Zeno Effect (Frequent Inhibition of the Effector Cells Regulators) in Cancer Therapy

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Recently Brutovsky and Horvath suggested a strategy of the pure evolutionary self-destroying of the cancer without any active medical treatment. In this work we suggest a completely opposite strategy for cancer inhibition and eventually elimination. It is based on the frequent (many times repeated) application of an especial active medical treatment. This treatment represents such inhibition of the regulator cells (Th_1, Th_2, …) which causes hyper-activity of the effector cells (citotoxic limfocits, nature killer cells, …) that eliminate cancer cells (dirty inspector Harry effect). Conceptually, our strategy is similar to Zeno effect theoretically predicted and experimentally verified in the quantum mechanics (but which can be realized in practically any domain of the physics). According to Zeno effect a non-stable system, evolving during time from initial non-decayed to the final decayed state, can never decay by frequent (many times repeated) perturbation by measurement (representing an active evolution breaking treatment).

1. Introduction

Brutovsky and Horvath [1] suggested recently an original strategy against cancer diseases. They started, on the one hand, from unambiguous fact that the active medical treatment (chirurgic treatment, radiation or chemo-therapy) in the late phase of the disease can often cause late accelerated disease expansion instead of disease inhibition. In this sense active medical treatment behaves like a penalty function. On the other hand Brutovsky and Horvath supposed that the cancer growth can be considered as a dynamical evolution of the cancer cells population. This evolution, as an optimized strategy, becomes les and les efficient during time (or, cancer cells affect the normal cells les and les efficiently) which can finally cause a complete elimination of the disease.

More precisely, according to the some relevant theoretical analyses [2], [3] on the carcinogenesis Brutovsky and Horvath suggested an abstract theoretical mechanism "keeping in mind an eventual therapeutic application" and "focus on those aspect of evolutionary optimization which decrease or inhibit efficiency of the optimization process", even if "strict adherence to the optimization framework has lead us to counterintuitive implications" on the active medical treatment as penalty function. Thus, Brutovsky and Horvath suggested a strategy of the pure evolutionary self-destroying of the cancer without any active medical treatment.

In this work we shall suggest a completely opposite strategy for cancer inhibition and eventually elimination. It is based on the frequent (many times repeated) application of an active medical treatment. This treatment represents such inhibition of the regulator cells (Th_1, Th_2, ...) which causes super-activity of the effector cells (citotoxic limfocits, nature killer cells, …) that eliminate cancer cells (dirty inspector Harry effect). It represents further development of our previous ideas and observations [4] on the opposite functioning of the cancer and hyper-immune diseases, e.g. multiple sclerosis. Conceptually, our strategy is similar to Zeno effect theoretically predicted [5] and experimentally verified [6], [7] in the quantum mechanics, but which can be realized in practically any domain of the physics [8]. According to Zeno effect a non-stable system, evolving during time dynamically from initial non-decayed to the final decayed state, can never decay

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by the frequent (many times repeated) perturbation of the dynamics by the measurement (representing an active dynamical evolution breaking treatment).

2. Zeno effect (frequent inhibition of the effector cells regulators) in cancer therapy

Brutovsky and Horvath strategy against cancer can be simplify presented by the following population dynamics equation

(1) $dp/dt = (a\text{-}bt)p$

with simple solution

(2) $p = p_0 \exp[at\text{-}bt^2/2]$.

Here p represents the cancer cells population in the time moment t, p_0 - initial cancer cells population, a – time independent cancer cells population growth parameter, and, bt – linearly time dependent cancer cells population decrease "parameter". It can be considered that growth parameter a is characteristic for the type of the cancer cells and the type of the human individuals organs affected by cancer cells. Also, it can be considered that decrease "parameter" bt refers on the decrease of the cancer cells attack efficiency (caused by mutation by cancer cells) only.

It is not hard to see that the cancer cells population (2) grows up till time moment

(3) $T = 2a/b$

after which the given population decreases toward zero (tends toward zero in limit when t tends toward infinity). It means that for t significantly larger than T cancer cells realize a complete self-destruction.

