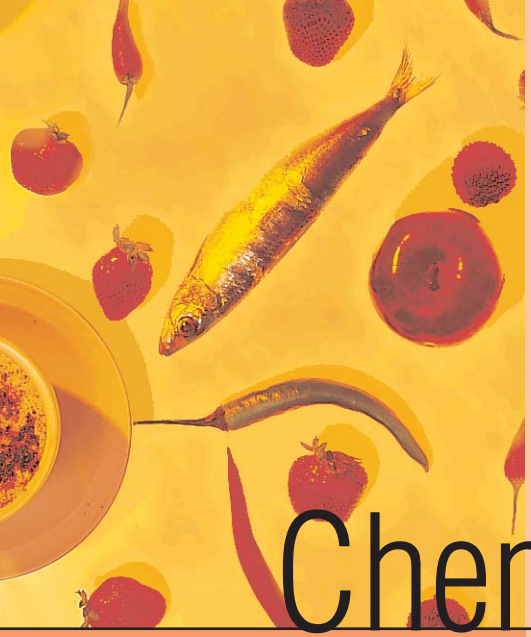

Chemo Sense

EDITORIAL

Breath-taking Advances

By Graham Bell
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Knowledge created by the science of olfaction is heading toward breath-taking technological achievements.

The smell of a patient has long offered a source of diagnostic information. Applying modern analytical tools (including e-noses) to the smell of a person's breath may provide diagnostics for several human pathologies. Of these, early detection of lung cancer stands as a compelling objective, which promises to save millions of lives every year. Olfactory science can supply the means by which this goal may be reached, as reviewed by Tran, Jackson and Thomas in this issue.

Another area of breath-taking importance, emerging from olfactory science, is the potential use of olfactory stem cells. Australian scientist, Alan Mackay-Sim, has captured the financial backing of people who wish to see progress in adult stem cell research, and they have backed him with AUD$22 Million in resources. We draw breath, Alan, on your spectacular achievement. Congratulations!

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Biomarkers in the Breath Associated with Lung Cancer

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Lung cancer is often diagnosed at an advanced stage and as a result has poor survival rates. The present methods for diagnosing lung cancer are time-consuming, expensive and invasive. There is a need for tests capable of early lung cancer detection. Recent studies describe exhaled breath condensate (EBC) as a potentially useful, non-invasive method of sampling the airways for assessing inflammation of the respiratory system, and possibly for the early detection of lung cancer.

Until the twentieth century, lung cancer was a relatively uncommon disease, but lung cancer death rates have risen dramatically and it is now recognised as a leading epidemic worldwide (Miller, 2005; Schwartz & Ruckdeschel, 2006; Spiro & Silvestri, 2005). Lung cancer ranks as the number one cancer in men and has recently overtaken breast cancer to become the most common cancer in women, usually affecting those 65 years of age or older (AIWH, 2003; Australian Social Trends, 2002; Jemal et al., 2003). With over a million people diagnosed with the disease per year worldwide, generally about 5-8%, and at best 15%, of those diagnosed will survive 5 years - a rate that has changed little in

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EDITORIAL CONTINUED

Breath-taking Advances continued

Our joy gives way to sadness with the recent deaths of two eminent chemosensory scientists, who were both in the prime of life: David Smith and L.E.L. (Bets) Rasmussen. Both have participated in the Heron Island meetings hosted by the Australasian chemosensory community (AACSS). Humanity is enriched for what they have researched, taught and shared. *ChemoSense* conveys condolences to their families and friends ■

AACSS Heron Island 2005

Biomarkers in the Breath Associated with Lung Cancer continued

the last three decades (Brambilla et al., 2003; Jett & Miller, 2006; Spiro & Silvestri, 2005). In Australia, 11% of male and 14% of female lung cancer patients live to five years post-diagnosis, statistics which are in stark contrast to the five year survival rates of 84% and 83%, in breast and prostate cancer respectively (ABS, 2004).

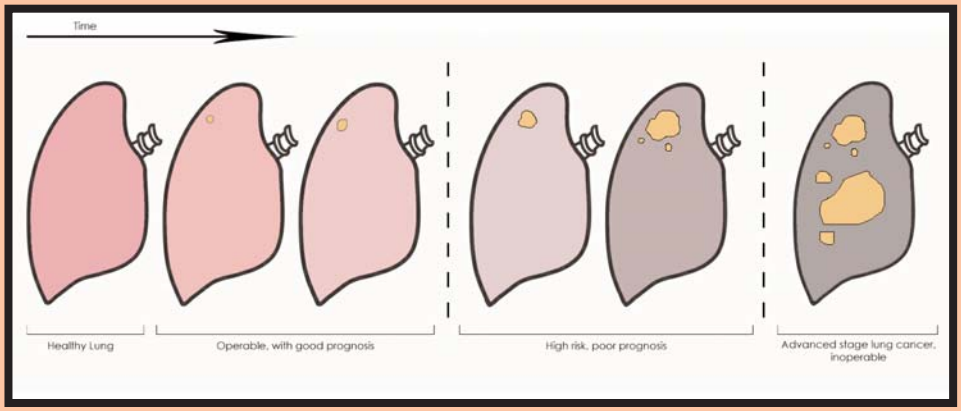

Fig.1: Schematic of development of lung cancer lesions (shown in yellow). If the cancer is detected before attaining a size of approximately 10-15mm in diameter, it can be removed surgically and the patient has a good prognosis. At this size the cancer is extremely difficult to detect by known methods. With further growth, to a size at which the lesion is commonly detected, the prognosis is poor. This exemplifies the need for new discovery of detection methods in the early, operable stage of lung cancer development.

Tobacco smoking is the main cause of lung cancer (Godtfredsen et al., 2005; Thompson, 2005; Vineis et al., 2005), but environmental carcinogens including substances such as asbestos, arsenic, radon, chromium, nickel, zinc and polycyclic hydrocarbons are also known causes. Asbestos was used formerly in housing developments, whilst radon is a naturally occurring radioactive substance found in rock and soil (Darby et al., 2005; Frumpkin & Samet, 2001). The increase in risk for an individual when exposed to asbestos is synergistic with tobacco smoke exposure (Nelson & Kelsey, 2002).

