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Mini Review

Telomerase Activity as a Connection Ring Between Oncology, Cellular Ageing, 3D Bioprinting and Vaccine Manufacturing

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Abstract

Cellular mortality and uncontrolled mitotic divisions are the main characteristics of cancer, as they give it, in addition to other factors, the ability to outbreak in the patient's body which hardens the curability of cancer while cellular ageing is the main reason behind many ageing diseases. In the last few decades researches showed that telomerase enzyme activity is the main controller of cellular mortality and ageing as its ability to make the cell exceed the hayflick's limit or the normal number of mitotic divisions that normal cells can do. This discovery not only opened the doors to many new cancer treatment techniques but also gives us new medical prospects capable of changing organ transplantation in the future.

Keywords: *Cancer; Cellular Ageing*

Introduction

Cancer and cellular aging as known relate to the limitation of cellular divisions; cancer cells, infinitely divide in contrary to cellular ageing in which cells lose their ability to divide. But the question is: What are those factors that control division?

Actually, the answer to this question took decades of researches, first about what difference there is between cancer cells and aged ones. To answer this question, we should know how normal cells divide and how they age or become cancer cells then the connection ring between them becomes clear.

Normal cells divide by mitosis and within every mitotic division [1], the length of telomere in the end of cell DNA gets shorter till definite limit called hayflick's limit. At this limit cells cannot undergo further divisions [2].

In cancer cells, in addition to major activation of oncogenes and suppression of P53 "tumor suppressor gene", there is an enzyme called telomerase enzyme that is activated which as a result, increases the length of telomere so that cancer cells can divide continuously [3-5].

Without telomerase enzyme, cancer cells will age like normal ones and will be localized so cancer will lose its major characteristics of metastasis or malignancy.

About 90% of cancer types show expression of telomerase enzyme which makes telomerase inhibition one of the possible mechanisms to control the outbreak of cancer in the patient's body [6].

Many cancer drugs depend on their mechanism as inhibitors of telomerase activity but side effects are painful as these drugs affect normal cells that have levels of telomerase expression since these cells frequently divide more than other cells such as "hair follicle cells – cells lining mouth… etc". [7,8].

Unlike cancer cells, aged cells show no expression of telomerase enzyme, so every mitotic division causes erosion of cells' telomere with no ability to reconstruct the missing parts lacking telomerase enzyme [9].

Cells, with each division, get closer to a limit that there are no more telomere parts to be lost. As a result, cells would then lose their ability to divide making them become larger in size and prone to programmed cell death by apoptosis [10].

So, the connection between aged cells and cancer cells is telomerase activity.

Telomerase enzyme is a complex enzyme formed of two main parts: telomerase reverse transcriptase (TERT) and telomerase RNA (TER) [11].

Telomerase reverse transcriptase uses telomerase RNA as a template to build up new parts on 3' end of DNA "telomere" as shown in Figure 1 [12].

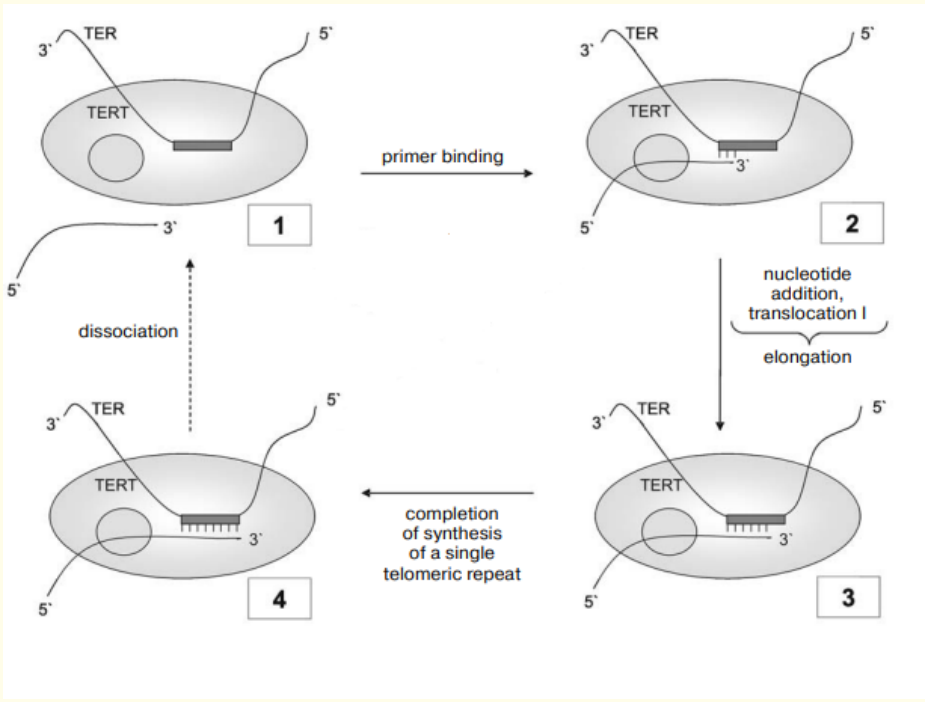

Figure 1

Telomerase activated in cancer by activation of telomerase enzyme genes which is found on chromosome 5 and formed of 16 exons and 15 introns [13].

The translation of telomerase gene is affected by epigenetic effects and many factors that regulate transcription process.

Epigenetic effects on chromatin structure and reshaping of the telomerase gene region that resembles the first control of telomerase regulation [14]. In contrary to the base of epigenetic control that methylation makes genes silent and couldn't be expressed, telomerase gene region in cancer cells is hyper methylated and that seems to help in promotion of transcription process [15] with the help of Histone acetylation [16,17].

In addition, there are many proteins that are believed to be responsible for transcription promotion like c-Myc protein family [18-20].

In addition, there are many viruses that have ability to activate telomerase gene like cytomegalovirus (CMV), Epstein-Barr virus (EBV), Kaposi sarcoma-associated herpes virus (KSHV), human papillomavirus (HPV), and hepatitis B, C virus [21-25].

The development of 3d bioprinting was promising to build up organs from the same body cells which will make organ transplantation without any hypersensitivity side effects but there is one big problem hinders that project is to find continuous source of cells [26-28].

Stem cells were a reasonable solution but it is still so difficult to use stem cells to build up 3 – 6 different types and maybe more of tissues to build up an organ but using safe activation of telomerase will lead to a huge jump in this field as it will give you the ability to build up a complete tissue from few cells.

Vaccine manufacturing is a complex industry but in general, it entails injecting a host by targeted virus and allowing the virus to propagate and then making a collection of all produced viruses. By using chemicals or other methods, viral infectivity will be removed then you will have a suitable antigens for immune system [29].

The host mostly is a mammalian cell line. So, in this industry, you should have a continuous source of cells. Using primary cell lines is expensive and badly effects on the stability of production.

The viral activation of telomerase is the key factor in this industry nowadays. Using tumor viruses to activate telomerase enzyme in host cells will give a cell lines called immortalized cell lines which will resemble an infinite source of host cells [30].

Conclusion

Finding the method of achieving full control of telomerase activity will open doors for development in many scientific and medical aspects.

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