

Protein links eyes and brain in Down syndrome

In Down syndrome, triplication of chromosome 21 invariably includes the gene (21q21) encoding the Alzheimer's disease amyloid precursor protein, accelerating expression of this protein and leading to cerebral accumulation of amyloid precursor protein-derived amyloid- β peptides (A β), early-onset Alzheimer's disease neuropathology, and age-dependent cognitive sequelae.

The Down syndrome phenotype complex also includes distinctive early-onset cerulean cataracts of unknown aetiology. Increased A β accumulation, co-localizing amyloid pathology and disease-linked supranuclear cataracts have been reported in the ocular lenses of subjects with Alzheimer's disease. A study performed at Brigham and Women's Hospital, Harvard, USA,

looked at whether related Alzheimer's disease-linked A β pathology underlies the distinctive lens phenotype associated with Down syndrome (Moncaster et al, 2010).

Ophthalmological examinations of Down syndrome subjects were correlated with phenotypic, histochemical, and biochemical analyses of lenses obtained from subjects with Down syndrome, Alzheimer's disease and normal controls.

Evaluation of Down syndrome lenses revealed a characteristic pattern of supranuclear opacification accompanied by accelerated supranuclear A β accumulation, co-localizing amyloid pathology, and fibre cell cytoplasmic A β aggregates (~5–50 nm) identical to the lens pathology identified in people with Alzheimer's disease. Peptide sequencing, immuno-

blot analysis and enzyme-linked immunosorbent assay confirmed the identity and increased accumulation of A β in Down syndrome lenses.

These results establish the genetic aetiology of the distinctive lens phenotype in Down syndrome and identify the molecular origin and pathogenic mechanism by which lens pathology is expressed in this common chromosomal disorder.

Moreover, these findings confirm increased A β accumulation as a key pathogenic determinant linking lens and brain pathology in both Down syndrome and Alzheimer's disease.

Moncaster JA, Pineda R, Moir RD et al (2010) Alzheimer's disease Amyloid- β Links Lens and Brain Pathology in Down Syndrome. *PLoS ONE* 5(5): e10659. doi:10.1371/journal.pone.0010659

Erectile dysfunction and heart disease link emphasized

Led by the Sexual Advice Association, 12 international experts are calling for recognition of the critical link between erection problems and cardiovascular disease (Jackson et al, 2010). In around two thirds of men, the onset of coronary artery disease is preceded by erectile dysfunction. The time between the start of erectile dysfunction and a heart attack or stroke is estimated to be 3–5 years. The authors are appealing for greater awareness of this subject from the medical community and the general public to help save lives.

Dr Graham Jackson, Consultant Cardiologist, London, is the lead author of the article and Chair of the Sexual Advice Association. He says: 'Erectile dysfunction affects 40% of men over the age of 40 and one in three men over 70 years. Whereas publicity around erectile dysfunction has increased over the last decade as new treatments have become available, there is still very limited awareness that erectile dysfunction can be an early warning sign of cardiovascular disease and that erectile dysfunction can be caused by cardiovascular disease.'

Jackson G, Boon N, Eardley I et al (2010) Erectile dysfunction and coronary artery disease prediction: evidence-based guidance and consensus. *Int J Clin Pract* 64(7): 848–57

Early results from breast ultrasound clinical trial

SuperSonic Imagine has unveiled some preliminary results of the largest clinical breast study ever undertaken in ultrasound imaging. The worldwide multicentre study is assessing the clinical benefits of ShearWave elastography in the ultrasonic evaluation of breast lesions. It is hoped that the results will be published later this year.

The study was launched in April 2008 with 17 American and European sites, and conducted under the leadership of

Professor David Cosgrove, Imperial College, London.

The first phase of the study was to define a scientific model on 1000 cases, to determine if ShearWave elastography information can complement ultrasound information in order to improve a diagnosis.

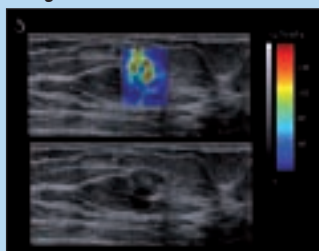
To undertake this, it was necessary to identify the criteria of an elastography image that would, when added to ultrasound criteria, improve lesion characterization (in sensitivity and specificity when compared to ultrasound alone) and eventually improve a BI-RADS score. The ShearWave elastography criteria or features studied for each lesion were: size, shape, average value of elasticity, homogeneity, orientation and contrast of elasticity between lesion and fatty tissue.

The second phase of the study, which is ongoing, will test this model on an independent set of lesions.

ShearWave elastography is reproducible both qualitatively (87% of consecutive repeated ShearWave elastography exams were 'similar', 'reasonably similar' or 'very similar' in appearance) and quantitatively (intra-observer reproducibility rates for ShearWave elastography measurements were 0.91).