Current Diagnostic Procedures

The poor prognosis for lung cancer is associated with its late detection. Many efforts have been channeled into the improvement of diagnostic procedures and therapy, but survival rates have seen little improvement (Hamilton et al., 2003; Wilkinson et al., 2003). Current screening and detection systems are unable to identify malignant lung masses until they have developed considerably. A screening or early diagnostic test would allow early detection and treatment, before a cancer becomes inoperable or unresponsive to other treatments.

Classical screening procedures, such as chest radiography and sputum cytology, have not reduced the number of deaths due to lung cancer (Marcus et al., 2000; Lau & Harpole, 2000; Humphrey et al., 2004; Bastarrika, 2005). In CT (computed tomography) scanning, up to 60% of lesions identified have not been cancerous, resulting in unnecessary invasive investigations (MacRedmond et al., 2004). However, CT scanning is a modern development that has shown promise in sensitivity in detecting lung cancer, especially early stage disease. From 60% to 85% of lung cancers can be detected at Stage 1, compared with just 15% to 20% of cancers using current practice (Pinsky et al., 2005). There are several limitations to CT scanning though, including, over-diagnosis, interval cancers and false positives. Furthermore, there are data to suggest that diagnostic X-rays contribute from 0.6% to 1.8% of cancer cases, which is an issue of concern (Mayo et al., 2003; Brenner, 2004).

Sputum cytology analysis can also be a useful method of diagnosing lung cancer, particularly in those unable to undergo invasive procedures, but this approach is still not associated with improved outcome (Spiro & Silvestri, 2005). The development of more reliable molecular analysis techniques means that sputum can be studied at the molecular level, and changes

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Biomarkers in the Breath Associated with Lung Cancer

continued

in gene expression have been detected (Tockman, 2000). Belinsky et al. (2006) found that the levels of gene methylation had an inverse relationship to time to lung cancer diagnosis, when sampled eighteen months prior to clinical diagnosis, showing the possibility of using molecular abnormalities (loss of regulatory factors, genomic instability, abnormal protein expression and methylation) to predict lung cancer in high-risk individuals (Belinsky et al., 2006). Other studies have looked into the possibility of using sputum cytology as a diagnostic tool for investigating inflammatory factors found in lung cancer and other respiratory disorders, including chronic obstructive pulmonary disease (COPD) and asthma (Cataldo et al., 2000; Roland et al., 2001; Brightling, 2006; Thunnissen; 2003). However, this approach is hampered by samples frequently contaminated with cellular debris and background material.

Although novel imaging techniques such as low-dose helical computed tomography hold promise, there are issues regarding cost and over-diagnosis. Currently, the most promising diagnostic combination appears to be the use of an annual chest radiograph combined with sputum cytology examination every four months because this increased survival when compared to annual chest radiography screening alone (Manser et al., 2003).

Given the issues described above, it is clear that there is a need for non-invasive diagnostic procedures that can potentially be adapted in screening programs. Ideally, such tests would allow biomarkers of lung cancer to be detected at an earlier stage, hence increasing the number of curable cases and improving the chances for survival.

EXHALED BREATH MARKERS

One possible source for detection of markers, and which would be non-invasive to collect, is exhaled breath, because it samples tissues where the disease occurs (Kharitonov & Barnes, 2001; Montuschi & Barnes, 2002; Giardina & Olesik, 2003). Differences in exhaled breath components between healthy individuals and those with other pulmonary diseases have been reported, however, studies investigating the use of this technique for diagnosis of lung cancer are limited.

The collection of exhaled breath can be divided into two phases: the gaseous phase and the liquid phase.

Gaseous Phase

Gaseous phase analysis of breath can include studies of carbon monoxide (CO) and nitric oxide (NO). CO is a product of organic oxidation, and produced by the enzyme haem-oxygenase (Ryter & Otterbein, 2004). Higher levels of CO have been found in the exhaled breath of asthma, cystic fibrosis (CF) and chronic obstructive pulmonary disease (COPD) patients (Kharitovnov & Barnes, 2001; Kharitovnov & Barnes, 2002). Whether this effect happens in exhaled breath of lung cancer patients has not yet been assessed, but may well be worth pursuing, because elevated CO levels are associated with inflammatory diseases of the lung. However, caution may be needed because smoking itself can affect CO levels, and might confound results (Deveci et al., 2004).

Nitric oxide is a product of L-arginine and oxygen metabolism, and synthesised by NO synthases. NO is involved in vascular tone and inflammatory processes (Masri et al., 2005; Yates, 2001). Measurement of exhaled NO is a highly sensitive test for respiratory disease. Preliminary results obtained from lung cancer patients have shown no significant differences when this group is compared with subjects matched for smoking history (Thurston, 2005). However, these results need further confirmation because it was also found that ambient NO gas levels can have a profound effect on results.

In addition to CO and NO, other substances that have been measured in the gaseous phase of exhaled breath are volatile organic compounds (VOCs). Phillips