Also, according to (2), for two time moments t_1 and t_2 that satisfy condition $0<t_1<t_2<T$, it follows

(4) $p(t_1) < p(t_2)$.

It implies that the quick (realized in a time interval much smaller than T) reduction of the cancer cell population using some active medical treatment (e.g. chirurgic treatment, radiation or chemo-therapy) can be considered as a "time reduction" too. Formally speaking, it forbids that the time moment t become larger than T and, in this way, it forbids complete self-destruction of the cancer cells. For this reason Brutovsky and Horvath strategy needs counterintuitive complete rejection of any active medical treatment.

A possible problem of the Brutovsky and Horvath strategy is that cancer disease healing, except (2), needs a natural limitation

(5) $p \leq p_L$

where p_L represents the critical cancer cells population that almost certainly causes quick lethal effect. Also, there is practically unambiguous empirical (clinical) fact that time moment t_L corresponding to p_L is significantly smaller than T, i.e.

(6) $t_L << T$.

All this implies that in the real situations population dynamics (1) must be reduced in the form

(7) $dp/dt = ap$ for $t \leq t_L << T$

with simple solution

(8) $p = p_0 \exp[at]$ for $t \leq t_L << T$.

Obviously, in the limit when t tends toward t_L, p tends toward p_L corresponding to lethal finish.

So, it seems that in the realistic situations we must use cancer cells population dynamics described by Eq. (8).

A possible strategy against the cancer disease with population dynamics (8) holds, firstly, to the discrete reduction of p in a smaller value p_R by a fast (or discrete, i.e. with duration significantly smaller than t_L) and strong (with high affectation at cancer cells and somewhat smaller affectation at normal cells) active medical treatment. Given treatment is realized by the external (without human individual physiology domain), physical or chemical means (e.g. chirurgic intervention, radiation or injected chemo-therapy). This strategy holds additional continuous (during complete time of the cancer cells population evolution) reduction of a in a smaller value a_R by a not so strong, active medical treatment. Given treatment (with not so high affectation at cancer cells and somewhat smaller affectation at normal cells) is realized by the external (without human individual physiology domain), physical or chemical means (e.g. oral chemo-therapy) too.

Basic problem for mentioned strategy is, of

course, its strong character. Namely, for strong affectation at the normal cells, not only cancer, strong active treatment can be applied only in a small time interval, i.e. quickly. In the opposite case given treatment itself can cause hard consequences including patient dead. For this reason time interval necessary for reveal of the normal cells before eventual repetition of strong treatment can be too large in sense that it can admit a successful growth of cancer cells by means of their population dynamics. On the other hand, continuous, not so strong active treatment (oral chemo therapy), because of its no so strong character (i.e. limited efficiency), cannot reduce a in a smaller value a_R in sufficiently satisfactory way.

All mentioned needs a new strategy with active treatment realized by internal (within human individual physiology domain) means. Namely, simply speaking, cancer originates when few cancer cells, by developing a mimicry, becomes unrecognizable (as the defect cells) for effector cells (citotoxic limfocits, nature killer cells, …). Then effector cells cannot destroy given cancer cells which continue to reproduce rapidly. There are many attempts of the stimulation of effector cells for a more sophisticated recognition and elimination of the cancer cells as defect cells. It, in fact, represents an attempt for anti-cancer vaccine development. But, it seems that anti-cancer vaccine must be developed by any human individual, after the moment when cancer start to grow. It implies that today, by existing physical, chemical and medical technology, such individual anti-cancer vaccine can be developed during the relatively large time interval comparable with t_L (There is opinion that individual anti-cancer vaccine developing time can be much smaller in the near future after more successful application of nano-technology in medicine.)

All mentioned facts imply that there is no sufficiently satisfactory strategy against cancer disease today.

Nevertheless, we shall suggest an original strategy against cancer disease that can be useful in at least some situations.

Consider a small time interval τ at end of which, i.e. in time moment τ, cancer cells population (8) can be linearly approximated by

(9) $p = p_0 (1 + a\,\tau)$ for $a\,\tau << 1$ and $\tau << t_L$.

