Genome breakthrough allows scientists to identify and profile tumor cells from very small samples

May 6 2010

Researchers from Cold Spring Harbor Laboratory in the USA have developed a powerful new technique for analyzing the genome of single tumor cells. The breakthrough allows them to study in fine detail the biology of how tumors develop and has the potential to help doctors identify dangerous tumor cells from small samples such as fine-needle biopsies from the prostate or a non-invasive lesion in the breast.

Dr James Hicks from Cold Spring Harbor described the new technique at the IMPAKT Breast Cancer Conference in Brussels, Belgium.

"Tumors are complex populations of cells and they are not limited to the tumor mass itself," Dr Hicks said. "By the time a tumor is discovered there are almost certainly thousands of tumor cells in the circulation or hiding in places like bone marrow. The breakthrough here is that we have proven the concept of identifying tumor cells in very small samples and profiling them to see whether they are dangerous. In other words are there small populations of highly rearranged cells among the benign-looking ones?".

A major focus of cancer treatment at present is determining how aggressively to treat patients as methods for early cancer detection improve. The opportunity to use similar techniques to study the basic biology of tumor growth is more academic, but no less important aspect.

The technique developed at Cold Spring Harbor focuses on 'copy number variation' in cancer cells. These are changes to the expected number of copies of large sections of DNA. For example, genes that were thought always to occur in two copies per cell might sometimes be found in one, three or more copies.

Dr Hicks explained: "Most solid tumors, especially breast, lung, liver, bladder and prostate, exhibit varying degrees of chromosomal rearrangement. As cells progress from normal state where there are two copies of each chromosome, to become more cancer-like, they tend to accumulate more and more rearrangements that can be seen as copy number changes. The genetic history of a tumor cell is written in its DNA and much of that information can be extracted from its copy-number profile."

Many of these rearrangements are characteristic of different cancer types or sub-types and are beginning to be used in diagnosis and prognosis. However, most tumor samples are mixtures of tumor cells of potentially different types mixed together with other tissue, making it difficult to understand what is going on in specific tumor cells.

Dr Hicks and colleagues recently published a method for enriching tumor cells from small parts of tumor specimens, separating them by virtue of their aberrant DNA content, and determining that the patterns were present in individual cells. They called this process the 'single nucleus sequencing' method (SNS).

At IMPAKT, Dr Hicks reported that the researchers were able to use the technique to show the pathway of genetic changes that happened as two breast carcinomas developed.

"By profiling over 100 individual cells from a single tumor, we have obtained evidence that as cancer cells initiate their progression they

undergo drastic changes, sometimes losing as much as 25% of their genomic DNA through massive deletions, yet are still able to establish clones of identical cells that occupy large portions of the tumor mass," Dr Hicks explained.

"Ultimately, at least three major populations of cells, all genetically related, were found to occupy one particular tumor mass. We are now working to understand which of these cells can go on to form distant metastases."

Currently, the techniques used in this research are too expensive and time-consuming for use as routine diagnostics. "But we believe that the drastic increases in sequencing efficiency and sample multiplexing on the horizon will make this approach feasible in the near future," Dr Hicks said.

Provided by European Society for Medical Oncology