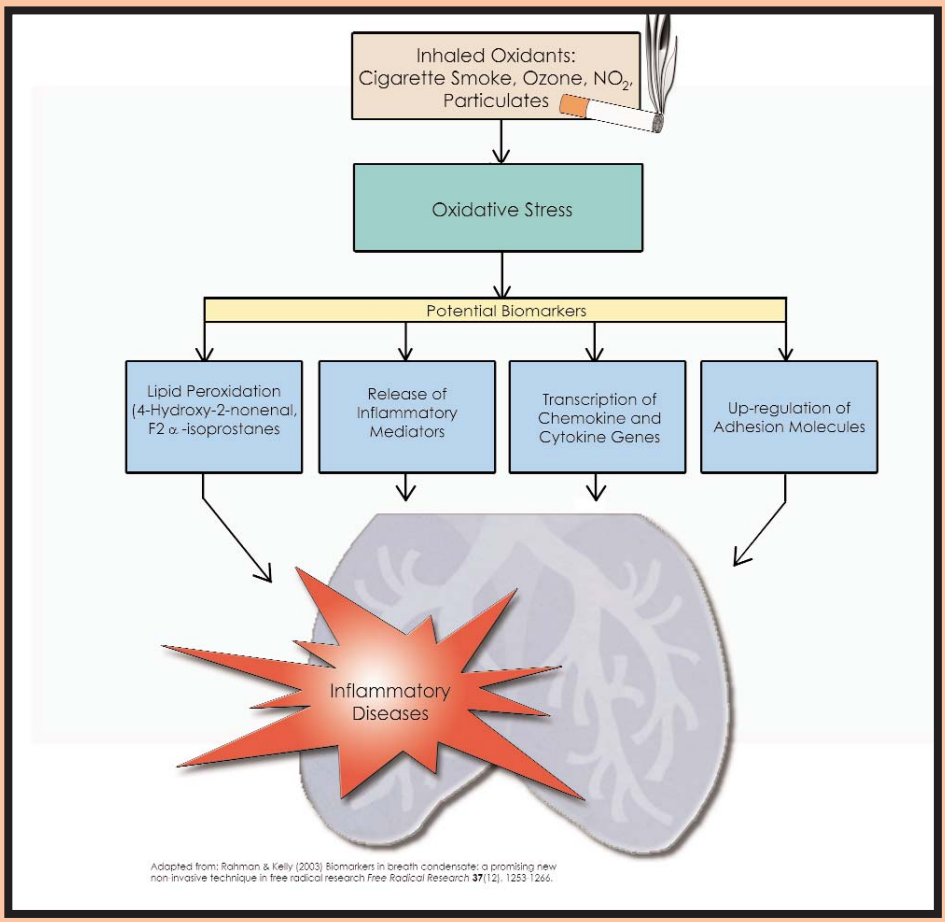

Fig.2: Potential bio-markers of inflammatory lung diseases from oxidative stress products. (Acknowledgement: Rahman and Kelly 2003).

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Biomarkers in the Breath Associated with Lung Cancer
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et al. (2006) conducted a study of possible biomarkers of pulmonary tuberculosis in breath. This mycobacterial infection induces oxidative stress and the authors hypothesised that a change in VOCs could potentially act as a marker for pulmonary tuberculosis. VOCs were captured from cultured Mycobacterium tuberculosis and 130 different compounds detected consistently, principally naphthalene, 1-methylhexane and cyclohexane. Breath samples obtained from 42 possible pulmonary tuberculosis cases and 59 healthy controls were then assayed using gas chromatography/ mass spectro-photometry (GC/MS). The study found that pattern recognition analysis for differentiating tuberculosis patients from healthy controls had 100% sensitivity and 100% specificity, with 82.6% sensitivity and 100% specificity for sputum cultures. Using exhaled breath to measure VOCs had the capacity to distinguish between pulmonary tuberculosis and control groups, and had possibly superior outcomes to sputum examination (Phillips et al., 2006).

The use of markers in exhaled breath for detection has also been applied to breast cancer and angina. VOCs in exhaled breath could distinguish breast cancer patients from normal controls with a sensitivity of 94.1% and a specificity of 73.8%, and 90% sensitivity with 73.7% specificity, for differentiating between unstable angina cases and healthy controls (Phillips et al., 2003b; Phillips et al., 2003c).

The analysis of VOCs in the breath of lung cancer patients has been limited. Phillips et al., (2003a) investigated levels of oxidative stress products such as alkanes and monomethylated alkanes, and found that examination of a combination of VOCs might improve sensitivity and specificity. Poli et al. (2005) set up a protocol for the identification of VOCs in exhaled breath of lung cancer patients versus healthy smokers, never-smokers and COPD patients. Using solid phase micro-extraction (SPME) and GC/MS, measurement of the levels of 13 selected VOCs (ranging from 10^{-12} M to 10^{-9M}) found none was unique to a particular study group (Poli et al., 2005). Measurements of ambient air and exhaled breath of healthy non-smokers demonstrated similar levels of VOCs, which may suggest a significant influence of ambient levels on exhaled VOCs.

An avenue of interest may be to investigate VOC levels upon repeated expirations, to determine if ambient air influences samples, and whether VOC-free air needs to be inhaled prior to sampling.

The Electronic Nose (e-nose)

The e-nose is an electronic detection system consisting of an array of coated sensors e.g. metal oxide electrodes coated with various rare earths, that can detect VOCs. The detectors can produce multi-dimensional 'smellprints' of various compounds, depending on variables such as molecular shape, mass or electrical properties. Breath samples are channeled through the machine, aided by a negative pressure gradient, to reach these sensors. Normally, an array of sensors are used with additional sensors to measure ambient temperature and humidity. An increase in the number of sensors in an array may further enhance the identification of complex mixtures of volatile compounds, or may simply add to redundancy and decrease the signal-noise ratio of markers to background. Currently , some e-nose researchers favour small arrays with minimal redundancy (Bell and Wu, 2006) where the make-up of the target odours is reasonably well known. Both approaches (small tailored arrays and larger, all-inclusive arrays) may need to be employed in the pursuit of exhaled breath markers of respiratory diseases and lung cancer.

The e-nose has proved to be useful in many settings, including the food and wine industry, and recently sewage systems and abattoirs use e-noses to monitor nuisance outdoor odour emissions (Bell and Wu, 2006). When elevated levels are reached, and/or an odour's pattern is recognised, the device can alert an operator to attend to the problem (Bell and Wu,2006; Thaler & Hanson, 2005).

