TUMOUR STEM CELLS

Generating colon cancer

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URLs
CD133
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=Retrieve&dopt=full_report&list_uids=8842

Colon cancer
http://www.cancer.gov/cancertopics/types/colon-and-rectal

One model of tumour growth proposes that tumours are hierarchically organized, wherein only a subset of cells, the so-called cancer stem cells (CSCs), are able to initiate and propagate tumour development. An opposing model suggests that every cell within a tumour has the capacity to initiate and sustain tumour growth. John Dick and colleagues now show that CSCs exist in colon cancer.

CSCs possess the capacity to regenerate themselves and produce non-CSC progeny. To examine whether colon cancer develops from CSCs, the group injected cell suspensions from 17 different colon cancer samples into immunodeficient mice. The resulting xenografts resembled the original tumours, showing common patterns of antigen expression and differentiation status. Can all cells derived from colon cancer initiate tumour development? The group performed limiting-dilution analyses, and showed that there was a minimum number of colon cancer cells that could form tumours in the mice. This indicates that only a subset of cells, termed the 'colon cancer-initiating cells' (CC-ICs), are capable of initiating tumour development, consistent with the CSC model. Furthermore, they showed that cells from the xenografts were able to initiate tumour growth in secondary and tertiary recipient mice, indicating that the CC-ICs can regenerate themselves.

The CSC model is also applicable to the development of brain and prostate cancers, for which the CSC fraction has been shown to overexpress the antigen CD133. Therefore, the authors fractionated the colon cancer cells according to CD133 overexpression before injecting them into the mice. Only the CD133-overexpressing ($CD133^+$) fraction was able to significantly induce tumours. Similarly, only the $CD133^+$ fractions from the xenografts were able to generate tumours in secondary and tertiary recipients. Moreover, the CC-ICs within the $CD133^+$ fraction had the capacity to re-establish the patterns of differentiation and CD133 expression of the tumour, which indicates that $CD133^-$ cells are derived from $CD133^+$ cells. Limiting-dilution analysis was used to determine that the CC-ICs were enriched 216-fold within the $CD133^+$ fraction compared with the unfractionated cell samples.

Similar results were found by Ruggero De Maria and colleagues.

The hierarchical organization of tumours has been shown to occur in acute myeloid leukaemia, cancers of the breast, prostate, brain and now the colon. The presence of CSCs could account for both metastatic and recurrent tumour growth.

Patients with colon cancer have the second highest mortality rate of all cancer patients, therefore John Dick and colleagues propose that further characterization of CC-ICs might reveal unique biomarkers that could have prognostic value. Furthermore, developing therapeutic strategies that specifically target the CC-ICs might improve patient survival.

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ORIGINAL RESEARCH PAPERS O'Brien, C. *et al.* Identification of a human colon cancer cell capable of initiating tumour growth in immunodeficient mice. *Nature* 19 November 2006 (doi: 10.1038/nature05372) | Ricci-Vitiani, L. *et al.* Identification and expansion of human colon-cancer-initiating cells. *Nature* 19 November 2006 (doi: 10.1038/nature05384)