Evolution of prostate cancer gene mutations

A whole genome sequencing study has challenged the notion that the genetic changes that mark prostate cancer occur gradually. Instead, the authors posited that the changes happen in bursts; coordinated actions in which a range of chromosomes are re-ordered at the same time. So rather than a gradual build-up of alterations and mutations, there is a series of discrete events, folding into a process the authors characterised as "punctuated cancer evolution".

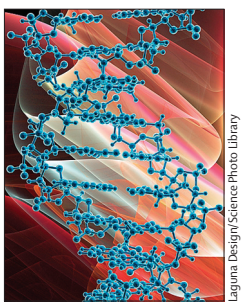
The multicentre study started by sequencing the entire genome of 57 localised prostate tumours of various grades and stages. The researchers compared the findings with DNA from healthy tissue: the cancer cells showed 356 136 base-pair mutations, and more than 5500 rearrangements that do not appear in healthy DNA. With sophisticated computer modelling techniques, the researchers were able to create a picture of the genetic make-up of prostate cancer.

"We found complex derangements that led to chains of rearrangements that involved cancer genes", explains co-author Mark Rubin, Weill Cornell Medical College of Cornell University, New York, USA. "It represents a novel way that cancer cells can incorporate a number of changes; these do not accumulate gradually but occur in a single cell cycle". The authors named this process chromoplexy and added that it occurs in most prostate cancers, and follows a course by which cancer-fighting genes are eliminated. In which case, the genes that remain might be those which drive the disease.

Chromoplexy remains an inference taken from computer modelling—the mechanism behind it has yet to be shown—but Phillip Febbo (University of California, San Francisco, USA) points out that it is a compelling theory and one that has been the subject of expert speculation for a while. "This is an important paper", affirmed Febbo. "We are really starting to build up a catalogue of genetic events that represent prostate cancer, and there is the opportunity to anticipate what genes, proteins and pathways we need to target." However, he noted that there is quite a difference between identification of a target and development of an appropriate therapeutic.

Rubin believes that the findings will stand up against other tumour types, opening up further possibilities. He conceded that a limitation of the study was its focus on a static shot. "We are currently working on taking biopsies from individuals along the course of their treatment—hopefully we should be able to gain some insight into what happens to individual tumours over time", he concluded.

Talha Khan Burki



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Prognosis of breast cancer during pregnancy

The prognosis of women with primary breast cancer diagnosed during pregnancy is similar to that of non-pregnant patients with primary breast cancer, according to a recent cohort study.

Frédéric Amant (University Hospitals Leuven, Belgium) and colleagues compared the disease-free survival and overall survival of 311 patients diagnosed with breast cancer during pregnancy with 865 non-pregnant patients. After a median follow-up of 61 months, the researchers found no evidence of worse prognosis for patients diagnosed with breast cancer during pregnancy in terms of disease recurrence (hazard ratio [HR] 1·34, 95% CI 0·93–1·91, p=0·14) or overall survival (1·19, 95% CI 0·73–1·93, p=0·51).

Amant told *The Lancet Oncology:* "The main message is that pregnancy does not alter the maternal prognosis of breast cancer. Historically, it was believed that the high hormone levels [during pregnancy led] to a worse outcome." He continued "We compared two groups with similar characteristics; the only difference was the pregnant state. And the outcome is similar. We believe this information is important when pregnant breast cancer patients are counselled."

On the basis of these data, and those published recently in *The Lancet Oncology*, Amant states that when breast cancer is diagnosed during pregnancy, women should not abort the pregnancy, should receive standard breast cancer treatment, and deliver their baby when the fetus has reached term.

Sibylle Loibl (German Breast Group, Neu-Isenburg, Germany) a senior author on the paper, concurs, stating that: "treatment for breast cancer during pregnancy is still not the same as for non-pregnant women in many countries and hospitals" despite growing evidence that this is not the best course of action.

Fedro Alessandro Peccatori, European Institute of Oncology, Milan, Italy, says that "The clinical implications of this study are important, as women can be reassured that pregnancy per se does not influence prognosis if [they are] appropriately treated during pregnancy". Peccatori states that further work is needed for us to gain "a better understanding of the aetiology of breast cancer occurring at young age and the relationship with pregnancy, which could help women and clinicians implement more effective treatment strategies".

Holly Baker

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For more on **breast cancer and pregnancy** see **Articles** *Lancet Oncol* 2012; **13:** 256–64 and **Articles** *Lancet Oncol* 2012; **13:** 887–96