The sensitivity and reproducibility of e-noses have stimulated interest in possible medical applications. Recent studies have used e-noses to analyse gaseous and other compounds found in exhaled breath (Chen et al., 2005). Breath samples analysed by e-noses yielded significantly different results between control groups and lung cancer patients (Thurston, et al., 2005). A sensitivity of 71.4% and specificity of 91.9% for e-noses in detecting lung cancer has been described (Machado et al., 2005). Other studies have employed a device comprised of quartz microbalance gas sensors coated with different metalloporphyrins. These sensors can detect alkanes and aromatic compounds, and had a good sensitivity to unspecified markers believed to be indicative of lung cancer (Di Natale et al., 2003).

In more recent studies, a hand-sized electronic nose (Cyranose® Smith's Detection Inc. Pasadena, California) has been used to produce a smellprint of VOCs from the exhaled breath of lung cancer patients, and showed a positive predictive value of 66% and a negative predictive value of 92% (Phillips et al., (2005). It is not yet known whether studies of patients with conventionally detectable, and therefore inoperable lung cancer, will provide the essential markers for earlier, operable stages of the disease. A strategy is suggested here, (provided by Graham Bell of E-Nose Pty Ltd) by which e-noses might be used to characterise the breath of patients with lung cancer, at an early stage and while treatment may result in survival for a normal life span.

The proposed strategy involves a long-term series of regular breath recordings with a large-array e-nose, of a sufficiently large group of high-risk people (long-term smokers) over a period long enough for lung cancer to manifest in some of them (and to be detected and reported in the normal way). This may well require several years and several thousand subjects. Data from the participants who become cancer patients, taken prior to the detection of the disease will then be compared with that of people who have not manifested the disease. A number of statistical methods exist for making the comparison, including the training of an artificial neural network using the two categories of data to train the network (see Levy and Naidoo, 1999). Any new breath data taken in a similar manner, from people at risk, may then be assessed by the resulting classifier, which will be an effective diagnostic device for the early detection of lung cancer and provide a rapid and inexpensive screening system.

The use of electronic noses for diagnosing

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Biomarkers in the Breath Associated with Lung Cancer

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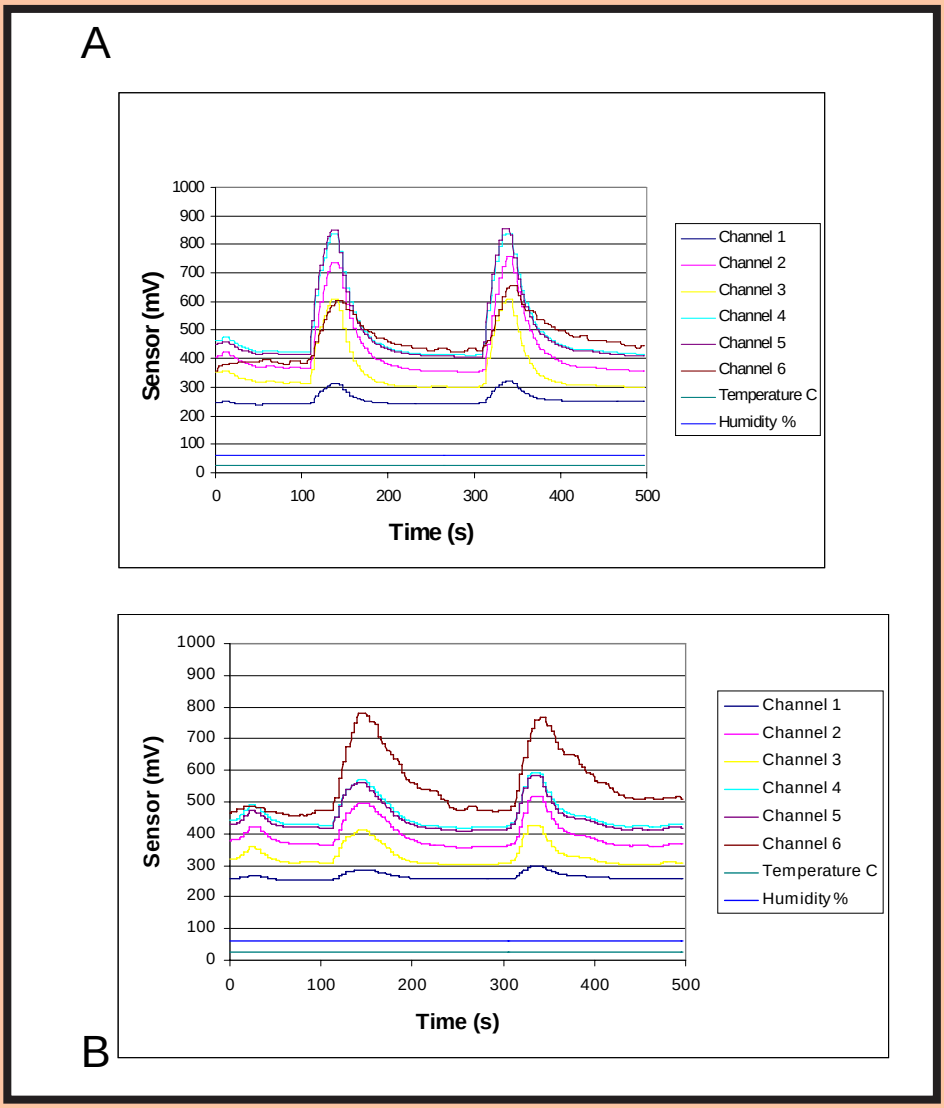

Fig.3: Breath records made with an electronic nose, from a healthy person (A) and one with lung cancer (B). (From Thurston et al., 2005).

lung cancer requires further investigation.

The Liquid Phase - Exhaled Breath Condensate (EBC)

Collection of exhaled breath condensate (EBC) is emerging as a novel and non-invasive technique which allows the liquid phase of breath to be examined (Horvath et al, 2005; Liu & Thomas, 2005). Several studies have assessed its practicality, with results indicating that disease markers can be detected in EBC. Consequently, it has been proposed that EBC analysis might be a potential tool in diagnosing lung cancer.