Suppose that in the same moment a fast (for time interval significantly smaller than τ), internal active treatment action (whose nature will be discussed latter) can be realized.

Suppose that given treatment reduces p into kp so that $k(1 + a\,\tau)$ is smaller than 1, i.e.

(10) $k(1 + a\,\tau) < 1$ for $a\,\tau << 1$.

Or, by given treatment, cancer cells population (9) turns out discretely in

(11) $p_R = p_0\, k(1 + a\,\tau) < p_0$ for $a\,\tau << 1$.

On the other hand these half-strong character of given treatment means that after application of given treatment normal cells reveal occurs during a time interval τ.

It means that n times repeated given fast, half-strong, internal active treatment with period τ yields the following cancer cells population

(12) $p_{Rn} = p_0 (k(1 + a\,\tau))^n < p_0$ for $a\,\tau << 1$

where n represents a natural number 1, 2, … . Obviously, (12) tends toward zero when tends to be very large, or, formally

(13) $\lim_{n\to\infty} p_{Rn} = 0$ for $a\,\tau << 1$.

But, really, n can be relatively small if $k(1 + a\,\tau)$ is relatively small too. For example, for $k(1 + a\,\tau) = 0.8$ and n=10 it follows $p_{Rn} \approx 0.1\, p_0$ that represents a very satisfactory result.

It can be seen that described fast, half-strong treatment conceptually corresponds to Zeno effect, theoretically predicted [5] and experimentally verified [6], [7] in the quantum mechanics, but existing in practically any domain of the physics [8].

Meanwhile, there is a principal question what really can represent mentioned fast, half-strong treatment from the point of view of physiology. We shall suggest a possible answer on this question.

In our previous work [4] it has been observed that cancer and auto-immune diseases, e.g. multiple sclerosis, act, in some sense, oppositely. It implies that a mechanism similar to auto immune disease

functioning can be used for fast, half-strong treatment.

Concretely, suppose that system for effector cells regulation, precisely suppression is inhibited by an external chemical influence during a small time interval τ_{inh} many times smaller than τ. It will cause hyper-activity of the effector cells (which will be called metaphorically dirty inspector Harry effect) that internally, i.e. as the part of human individual physiology, attack all cells, normal and cancer. There is a probability that such attack can do larger damage cancer cells than normal cells.

Suppose further that after τ_{inh} inhibition of the suppression cells is stopped, i.e. that after normal activity of the suppression cells is restored during next time interval τ.

It can be added that during time interval τ suppression cells can be additionally activated by external chemical simulation. It causes additional suppression of the effector cells activity which, maybe, can make the mimicry mechanism by cancer cells passive. Then, by suppression cells inhibition and effector cells hyper-activation during τ_{inh}, elimination of the cancer cells can be more efficient. In other words, we suppose that here the analogy with therapy against chronic hepatitis B maybe exists. Namely, in some cases, before medicament therapy against chronic hepatitis B, during a time interval there is an external chemical suppression of all immune processes in the human organism. After given suppression medicament therapy becomes more efficient.

Finally, suppose that this alternation of the regulator cells inhibition and normal activity is repeated many, i.e. n times, where n represents a relatively large natural number.

In this way we obtain a concrete model of the fast, half-strong, active internal treatment against cancer disease.

3. Conclusion

In conclusion we can shortly repeat and point out the following. Recently Brutovsky and Horvath suggested a strategy of pure evolutionary self-destroying of the cancer without any active medical treatment. In this work we suggest a completely opposite strategy for cancer inhibition and eventually elimination. It is based on the frequent (many times repeated) application of an especial active medical treatment. This treatment represents such inhibition of the regulator cells (Th_1, Th_2, …) which causes hyper-activity of the effector cells (citotoxic limfocits, nature killer cells, …) that eliminate cancer cells (dirty inspector Harry effect). Conceptually, our strategy is similar to Zeno effect theoretically predicted and experimentally verified in the quantum mechanics (but which can be realized in practically any domain of the physics). According to Zeno effect a non-stable system, that during time evolves from initial non-decayed in the final decayed state, can never decay by frequent (many times repeated) perturbation by measurement (representing an active evolution breaking treatment).

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