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A mathematical light on initiation of colorectal and intestinal cancer

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Rapidly dividing tissues, like intestinal crypts, are frequently chosen to investigate the process of tumour initiation, because of their high rate of mutations. To study the interplay between normal and mutant as well as immortal cells in the human colon or intestinal crypt, we developed a 4-compartmental stochastic model for cell dynamics based on current discoveries. Recent studies of the intestinal crypt have revealed the existence of two stem cell groups. Therefore, our model incorporates two stem cell groups (central stem cells (CeSCs) and border stem cells (BSCs)), plus one compartment for transit amplifying (TA) cells and one compartment of fully differentiated (FD) cells. However, it can be easily modified to have only one stem cell group. We find that the main deficiency occurs when CeSCs are mutated, or an immortal cell arises in the TA or FD compartments. The probability of a single advantageous mutant CeSC being able to transform all cells into mutants is more than 0.2, and one immortal cell always causes all FD cells to become immortals. Moreover, when CeSCs are either mutants or wild-type individuals, their progeny will take over the entire crypt in less than 100 days if there is no immortal cell. Unexpectedly, if the CeSCs are wild-type, then non-immortal mutants with a higher fitness are washed out faster than those with a lower fitness (net reproduction rate). Therefore, we suggest one potential treatment for colon cancer might be replacing or altering the CeSCs with the normal stem cells.

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