EBC is obtained by collecting exhaled breath into a condensing chamber (at -20°C to 4°C) (Thurston, 2005 unpublished data; Montuschi, 2002; Horvath et al, 2005). Collection usually requires ten minutes of quiet breathing, at normal frequency and tidal volume. Markers such as hydrogen peroxide, nitrite/nitrates and nitrotyrosine can be detected (Liu & Thomas, 2005; Montuschi & Banes, 2002), as well as other compounds such as adenosine, ammonia, isoprostanes, leukotrienes, peptides, cytokines, hydrogen ions (pH), and other larger molecules.

Molecular markers in EBC

Small molecules and proteins are therefore detectable in EBC and some reports suggest macromolecules such as DNA can also be detected. DNA markers of tumours include microsatellites. A microsatellite is a segment of DNA sequence that has multiple repetitions within the genome of a particular organism. Microsatellite alterations (MA) occur when these repeats are either amplified or deleted as a result of imprecise division processes within cells. A recent study has provided evidence that (MA) already described in lung cancer, can be detected in EBC from patients with non-small cell lung cancer and in healthy subjects (Carpagnano, 2005).

Capagnano et al. (2005) discovered a higher incidence of MA in patients with histological evidence of NSCLC. In this study, an MA in the chromosome arm of region 3p was identified. From a subject pool of 30 lung cancer patients and 20 healthy people, lung cancer patients showed 53% of MA in EBC and 10% in whole blood for lung cancer patients, as opposed to 13% in EBC and 2% in healthy subjects. The increased MA levels when comparing EBC of lung cancer patients and healthy controls indicates the possibility of correlation with disease process. Moreover, the amount of MA found in EBC exceeded the concentrations in whole blood (Carpagnano et al., 2005).

Nitrite/Nitrate(NOx)

Lung diseases can increase the levels of NOx and exhaled NO levels (Massimo, 2002). A twenty-fold increase in nitrite/nitrate (NOx) levels has been found in bronchoalveolar lavage fluid (BLF) from patients with NSCLC, when compared with control subjects (Arias-Diaz et al., 1994). However, 5 out of 8 control subjects had other known respiratory diseases (Arias-Diaz et al., 1994), so the specificity of the effects was unclear. NOx levels have also been analysed in bronchoalveolar lavage fluid, and pleural effusions of lung cancer patients (Chen et al., 1998), although levels in EBC have yet to be done. Some studies have indicated increased levels of nitrite in the BLF and lung cancer patients in comparison with smoking controls.

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Biomarkers in the Breath Associated with Lung Cancer

continued

Limitations of EBC

Although breath analysis is rapidly becoming a promising alternative for lung assessment, collecting EBC samples from patients requires further standardisation. Sources of variance can include quantities of individual compounds, breathing too forcefully, or breathing through the nose while collecting the sample, because high levels of nitric oxide reside in the vicinity of the nasal epithelium (Liu & Thomas, 2005).

Testing for a combination of markers could incorporate a gaseous phase analysis for volatile compounds in addition to a liquid phase analysis examining exhaled breath condensate for non-volatile markers, such as tumour markers.

TUMOUR MARKERS

Cancer cells produce enzymes, serum proteins, hormones and metabolites which may become elevated during neoplastic growth. In addition, they can express different cell surface components to normal cells that allow their migration and invasion into surrounding tissues. These cell surface components and cancer cell products may act as tumour markers (Way & Kessler, 1996).

Some known tumour markers of lung cancer which might be targeted by analysis of EBC, and which have previously described in immunohistochemistry, serum and blood studies will be discussed here.

The effectiveness of serum neuron specific enolase (NSE), tissue polypeptide antigen (TPA) and carcino-embryonic antigen (CEA) as lung cancer markers was analysed by Spinazzi et al. (1994) and Buccheri and Ferrigno (1995). These studies showed that greatest positivity was found for NSE in SCLC (88%), and TPA in NSCLC (62%). Similarly CYFRA-21-1 and another tumour marker, tissue polypeptide antigen (TPA), are tumour markers which show highest sensitivity for NSCLC and a strong correlation with overall survival (Kasimir-Bauer et al., 2003; Foa et al., 1999).

Romero et al. (1996) looked at three tumour markers in serum and pleural fluid, two of which were CEA and CYFRA 21-1. Fifteen of the 120 subjects recruited had lung cancer. Serum measurements indicated sensitivities for malignancies of CEA (36%) and CYFRA 21-1 (31%) in comparison to pleural fluid analysis, where CYFRA 21-1 showed 32% sensitivity, 82% specificity and CEA with the highest sensitivity (57%). The study found that determining all three markers in serum produced an increased accuracy of 88% compared to 38% sensitivity when tested alone.

Of the markers mentioned, thyroid transcription factor 1 (TTF-1), CK7 and cytokeratin 20 (CK20)CK20 have been widely applied in immunohistochemistry (Johansson, 2004). A recent study employed antibodies against these markers in order to ascertain differential staining patterns between primary and metastatic lung carcinomas (Su et al., 2006). Sixty-six adenocarcinoma patients were included in this study, comprising patients diagnosed with primary lung adenocarcinomas (n = 40), metastatic breast adenocarcinomas (n = 12), metastatic colon adenocarcinomas (n = 13) and metastatic stomach adenocarcinoma (n = 1). The tests found that primary lung adenocarcinomas stained positive for TTF-1 (73%), while adenocarcinomas of different origin lacked TTF-1 staining. A higher level of CK7 expression occurred in adenocarcinomas of the lung and breast ($p < 0.001$), whilst CK 20 appeared more frequently in colon cancer specimens in comparison to pulmonary ($p < 0.001$) and breast ($p < 0.001$) carcinomas. Drawing from the results of this study, these markers may be used in differential diagnosis of primary lung cancer. Several factors may be extended to further determine sensitivity, such as extending the study to carcinomas of different origins, and perhaps studying the other subtypes of primary lung cancer (Su et al., 2006).

Overall, current data demonstrate elevated expression of TTF-1 and CK7, with CK20 as negative control in pulmonary carcinomas; NSE in SCLC; CYFRA 21-1 in NSCLC, and specifically CEA in adenocarcinomas of the lung.

