

Mathematical investigation of change in the size of a cancerous tumour when its cells are being destroyed by T-lymphocytes

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Abstract

Mathematical investigation of change in the size of a cancerous tumour under the conditions of the body's immune response is performed. When the cancerous tumour is attacked by T-lymphocytes, its cancer cells are destroyed. Then, under certain conditions, the cancerous tumour shrinks. This process is described by the system of dynamic differential equations constructed in this research. It makes it possible to determine the conditions for the destruction of cancer tumours.

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1. Introduction

The cause of death of a large number of patients is cancer worldwide since many patients find out about the presence of cancer already at a late stage of its development. To overcome this disease, the scientific research (including mathematical research [1]) is very important and relevant. In the research and treatment of cancer patients, many world scientists noticed very important role of T-lymphocytes in the destruction of cancer cells ([2], [3]).

In 2018, James P. Allison and Tasuku Honjo became laureates of the Nobel Prize in Physiology or Medicine for a completely new principle of cancer therapy, a new type of cancer treatment that is immunotherapy. The immunotherapy works by blocking the inhibitory proteins of the

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immune system which includes a special variety of white blood cells -- T-lymphocytes. T-lymphocytes recognize and destroy foreign and mutated cells ([4], [5]).

The immune response of the human body consists in the fact that it produces T-lymphocytes that destroy cancer cells. However, when the immunity is weakened, the human body produces an insufficient number of T-lymphocytes. Then with intensive transformation of cells into cancer ones due to various causes, cancer cells can lead to the appearance and growth of a cancerous tumour.

In this article, we mathematically analyze the process of changing the size of the cancerous tumour when cancer cells are being attacked by T-lymphocytes. It makes it possible to determine the conditions for the destruction of cancerous tumours.

2. Research Method and Results

Cancerous tumour cells contain special substances (antigens) that cause a strong immune reaction in most people. This reaction consists in the production of T-lymphocytes that attack and destroy cancerous tumour cells.

We operate with such variables as (in all cases, we mean the size of the named cell population)

- T_l are free T-lymphocytes on the surface of the cancerous tumour;
- c are cancer cells inside the cancerous tumour and on its surface;
- c_s are cancer cells on the surface of the cancerous tumour;
- $\bar{c}_s$ are cancer cells on the surface of the cancerous tumour not bound by T-lymphocytes (free cancer cells on the surface of the cancerous tumour);
- $\bar{c}$ are cancer cells inside the cancerous tumour and on its surface not bound by T-lymphocytes (free cancer cells inside the cancerous tumour and on its surface).

Let us take T_l and c as the main variables.

The interaction of cancer cells with T-lymphocytes occurs only on the surface of the cancerous tumour. Thus, it is obvious that free cancer cells inside the cancerous tumour and on its surface ($\bar{c}$) are the difference between cancer cells inside the cancerous tumour and on its surface (c)

and cancer cells bound by T-lymphocytes on the surface of the cancerous tumour $(c_s - \bar{c}_s)$, i.e.

$$\bar{c} = c - (c_s - \bar{c}_s)$$

or

$$c = \bar{c} - \bar{c}_s + c_s. \quad (1)$$

Let us assume for simplicity that the cancerous tumour has a ball-like shape.

Suppose that the ball-like shape of the cancerous tumour does not change. Therefore,

$$c = \rho V = \rho \left(\frac{1}{6} \pi D^3 \right),$$

$$c_s = \rho_s S = \rho_s (\pi D^2)$$

whence

$$D^2 = \frac{c_s}{\pi \rho_s}, \quad (2)$$

$$\sqrt[3]{c} = \sqrt[3]{\frac{1}{6} \pi \rho D},$$

$$\left(\sqrt[3]{c} \right)^2 = \left(\sqrt[3]{\frac{1}{6} \pi \rho} \right)^2 D^2$$

whence

$$D^2 = \frac{\left(\sqrt[3]{c} \right)^2}{\left(\sqrt[3]{\frac{1}{6} \pi \rho} \right)^2}. \quad (3)$$

Taking into account formulas (2) and (3), we write

$$\frac{c_s}{\pi \rho_s} = \frac{\left(\sqrt[3]{c} \right)^2}{\left(\sqrt[3]{\frac{1}{6} \pi \rho} \right)^2}$$

whence

$$c_s = \frac{\pi \rho_s}{\left(\sqrt[3]{\frac{1}{6} \pi \rho}\right)^2} \left(\sqrt[3]{c}\right)^2$$

or

$$c_s = P \left(\sqrt[3]{c}\right)^2 \quad (4)$$

where

$$P = \frac{\pi \rho_s}{\left(\sqrt[3]{\frac{1}{6} \pi \rho}\right)^2},$$

ρ is the density of cancer cells, ρ_s is the surface density of cancer cells, V is the volume of the cancerous tumour, S is the surface area of the cancerous tumour, D is the diameter of the cancerous tumour.

We recall that the interaction of cancer cells with T-lymphocytes occurs only on the surface of the cancerous tumour. Not all cancer cells fall under the action of T-lymphocytes. Therefore, only in some cases, when a free cancer cell and a free T-lymphocyte meet, binding occurs.