Regression models based on 1000 cases were statistically evaluated by an independent biostatistician from the Hammersmith Hospital and show that when two ShearWave elastography features are added to the ultrasound evaluation, correct breast lesion classification rates rise to 87%, thus leading to more accurate results.

Malignant lesion with a hard shell.



Improving mental health symptoms for psoriasis patients

New research published online in the *Journal of the American Academy of Dermatology* shows that treatment with ustekinumab (Stelara) significantly improves symptoms of depression, anxiety and health-related quality of life in patients with moderate to severe psoriasis compared to placebo (Langley et al, 2010). These results are from an analysis of prespecified quality of life measures from a large phase III trial for ustekinumab, PHOENIX 2.

Data from the 1230 patients included in the PHOENIX 2 study show comparable levels of depression and anxiety to previous studies in psoriasis patients, as analysed using the Hospital Anxiety and Depression Scale (HADS). At baseline, over a quarter of

patients reported symptoms of depression (27%; HADS-D \geq 8, mild to severe symptoms) and more than a third reported symptoms of anxiety (40%; HADS-A \geq 8). The mean baseline scores of depression and anxiety reported by patients (HADS-D=5.1; HADS-A=6.9) are comparable to or worse than those of patients diagnosed with breast cancer and chronic obstructive pulmonary disease, highlighting the overall impact of psoriasis on patients' health-related quality of life.

At week 12, 63.5% of patients (141 out of 222 patients) treated with ustekinumab reported improvements in symptoms of depression, defined as a change in HADS-D score from \geq 8 at baseline to a HADS-D score of

<8 (normal), compared with 29.9% of patients receiving placebo (29 out of 97 patients, $P<0.001$). Similarly, 47.9% of ustekinumab-treated patients (152 out of 317 patients) with symptoms of anxiety reported improvements at week 12, defined as a change in HADS-A score of \geq 8 at baseline (mild to severe anxiety) to <8 (normal) compared to 22.2% of placebo-treated patients (37 out of 167 patients, $P<0.001$). This response was maintained up to week 24 in the ustekinumab-treated group.

Langley R, Feldman S, Han C et al (2010) Ustekinumab significantly improves symptoms of anxiety, depression and skin-related quality of life in patients with moderate-to-severe psoriasis. *J Acad Am Derm* May 10 [Epub ahead of print] doi:10.1016/j.jaad.2009.09.014

Teenage booster for meningitis C vaccine

The Oxford Vaccine Group are calling for a booster injection against meningitis C to be given to teenagers, following findings that three out of four British children have no personal protection against the bacteria within 7 years of vaccination.

Treating gum disease may lower blood sugar levels in type 2 diabetes

A meta-analysis published in the *Cochrane Library* suggests that the treatment of serious gum (periodontal) disease in patients with type 2 diabetes may lower their blood sugar levels, thus reducing the risk of serious complications such as eye and heart disease.

Fixed dose combination therapy for benign prostatic hyperplasia

Combodart (dutasteride 0.5 mg/tamsulosin hydrochloride 0.4 mg), the first fixed dose combination of a 5-alpha reductase inhibitor and an alpha blocker, has been approved for the treatment of moderate-to-severe benign prostatic hyperplasia and reduction in the risk of acute urinary retention and benign prostatic hyperplasia-related surgery.

Doubled chance of sustained remission in follicular lymphoma with rituximab maintenance

Targeted antibody therapy rituximab (MabThera) halves the risk of disease progression in previously untreated patients with follicular lymphoma, the most common type of indolent non-Hodgkin lymphoma, compared to those who received no maintenance therapy.

These new data come from the PRIMA study and were presented at the American Society of Clinical Oncology annual meeting in June (Salles et al, 2010). They also demonstrate that when treated with rituximab alone for a 2-year period ('maintenance therapy') following initial treatment with rituximab plus chemotherapy, 82% of patients with previously untreated advanced follicular lymphoma were able to live without their disease progressing, compared to 66%

of those who did not receive maintenance therapy.

PRIMA is an international, open-label, randomized, phase III study in patients with previously untreated advanced follicular lymphoma. It was conducted at 223 study sites across 25 countries, 9 of which were in the UK. A total of 1217 patients with previously-

Dr Robert Marcus, Consultant Haematologist, King's College Hospital, London



untreated advanced follicular lymphoma were involved.

Dr Robert Marcus, Consultant Haematologist at King's College Hospital, London, commented: 'The PRIMA study results show a significant improvement in progression-free survival in those patients who received rituximab maintenance therapy compared to those who did not. These data could change both our practice and our perspective on what is, in the majority of patients, a condition that should be controllable with intermittent and relatively non-toxic therapy.'

Salles GA, Seymour JF, Feugier P et al (2010) Rituximab maintenance for 2-years in patients with untreated high tumor burden follicular lymphoma after response to immunochemotherapy. Presented at the American Society of Clinical Oncology, Chicago, USA: 4-8 June