Conclusions

It is very likely that any future screening for lung cancer will require testing for several markers that may incorporate analysis in both the gaseous phase and liquid phase for specificity and sensitivity, rather than relying upon a single marker. These markers, and in particular CYFRA 21-1 which has already been established as a promising marker in terms of both sensitivity and specificity, are candidates for lung cancer detection in EBC studies.

Using breath analysis to detect biomarkers of lung cancer appears to be a promising proposition. If these markers can be detected, there will also be a need for development of standard methods for sample collection and analysis, to allow implementation into a reliable and inexpensive screening system ■

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NEWS

Historic Recognition for Australian Chemosensory Science

In what is possibly the largest single grant to an olfactory project in the history of modern science, Griffith University in Brisbane, the Government of Queensland, and the Australian Federal Government, announced recently the funding of a $22 Million **Adult Stem Cell Research Centre**, which will be directed by olfactory scientist Alan Mackay-Sim, for the study of adult stem cells derived from olfactory tissue.

The funding recognises the excellence of Griffith's scientific and clinical research led by Professor Alan Mackay-Sim and Professor Peter Silburn at Griffith's Eskitis Institute for Cell and Molecular Therapies.

Last year Alan Mackay-Sim and his team showed that adult stem cells from the olfactory muscosa could be grown in the laboratory into many different types of cells, including heart, muscle, liver, kidney and blood cells. These olfactory cells have potential clinical application in human transplantation therapies and tissue reconstruction and will be used to understand and ultimately develop treatments for brain diseases such as Parkinson's disease, motor neurone Disease and schizophrenia.

The Centre will be part of Griffith's Eskitis Institute for Cell and Molecular Therapies which has capabilities for high throughput screening for drug discovery and development ■

Alan Mackay-Sim

Vol. 8 No.4 October 2006

Useful Chemical Senses Book

Tastes and Aromas: The Chemical Senses in Science and Industry, Edited by Graham Bell and Annesley J. Watson. 214 pages. Published by UNSW Press and Blackwell Science, 1999. ISBN: 0-86840 769 0. Hard Cover. Price: US$ 30 / AUD$ 40 (includes tax if applicable, postage and handling). Order from: g.bell@atp.com.au

A limited number of this extremely useful volume are, for a short time only, available at a 50% discount. *Tastes and Aromas* has been hailed as a great teaching aid and resource for the practicing sensory scientist. Written by leaders in their fields as fundamental information, the volume retains its value and is rich in scientific and practical quality. Beautifully packaged in hard cover, it will continue to be a durable reference for many years to come.

Chapters include mini-reviews by (first authors) Stoddart; Bartoshuk; Youngentob; Prescott; Lyon; Weller; Bell; Saito; Lambeth; Noble; Morgan; Best; Barry; Sullivan; Key; Mackay-Sim; Atema; Hibbert; Barnett; and Levy.

Content covers the chemical senses in human culture; fundamentals of smell; taste; pungency; oral touch and pain; applied sensory evaluation; cross-cultural studies; perfumery and flavour chemistry; wine preference; psychophysics; sensory mapping; physiology of odour encoding; anatomy, growth and aging; emerging chemosensory technologies; sensors; marine chemical signals; electronic noses and chemosensory machines.

Avail yourself of a copy while these limited stocks last.

Every sale will support *ChemoSense.*

Order from: g.bell@atp.com.au ■

ISOT 2008

International Symposium on Olfaction and Taste

Hyatt Regency Hotel
At the Embarcadero
San Francisco CA

Monday July 21 to Saturday July 26, 2008

CALL FOR SYMPOSIA & SATELLITE MEETINGS

Proposals for Symposia and Satellite Meetings should include:

(1) a synopsis of the symposium/meeting theme;
(2) a tentative list of speakers, including institutional affiliations, and topics; and
(3) a rationale for the symposium explaining why this topic and this group of speakers are particularly appropriate for an international symposium.
(4) Ideas for potential sponsors including corporations, government agencies or non-profit organizations.

In evaluating proposals, the program committee will favor proposals whose topics concern newly emerging fields. In particular, the committee would like to encourage the inclusion of young investigators as well as geographic diversity in the speakers and discussants.

Please send suggestions to the ISOT Meeting Organizer:

Thomas Finger
Dept. Cellular and Structural Biology MS 8108
University of Colorado at Denver and Health Sciences Center
PO Box 6511
Aurora, CO 80045 U.S.A.
Tom.finger@uchsc.edu

Proposals can be sent as paper copies by mail or as e-mail attachments in Word, RTF or PDF format.

INFORMATION REGARDING SATELLITE MEETINGS

The proposer of a Satellite Symposium can either organize the entire meeting on his/her own, or plan the symposia in conjunction with the ISOT Meeting Organizer. If you plan to organize the event independently, it is not necessary to finalize the location before submitting the proposal, but it will be the proposer's responsibility to arrange for location, registration, meeting materials, audiovisual, etc. The Satellite Symposium can be held for half, one or 2 days. The proposer will be responsible for securing all necessary financial support for the Satellite Symposium.

Those requesting ISOT support must submit their proposals to the Program Chair to determine whether meeting space can be secured. Please include the following information in your proposal: (1) Dates/Time of event, and (2) Number of attendees expected. The Program Chair will work with the Satellite Symposium Organizer on further details.

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NEWS

Monell Passes Funding Target

In a great moment for science funding, Monell Chemical Senses Centre, in Philadelphia, USA, recently reached and exceeded the target it had set itself to raise US$ 10.9 Million, by announcing a final total of US$11.2 Million. The Centre is a nonprofit basic research institute, devoted to investigation of taste, smell and chemosensory irritation. Its first capital campaign funds will be used to employ a number of new scientists and construct two state-of-the-art laboratories including a new human sensory testing wing in a recently acquired building adjacent to the existing Market Street building. Over a million dollars of the funds raised came from individual donors including the Centre's Board members, alumni, employees and friends. The bulk of funds (US$4.2M) came from food, flavour and fragrance industries and the National Institutes of Health (US$3.6M) which added to substantial donations from two large private foundations: The Ambrose Monell (US$1M) and The Kresge (US$0.6M). New wings in the Centre will facilitate research integrating molecular biology and human sensory studies. We can look forward to new knowledge that will be produced at Monell on the genetic determinants of chemosensory perception. Centre Director, Gary Beauchamp concluded: "The end result will be greater knowledge of how taste and smell function and how these senses contribute to human health, well-being and quality of life."

