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Trends in Cancer

Why Tumor Genetic Heterogeneity May Require Rethinking Cancer Genesis and Treatment

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This paper proposes a novel approach to cancer treatment, by examining tumor genetic heterogeneity, that also challenges current cancer hypotheses, which are predominantly based on a mutation-centric hypothesis and its related treatment approaches. The hypothesis proposes that tissue genetic heterogeneity, is a built-in natural consequence of the temporary reduction of DNA repair efficiency, that occurs very early in human development. This results in a small minority of cells within normal tissues acquiring cancer-associated genes to create precancerous cells that remain dormant. Cancer then only develops when these precancer cells are selected for by altered cancer-promoting tissue microenvironments. Moreover, similar scenarios occur when metastases and therapeutic resistance emerge in established cancers.

The authors therefore suggest a “normal cell selection treatment approach” to cancer treatment:

1. based on preferentially selecting normal cells within tumors by returning malignant tissue microenvironments that select cancer cells to precancer conditions that select normal cells and similarly;
2. in metastatic and resistant-to-treatment tissues , by restoring and then maintaining tissue microenvironments that can select normal cells for proliferation in favour of cancerous cells.

Thus, rather than focusing on the destruction of cancer cells, this approach seeks to alter tumor microenvironments so that normal cells are competitively selected in preference to cells with mutations that can drive carcinogenesis.

Therefore, in order for such a plan to be executed, it will be necessary to establish the factors responsible for returning tumor microenvironments to a state where selection of normal cells wins out over cancer cells. While, there are a number of outstanding questions still to be addressed through further research, the idea is to pursue treatment options designed to promote the proliferation of normal cells, rather than the destruction of cancer cells.

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