Mathematical modeling of Chronic Myeloid Leukemia

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Abstract

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The Chronic Myeloid leukemia (CML) is a blood cancer attributed to mutations in the white blood cells. The leukemic cells tend to proliferate rapidly and to have better survival capacities than healthy cells. Since the immune system plays an important role in the long term response, we develop a model which describes the interactions of the leukemic cells with the immune.

Based on a model of ODE that was developed by Apollos Besse [1] during his PhD, we constructed a system of PDEs structured in maturity in order to describe the dynamics of differentiated leukemic cells in a continuous way. The purpose of this work was primarily to see if the PDE model can better describe the real distribution of differentiated cells and do the stability analysis.

The model is based on a non-monotonic immune response. At low levels, immune response increases with the tumor load whereas for high levels tumor is suppressing the effect of immune response (immunosuppression). In particular, under certain hypothesis, immune response grows fast at intermediate levels (in the 'immune window').

In an ODE framework, the equilibrium points where classified according to the concentration of 'mature' cells (differentiated non-stem leukemic cells). It has been established that the generic situation is the following :

1. One disease free steady state (unstable).
2. One low level steady state (under the immune window) (stable).
3. Several (or none) steady state above the immune window (with alternated stabilities, the highest being stable).

With the PDE model we also find a stable healthy equilibrium point and the structure of the high equilibria is preserved. This means that whenever they exist, their stability is alternated, the highest one being stable. On the other hand, for the low equilibrium point the stability is not guaranteed. There are cases where this point is stable and others where stability is perturbed. The aim is to find conditions on parameters that entail stability to investigate the robustness of the stability result.

References

[1] Apollos Besse, Geoffrey D.Clapp, Samuel Bernard, Frank E.Nicolini, Doron Levy,Thomas Lepoutre *Stability analysis of a Model of Interaction Between the Immune System and the Cancer Cells in Chronic Myelogeneous Leukemia*