Source: The Monell Connection, Summer issue, 2006.
Web: www.monell.org ■

Vale: Bets Rasmussen

"Bets" Rasmussen

We must report with great personal and collective sorrow, the passing of a truly great human being and member of the community of chemosensory scientists: L.E.L.."Bets" Rasmussen, known affectionately across the world as "The Elephant Lady", who died at the age of 67, on Sunday, Sept. 17.

Bets is well-known for her identification of elephant sex pheromones and the molecular mechanisms (perireceptive events) by which they were transferred from the female elephant to the male. One of her most recent papers with David R Greenwood (*ChemoSense*, 2005, 8(1) 1-4) describes the behavioural and biological foundations of precise chemical signalling between elephants and their social consequences. Their work has been recently communicated in *Science and Nature*.

Papers by Bets were the epitome of good science, despite the obvious difficulty of working with such large animals. There was, however, some advantage in the quantities of material available which Bets made use of, including her personal collection of substantial quantities of elephant urine. She attended two AACSS meetings in 2002 and 2005 and dramatically enhanced them with highest quality science and wonderful pictures of her subjects.

She was on a first name basis with many of the elephants in zoos in America and especially with those in Riddle's Elephant and Wildlife Sanctuary in Arkansas. Bets was a wonderful person, full of enthusiasm for all things – an avid swimmer, diver and scientist. We (and the elephants) will miss her greatly –both scientifically and personally.

Acknowledgement: Tom Finger, AChemS ■

NEWS

Vale: David V. Smith (1943-2006)

Readers of ChemoSense who attended the AACSS 2002 Heron Island meeting had the pleasure of meeting David and Michiko Smith. They, and the greater chemosensory community will be saddened to hear that a great contributor to taste research, David Smith, died of brain cancer on September 30, 2006 in Memphis, Tennessee. He is survived by his loving wife, Michiko, and his three children, Bryan, Laurie and Charles.

The following is extracted, with thanks, from an obituary published by AChems:

Over the course of his distinguished research career, David's true and abiding passion was the study of sensory coding. The puzzle posed by the neural mechanisms responsible for taste quality coding piqued his interest early on, and though some of us heard him "swear off" of the topic any number of times, he never abandoned it. David studied several other aspects of taste processing but the most pervasive goal of his studies was to understand how taste information is extracted by gustatory receptor cells and encoded into neural activity, how this code is maintained during receptor cell turnover and synaptogenesis, and how these processes lead to taste quality perception.

One of the defining characteristics of his career was to use a variety of experimental approaches to achieve his aims. His first scientific paper, resulting from his dissertation entitled; "Gustatory cross-adaptation: does a single mechanism code the salty taste?", employed a clever paradigm of cross-adaptation in human subjects to begin to discern the underlying neural complexity necessary to code a unique, seemingly unitary taste quality. That same basic interest drove the recent work that he did using central single unit recording and signal-detection theory to assess the role of individual or multiple central neurons in conveying the quality message.

His work spanned human psychophysics, animal behavior, electrophysiological experiments using patch recording of taste receptor cells, *in vivo* and slice recording of central gustatory neurons, and anatomical and immunohistological techniques. His studies were characterized by clear conceptualization, experimental rigor, and a mathematical orientation.

Among the many honors and awards David collected throughout his illustrious career were the Claude Pepper Award (1989-1991) and Jacob K. Javits Neuroscience Award (1984-1991) from the NIH, the Frito-Lay Award for Excellence in Taste Research (1994), and the Mannheimer Lectureship (Lifetime Achievement Award) from Monell Chemical Senses Center (2004).

Born in Memphis, Tennessee, on April 21, 1943, David received his B.S. and M.A. degrees in Psychology in from the University of Tennessee, Knoxville, in 1965 and 1967, and his Ph.D. in Psychobiology from the University of Pittsburgh in 1969. His Ph.D. advisor was Donald H. McBurney. After completing his doctorate, David embarked on a postdoctoral fellowship with Carl Pfaffman at Rockefeller University.

David established his own laboratory as an Assistant Professor in the Department of Psychology at the University of Wyoming in 1971. Having obtained the rank of Professor with tenure at Wyoming, he moved in 1984 to the Department of Otolaryngology-Head and Neck Surgery at the University of Cincinnati, College of Medicine, where he served as Professor until 1994. From 1994-2002, he served as Professor in the Department of Anatomy & Neurobiology at the University of Maryland School of Medicine, and Vice Chair from 1997-2002.

David came home in a very real sense to his native Tennessee in 2002, accepting a position as the Simon R. Bruesch Professor and Chair of the Department of Anatomy & Neurobiology, University of Tennessee Health Science Center in Memphis. He served in this role from 2002 to his death in 2006; during this time he was also the Director of the Neuroscience Institute. Throughout his career, David authored over 130 publications, mentored many students and fellows, held editorial posts (including Executive Editor of *Chemical Senses* from 2001 - 2006) and served both the NSF and NIH in review and administrative capacity. David was one of the founding members of the Association for Chemoreception Sciences in 1983, and served as its Executive Chairperson in 1985.

His loyal support enhanced numerous careers and created lasting friendships. He had a fine sense of humor, as well as an artistic flair.

