Promising new insights into early cancer growth

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In a significant advance in cancer research, US scientists have pioneered a new technique to record the earliest stages of a tumour's development. Using microscopic pictures, Duke University scientists recorded the tumour's early growth through glass "windows" placed in the sides of live mice. The results showed that tumours began to sprout blood vessels—a process known as angiogenesis—at a much earlier stage than previously thought.

Furthermore, the US scientists used the technique to test a new class of anti-angiogenesis drugs, which were shown to stunt the growth of tumours by literally starving them before they spread. The finding has important implications for the development of a new anti-cancer treatment.

Published in the Journal of the National Cancer Institute in January, the study featured a photo series taken from video-microscope footage showing day-by-day growth of a tumour. In less than eight days, the cancer cells multiplied, forming a tumour and its own blood vessels. The first evidence of blood vessels was seen on day six, when the tumour mass increases to between 100 to 300 cells. By day eight, the tiny vessels were observed to be fully functional with red blood cells clearly visible on the recorded video images.

The study has also provided a new insight into how newly formed tumours attach to the body's blood vessel system. According to the scientists, during the first 20 days of tumour development, the cancer cells showed a definite orientation or movement towards the body's own system of blood vessels. That is, the cancer cells actually migrated towards the surrounding blood vessels. This phenomenon indicates significant interaction takes place between the cancer cells and blood vessels—most likely through a type of "chemical signal".

There is also clear evidence of "chemical signals" operating between the blood vessels formed by the tumour, and the tumour's own cell growth. In other words, the growth of a tumour is intimately bound up with the development of vessels formed by the tumour itself.

The study conducted each experiment ten times to verify the findings, and strongly contradicts the previous estimate of roughly one million cancer cells (a tumour that is one millimetre in diameter) before angiogenesis could commence. The study's findings are another indication that new anti-angiogenesis drugs will be an effective form of cancer treatment.

In fact, the Duke University scientists made major strides in evaluating these drugs. An engineered anti-angiogenesis drug called "ex-flk 1" was tested to see whether the process of angiogenesis is essential for tumour survival and growth. Once injected into the mouse, tumour growth was monitored continuously. It was found that the drugs effectively inhibited tumour cell proliferation right from the beginning. All tumour cells had disappeared within the first five days of implantation with no evidence of any blood vessel formation whatsoever.

The results of the study underscore the significance of technological advances in the field of in-vivo experiments—that is, real time experiments in living organisms rather than in test tubes. Scientists were able to develop a new technique involving the use of a fluorescent protein to observe the live cells. In fact, the Duke University scientists explain that the same test done under in-vitro, or test tube conditions, produced inferior and inconclusive results.

The mouse cancer cells were viewed with a green protein, called Green Fluorescent Protein (GFP), extracted from a species of jellyfish, *Aequorea victoria*.

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The protein is genetically engineered, that is genetically manipulated, into the mouse cancer cells so that they fluoresce or glow when exposed to a special external light. As the GFP becomes part of the genetic structure of the mouse cancer cells, they continue to fluoresce, even as they continue to divide and multiply.

The use of the fluorescent protein for cancer research is a major advance in biotechnology, as well as in the field of imaging technology. Cancer cells can be viewed in real time, without disturbing the cells or causing any physiological changes to the animal. Current technology, including X-rays, MRI, and ultrasonography (ultrasound) is limited in its ability to investigate internal tumour growth. Monitoring cancer using these methods is impractical as they use potentially harmful irradiation. Furthermore, optical imaging of cancers has so far been a major challenge as tumours are generally indistinguishable from normal tissue. The GFP technique is a major advance as the actual target tumour is the source of light.

The use of GFP in mice is also effective because all that is needed is a blue light to illuminate the cells for viewing under the video camera—thus leaving the cells undisturbed. A one millimetre diameter glass window is implanted into the side of the mice to facilitate the injection of tumour cells, as well as the viewing of the fluorescent cells under the videomicroscope—a video camera that enhances microscopic images. The technique has enormous potential for testing anti-cancer drugs.

The Duke University findings strongly support the research of other scientists, which have found positive results for anti-angiogenesis drugs. When Dr. Judah Folkman revealed the potential of the anti-angiogenesis drugs, Endostatin and Angiostatin, they were over-sensationalised in the media as drugs, which would provide a general cure for cancer in two years. While there is no evidence of complete “cancer-cures” in the near future, the findings of the Duke University scientists open the way for promising new lines of anti-cancer research.

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