It is obvious that

- the more cancer cells c_s are, the more free cancer cells $\bar{c}_s$ are;
- the more bound cancer cells $(c_s - \bar{c}_s)$ and T-lymphocytes are, the fewer free cancer cells $\bar{c}_s$ are.

Then we assume that on the surface of the cancerous tumour the following relation is true:

$$\bar{c}_s = k \frac{c_s}{(c_s - \bar{c}_s) T_l} \quad (5)$$

where k is some constant, and we substitute the value c_s from equation (4).

From formula (1), it follows that

$$\bar{c} = c + \bar{c}_s - c_s \quad (6)$$

where we substitute the values $\bar{c}_s$ and c_s from equations (5) and (4).

From equations (5) and (6), it follows that T_l and c can be taken as main variables.

Consider the relation $\frac{dT_l}{dt} / T_l$ where t is time. Then $\frac{dT_l}{dt}$ is the rate of T-lymphocyte production.

We assume that the value $\frac{dT_l}{dt} / T_l$ for the population of T-lymphocytes consists of two summands:

1. the constant value of the mortality rate γ_1 ;
2. the level of stimulation $\beta_1 \bar{c}_s \left(1 - \frac{T_l}{T_l^{max}}\right)$.

The expression 2) shows that

- $\left(1 - \frac{T_l}{T_l^{max}}\right) \rightarrow 1$ as $T_l \rightarrow 0$. Then stimulation of free T-lymphocytes increases linearly with the increase of $\bar{c}_s$,
- there exists the maximum population size $T_l = T_l^{max}$. Then the level of stimulation becomes zero.

It is obvious that the greater the constant value of the mortality rate γ_1 is, the smaller the ratio of the rate of production of T-lymphocytes to their number $\frac{dT_l}{dt} / T_l$ is. The greater $\bar{c}_s \left(1 - \frac{T_l}{T_l^{max}}\right)$ is, the greater the ratio of the rate of production of T-lymphocytes to their number $\frac{dT_l}{dt} / T_l$ is.

Thus, T_l satisfies the following dynamic differential equation

$$\frac{dT_l}{dt} / T_l = -\gamma_1 + \beta_1 \bar{c}_s \left(1 - \frac{T_l}{T_l^{max}}\right)$$

or

$$\frac{dT_l}{dt} = -\gamma_1 T_l + \beta_1 \bar{c}_s T_l \left(1 - \frac{T_l}{T_l^{max}}\right). \quad (7)$$

When $\bar{c}$ increases, then $\frac{dc}{dt}$ increases, and when $\bar{c}_s$ and T_l increase, then $\frac{dc}{dt}$ decreases.

Thus, we define the growth rate of the cancer cell population by the following dynamic differential equation

$$\frac{dc}{dt} = \gamma_2 \bar{c} - \beta_2 \bar{c}_s T_l. \quad (8)$$

The first element of the right-hand side of the differential equation (8) describes the growth of the cancerous tumour that is not being attacked by T-lymphocytes.

The second element of the right-hand side of the differential equation (8) takes into account the interaction of free T-lymphocytes with free cancer cells on the surface of the cancerous tumour.

Let us rewrite dynamic differential equations (7) and (8) in the form of the following system

$$\begin{cases} \frac{dT_l}{dt} = -\gamma_1 T_l + \beta_1 \bar{c}_s T_l \left(1 - \frac{T_l}{T_l^{max}} \right), \\ \frac{dc}{dt} = \gamma_2 \bar{c} - \beta_2 \bar{c}_s T_l \end{cases} \quad (9)$$

where $\gamma_1, \gamma_2, \beta_1, \beta_2$ are positive parameters and values $\bar{c}_s, \bar{c}$ are substituted into the obtained system of dynamic differential equations (9) from equations (5) and (6).

3. Conclusions

Thus, mathematical investigation of change in the size of the cancerous tumour under the conditions of the body's immune response is performed.

When the cancerous tumour is attacked by T-lymphocytes, its cancer cells are destroyed. Then, under certain conditions, the cancerous tumour shrinks. This process is described by the system of dynamic differential equations (9) constructed in this research.

Under some conditions, the solutions of this system of dynamic differential equations (9) will show a decrease in the size of the cancerous tumour over time until its complete disappearance. This is proved in many cases during the treatment of cancer patients with immunotherapy for some types of cancer by laureates of the Nobel Prize James P. Allison and Tasuku Honjo.

Note, that the dependence of the diameter D of the cancerous tumour on the size c of the population of cancer cells inside the cancerous tumour and on its surface is given in Eq. (3). The size c is determined from the system of dynamic differential equations (9).

Thus, this mathematical research makes it possible

- to analyze the process of changing the size of the cancerous tumour when cancer cells are being attacked by T-lymphocytes;
- to determine under what conditions T-lymphocytes will destroy the cancerous tumour.

Therefore, this mathematical research is important and relevant. It contributes to the possibility of overcoming cancer diseases that are the cause of death of a large number of patients worldwide.

4. Declarations

On behalf of the author of this article, the corresponding author states that there is no conflict of interest.

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