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The Common Genesis of All Cancers

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Abstract

It is a commonly held belief nowadays that cancer originates in tissue-specific adult stem cells. Most of the tissues in human body have adult stem cells at their base. The difference between embryonic stem cell and adult stem cell is that whereas the former, through a carefully orchestrated cellular program of development genes, can give rise to terminally differentiated cells of all types, the later can repair the terminally differentiated tissue by giving rise to cells of few types specific to the tissue. In a majority of tissues the adult stem cells are relatively quiet, swinging into action only on signals of damage or injury to tissue. One of the exceptions of this is the adult stem cell of intestinal epithelium, which is continuously in action as the differentiated cells of intestinal epithelium are continuously shed into the lumen. The adult stem cells have the property of self-renewal: they can undergo asymmetric cell division to give rise to two distinct daughter cells one of which is the exact copy of mother stem cell and the other is a partially differentiated progenitor cell or progeny, and symmetric cell division to give rise to two identical daughter cells which are exact replicas of mother stem cells. The progenitors further undergo cell division to yield terminally differentiated cells having specific morphologies and functions. The rates of self-renewal, apoptosis and differentiation of adult stem cells and their progenitor cells is very tightly regulated to achieve homeostasis, i.e. steady state where in the number of adult stem cells, progenitor cells and terminally differentiated cells attain a constant value. It has been suggested that cancer results by multiple mutations in adult stem cells and or progenitor cells which disturbs the balance between rates of self-renewal, apoptosis and differentiation leading to unsteady state.

Keywords

Carcinogenesis; Cancer stem cells; Self-renewal; Apoptosis

Introduction

Is there a genesis of cancer common to all cancers? His is a burning question if we dream of a single unique preventive therapeutic against all cancers. His is what ideally all researchers on carcinogenesis around the world aim at. Having a preventive therapeutic specific to the type of cancer does not help, at best what we can achieve with this effort is prevention of recurrence of a particular cancer type in a patient once he/she has been cured of that cancer type. In recent years the research on carcinogenesis has focused on adult stem cells [1]. It is the occurrence of multiple mutations cumulated over multiple stages in adult stem cells and progenitor cells that lead to their transformation to cancer stem cells (CSC) [1]. CSC by them is not cancer but in most of the cases it is CSC that initiates tumors. He reason for my belief is the similarity in fates and properties of adult stem cells and progenitor cells of all tissue types under both normal and carcinogenic conditions. In order to understand this mechanism I review five different types of cancers of five different organs respectively.

Colon Cancer

Colon is the name given to large intestine. He intestine (both small and large) is a long tubular structure with the inside hollow space known as lumen. Overlooking the lumen are millions of crypt-villus structures which have a lining of single sheet of epithelial cells on the outside [13]. He crypt-villus structure is a folded finger like structure protruding into the lumen. He top third of it is known as the villus and the bottom two-third constitutes the crypt. He top of the crypt is occupied by the multipotent progenitor cells. Below the progenitor are the adult stem cells. And at the very

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bottom below the stem cell population is Paneth cells- another terminally differentiated cell originating from the stem cell. He stem cells undergo asymmetric cell division to give one daughter cell which is the exact copy of the mother cell and another partially differentiated cell which is the multipotent progenitor.

Conclusion

In most of the cases of cancer the cause of a cancer is a pre-cancer single mutation in the otherwise healthy adult stem cell or multipotent progenitor. His single mutation, however, does not directly give rise to cancer but over a period of time multiple mutations occur in a sequence in multiple stages in the cell that initially had only single mutation, and thus a pool of small number of highly mutated cells are formed that have the same capacity of self-renewal as the healthy adult stem cell called the Cancer Stem Cell (CSC). CSCs do not always arise from adult stem cells and or multi-potent progenitors only, the mature cells also give rise to CSCs by undergoing a sequence of successive mutations that confer it the property of selfrenewal, like, for example, in liver. It is the CSC that initiates tumor and maintains the cells of the cancer blast. What is the gap between CSC and initiation of tumor, i.e. exactly what happens between the establishment of CSC and onset of cancer is the primary focus of this review. It is not possible to know this, or capture this moment, by any experiment.

References

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