

Stem cells provide clues to cancer spread

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Scientists have made a breakthrough in understanding how cancers spread in what could lead to new ways of beating the disease.

The University of Manchester study used embryonic stem (ES) cells to investigate how some tumours are able to migrate to other parts of the body, which makes the treatment of cancer much more difficult.

Dr Chris Ward, in the University's Faculty of Medical and Human Sciences, studied a crucial change that makes cancer cells able to start moving and spread into other tissues.

Normal cells, as well as early cancer cells, are called epithelial cells because they bind tightly to each other forming stable layers of tissue. However, as a tumour becomes more advanced, some of the cells change to become 'mesenchymal'.

Mesenchymal cells do not bind to each other, forming more disorganised tissues in which the cells can move around. Since this crucial change – known as the epithelial-mesenchymal transition, was first observed in the early embryo, Dr Ward theorised that embryonic stem cells might undergo a similar process.

Dr Ward, whose findings are published in the journal *Molecular Biology of the Cell*, said: "We have shown that ES cells spontaneously change in a manner that is remarkably similar to the epithelial-mesenchymal transition. They lose the proteins that cells use to bind to each other and have other protein alterations that are characteristic of spreading cancer

cells.

"Since ES cells can be grown in the laboratory where they keep the characteristics of the cells in the early embryo they can be studied in detail. By studying these ES cells we have already identified a novel component of this transition process. We expect the use of ES cells will lead to the identification of other unknown factors involved in cancer cell spread, hopefully leading to new avenues for cancer therapy."

Previously, it has been quite difficult to study this crucial transition in cancer cells as it only happened to a limited number of cells in a growing tumour. The team's discovery that it happens spontaneously in ES cells means that it can be studied more easily in the laboratory.

"Understanding how cancer cells start to spread is tremendously important for cancer research; tumours that do not spread are rarely, if ever, dangerous," said Dr Ward, who leads the stem cell research group in the School of Dentistry.

"It is the ability of tumours to invade into other tissues and spread around the body that makes them so dangerous. Finding out more about the mechanism that controls the spread of cancer cells will help us find new treatments that can prevent tumours spreading and make them essentially harmless."

The study, which was funded by the Association for International Cancer Research (AICR) and also involved the University's Immunology Group at the Paterson Institute for Cancer Research (PICR), used embryonic stem cells to investigate how the protein E-cadherin stopped cells from migrating during normal growth.

The team found that, as well as helping cells stick together, E-cadherin also blocked the action of another protein known to increase the mobility

of cells. This important dual function of E-cadherin opens up the potential for new targets to prevent tumours from spreading.

Derek Napier, Chief Executive of AICR, said: "Dr Ward's work will open the door to a detailed dissection of the process that makes cancers spread around the body.

"Scientific research occasionally makes sudden leaps forward when a new way of investigating something is discovered. We predict that this will lead to a huge growth in our understanding of cancer spread and the development on several new approaches to stopping it."

Source: University of Manchester

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