For further information: www.achems.org ■

Vol. 8 No.4 October 2006

IBRO Satellite:

Brain mechanisms, cognition and behaviour in birds

Heron Island, Queensland, Australia
Thursday, 19 –Monday, 23 July, 2007

http://workshops.med.monash.edu.au/birdbehaviour07

Including Session on Avian Olfaction

NEWS

Echoes of ECRO in Granada

Papers and posters numbering 353 and two excellent guest lectures, made up the serious side of a wonderful European Chemical Senses meeting (ECRO, 4-8 September 2006) held recently in Spain. Everything intellectually new and wonderful in the chemical senses was represented at this conference, which attracted participants from Europe, the Americas, Japan, Asia, Russia, Africa and Australasia. This was an ECRO to remember.

Like most conferences, this one let people loose to talk, display, strut and pound the network. A great program (including for accompanying persons) was arranged and published in a well-made booklet (the design and editing set a new standard for conferences). But there was an outstanding and enduring feature that made this conference different, and that was Spanish hospitality.

Oh la!

If you have never experienced genuine hospitality, go to a conference in Spain, and preferably one in Granada.

ECRO's 500 attendees were wowed by the beauty and grandeur of the world heritage sites of Granada, and were indulged by the most impressive warmth of hospitality imaginable. This has to rate as a "super-conference" in the annals of chemical sensory conferences. Congratulations to the ECRO organisers, and to the local secretariat, GESTAC and the wonderful volunteers and staff who coped so excellently.

Tappas on tap

Granada has the enviable reputation of being a city of pubs and sidewalk cafes where the snacks (tappas) come automatically and free when a drink is ordered. This alone deserves to place it at the top of the conference venues! To put this to the test, the conference organised a "tappas tour" and took several groups on a slow tour (later, more like a crawl) of many venues where different types of tappas were offered: fish, shellfish, meats and cheeses, and plenty of crusty bread.

In addition, there were two wonderful drinks parties, a magnificent dinner with Flamenco dancers and a night trip to the Alhambra. This all helped to make ECRO in Granada an exceptional conference, and one to be remembered ■

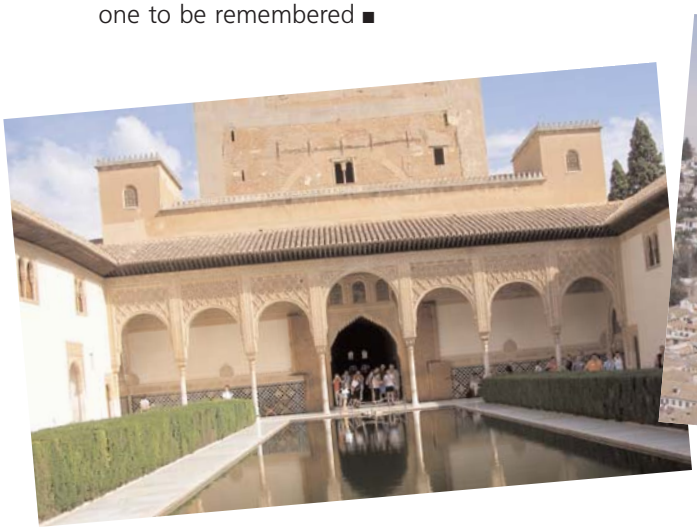

Photo courtesy of Ann Williamson

Upcoming Events

21-25 October 2006	**Society for Neuroscience** New Orleans Info: www.sfn.org
21-25 January 2007	**Keystone Symposium** "Chemical Senses: From Genes to Perception" Snowbird, Utah, USA Info: www.keystonesymposia.org
13-15 April 2007	**ISOEN** (International Symposium of Olfaction and Electronic Nose) St Petersburg, Russia Info: www.isoen.org
25-29 April 2007	**AChemS** Sarasota, Florida, USA Abstract Deadline: early Jan 07 Info: www.achems.org
7-9 June, 2007	**"Bacchus at Brock"** International Interdisciplinary Wine Conference St Catherines, Ontario Canada Info: www.brocku.ca/bacchus
19-23 July 2007	**IBRO Satellite on Avian Brain, Cognition and Behaviour** Heron Island, Queensland, Australia Contact: Marie.Gibbs@med.monash.edu.au
July 2007	**AACSS: 9th Annual Meeting** Adelaide, South Australia Contact: Stephen.Trowell@csiro.au
12-17 July 2007	**IBRO** (International Brain Research Organisation) Melbourne, Australia Contact: http://www.ibro2007.org
19-23 July 2007	**Avian Olfaction Symposium** IBRO Satellite on Avian Brain, Cognition and Behaviour Heron Island, Queensland, Australia Info: http://workshops.med.monash.edu.au/birdbehaviour07
28 July - 2 August 2007	**The 13th Australian Wine Industry Technology Conference** Adelaide, South Australia Contact Rae Blair: rae.blair@awitc.com.au
12-16 August 2007	**7th Pangborn Sensory Science Symposium** Hyatt Regency, Minneapolis, USA Abstract deadline: 31 January, 2007 Info: www.pangborn2007.com
6-8 May 2008	**Enviro 08** Melbourne Info: rvquitz@bigpond.com
21-25 July 2008	**International Symposium on Olfaction and Taste (ISOT)** San Francisco, USA Now calling for proposals for satellite meetings Contact Tom Finger: tom.finger@uchsc.edu ■

NZIFST

New Zealand/Australia Sensory Network Symposium- Auckland, NZ

30-31 January 2007
YMCA Shakespear Lodge
Shakespear Regional Park

- The purpose of this symposium is to increase networking and collaboration between Australia and New Zealand sensory and consumer science communities.
- Sessions and workshops based on recent sensory and consumer research.
- The programme is to be determined, but we hope to dedicate one day to sensory/consumer statistics (with an overseas presenter) and one day to research presentations.
- Total symposium cost for 2 Days will be as economical as possible. We are hoping to keep the cost under $600 NZD (including accommodation and food)
- Location of workshop and accommodation: www.arc.govt.nz/auckland-regional-parks/northern-parks/shakespear.cfm

In order to determine if there is enough interest in this workshop, please tick one of the boxes below and fax or email your interest to either Cynthia or Veronika before **10 November 2006**

- ○ I'm interested in attending the conference
- ○ I'm interested in speaking about my current research

For more information and to indicate your interest, please contact:

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