Gene linked to oestrogen levels and breast cancer risk

Scientists have found the first direct link between breast cancer risk and genetically-determined levels of oestrogen in younger women, according to new research (Johnson et al, 2012).

Sex hormones such as oestrogen are known to be important in breast cancer development. Previous studies have found that postmenopausal women with higher levels of particular hormones are at greater risk of breast cancer, but the direct evidence in premenopausal women has so far been inconsistent.

The study found an alteration in a gene that is involved in the breakdown of oestrogen and is also associated with a modest reduction in breast cancer risk in pre-menopausal women.

The scientists set out to find genetic variants involved in the synthesis or breakdown of sex hormones. They first measured markers of hormone levels in the urine and blood of more than 700 healthy premenopausal women, using a process that was specially designed to account for variation in levels during the menstrual cycle. They then examined the women's DNA, focusing on 42 genes that are known to be involved in the synthesis or breakdown of sex hormones.

When they compared women's hormone levels with each of the variants that they tested, they identified one genetic variant that was more common in women who had lower urinary levels of a particular oestrogen breakdown product called oestrone glucuronide. The variant was a single letter change in the DNA at position 7q22.1, not far from the CYP3A gene cluster. It was associated with a 22% reduction in urinary oestrone glucuronide levels.

The team then tested this variant in a further 10 551 breast cancer patients and 17 535 healthy controls, and found the DNA change was more common in healthy women. The variant was associated with a modest – 9% – reduction in breast cancer risk in women diagnosed at or before the age of 50 years, but not in older women.

Senior author Dr Olivia Fletcher from the Institute of Cancer Research's Breakthrough Breast Cancer Research Centre said: 'This is the first time anyone has found a DNA change that is directly associated both with hormone levels and breast cancer risk in younger women. Scientists have suspected this link exists, but no one has been able to prove it until now. This represents an important step forward in our understanding of the link between hormones and breast cancer. Ultimately, it may have implications for the way we monitor and treat breast cancer.'

Although this DNA change is only one part of a very complex picture of the relationship between hormones and breast cancer, variants such as this could potentially form part of a genetic test that could help predict young women's risk of breast cancer.

Dr Fletcher continued: 'This research has revealed that this set of genes warrants further investigation for the effect they may have on the way the body processes drugs'.

Johnson N, Walker K, Gibson LJ et al (2012) CYP3A variation, premenopausal estrone levels, and breast cancer risk. *JNCI J Natl Cancer Inst* 3 April (Epub ahead of print)

Improved flow could allow more efficient use of paediatric intensive care unit beds

The paediatric intensive care unit is a key component of patient flow. A new American study reveals that, while a large paediatric intensive care unit observed for the study delivered critical care services most of the time, periods of use for non-critical care services represented a barrier to access for new patients (Fieldston et al, 2012). At times when a bed was needed for a new patient, the paediatric intensive care unit had beds being used by patients who could have been cared for in other settings.

Led by Dr Evan Fieldston, of the Children's Hospital of Philadelphia and the Perelman School of Medicine at the University of Pennsylvania, researchers conducted a real-time prospective observational study in a convenience sample of days in the paediatric intensive care unit of an urban tertiary care children's hospital.

Three trained observers spent 5 non-contiguous weeks in the paediatric intensive care unit for 16 hours each day and also recorded what had happened overnight each morning. This created almost 20 000 bed-hours of data, which were then categorized as medical or nursing value-added, necessary logistics, non-value-added, or empty and unassigned time.

Results showed that the beds were being used for value-added purposes 82% of the time. While only 8% of the time was considered to be non-value-added, during 75% of the time when the paediatric intensive care unit was full, at least one bed was being used for a non-value-added purpose and 37% of the time, two beds were being used for non-value-added purposes.

'This topic affects the delivery of health care in all settings, but most notably inpatient settings,' Dr Fieldston concluded. 'This work is part of a larger stream that is merging operations management and other techniques to better describe and improve healthcare delivery and provides hospitalists and hospital leaders an approach to learn more about their operations.'

Dr Evan Fieldston, Children's Hospital, Philadelphia, and Perelman School of Medicine, University of Pennsylvania

Fieldston ES, Li J, Terwiesch C et al (2012) Direct observation of bed utilization in the pediatric intensive care unit. *J Hosp Med* 7(4): 318–24