Dynamics of cancer cells in HIV-infected patients for distinct immune responses

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Abstract. Patients infected with the human immunodeficiency virus (HIV) are more prone to develop certain types of cancer, than healthy people. These cancers define the final stage of HIV infection, and are known as acquired immunodeficiency syndrome (AIDS)-related cancers. Kaposi sarcoma, non-Hodgkin lymphoma (NHL), and invasive cervical carcinoma are included in this set. We propose a within-host model for the dynamics of AIDS-related cancers, under distinct immune responses, and varying treatments' efficacies for HIV and cancer. In immune function f_1, the cytotoxic T cells (CTLs) proliferate as a function of CTLs and infected CD4 T cells. In the other, f_2, CTLs proliferation rate is also dependent on their expansion. Numerical results show distinct trends of the cells' population and viral load, as the immune response is varied. Immune function f_1 seems more effective, having advantage in a more visible reduction of the viral load and the number of cancer cells.

Introduction

HIV is a retrovirus that destroys the body's immune system, by targetting the helper CD4$^+$ T cells. Cancer consists in an abnormal growth of cells, that divide disorderly, and invade and destroy normal body tissue. Cancer prevention is one of the biggest health challenges of the 21st century, apart from the new COVID-19 pandemic. People infected with HIV are predisposed to develop AIDS-related cancers. Antiretroviral therapy (ART) and highly antiretroviral therapy (HAART) have brought hope to HIV-infected patients, since late 20th century, by suppressing the HIV virus load and preventing the progression of HIV disease to AIDS. This has contributed to lower AIDS-related cancers' incidences, nevertheless, they remain high. As such, accurate and deeper information on the joint dynamics of cancer cells and HIV in the human body is needed. Suitable mathematical models can be useful [1, **?**]. With these ideas in mind, we developed a within-host model to analyse the interplay between cancer cells growth and HIV viral load.

The proposed model

The proposed compartmental model is divided in five cell populations: cancer cells, $C(t)$, healthy CD4$^+$ T cells, $T(t)$, infected CD4$^+$ T cells, $I(t)$, and HIV, $V(t)$, and cytotoxic T lymphocytes, $E(t)$. Cells and virus move between compartments according to the following rules. All cells have a growth rate, corresponding to the positive factors on the right side of the differential equations. Cells' and virus death rates are represented by μ_i. Chemotherapy is modelled by terms $P_j\left(1 - e^{-D(t)}\right)$, and ART efficacy by $(1 - e_1)$. where $i = 1, 2$ and $u(t) = 2.3869$, for $t = 21n$, $n \in \mathbb{N}$, and $u(t) = 0$, otherwise.

$$
\begin{aligned}
C'(t) &= r_1\left[1 - \left(\frac{C(t)}{C_0}\right)^{1/4}\right]C(t)^{3/4} - k_1 T(t)C(t) - \\
&\quad - P_C\left(1 - e^{-D(t)}\right)C(t), \\
T'(t) &= \lambda + T(t)\left[-pk_1 C(t) - k_2(1 - \epsilon_{RT})V(t) - \right. \\
&\quad \left. - P_T\left(1 - e^{-D(t)}\right) - \mu_T\right], \\
I'(t) &= k_2(1 - \epsilon_{RT})T(t)V(t) - P_T\left(1 - e^{-D(t)}\right)I(t) - \\
&\quad - \mu_I I(t) - k_0 I(t)E(t), \\
V'(t) &= N\mu_I(1 - \epsilon_P)I(t) - \mu_V V(t), \\
E'(t) &= f_i(I, E) - \mu_E E(t), \\
D'(t) &= u(t) - d_D D(t)
\end{aligned}
\tag{1}
$$

Discussion and Conclusions

The figure below depicts the response of the model (1) for two values of the transmission rate, k_2, and the two immune functions, f_1 and f_2. Higher values of k_2 ignite a more powerful immune response. Moreover, for function f_1 for the is observed a periodic behaviour, preceded by a Hopf bifurcation. For function f_2 is shown an increase in the number of cancer cells with k_2. The immune system response is crucial to fight HIV and prevent cancer progression. The two chosen immune functions reveal intriguing dynamics. Conclusions may aid clinicians adjust treatment efficacy for real patients.
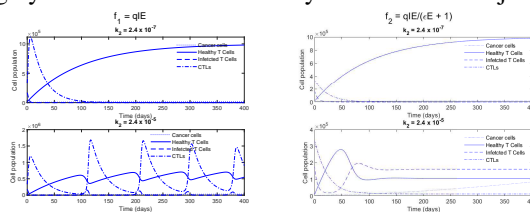
References

[1] Carvalho, A. R., & Pinto, C. M. (2018). New developments on AIDS-related cancers: The role of the delay and treatment options. Mathematical Methods in the Applied Sciences, 41(18), 8915-8928.