Mathematical model of T-cell lymphoblastic lymphoma: disease, treatment, cure or relapse of a virtual cohort of patients

Nathalie Eymard[*1]

[1]Lyon 1, UMR CNRS 5558, Laboratoire de Biométrie et Biologie Évolutive (LBBE) – Université Claude Bernard (Lyon 1) – France

Résumé

T lymphoblastic lymphoma (T-LBL) represents around 25% of all Non-Hodgkin Lymphoma (NHL) in children and is considered as a rare disease. Most patients with T-LBL typically present with mediastinal tumor. T-LBL starts in the thymus and causes an increase in its volume. The thymus is an important organ in the development of the immune system in very young children. Its action becomes negligible in adults. The cells causing tumors possess genetic lesion that promotes their proliferation and blocks their differentiation.

This work focuses on the development and the treatment of a T-LBL over a period of two years. This is the interval required to study the onset of the disease, the treatment of the acute phase and the maintenance treatment. Indeed, the therapy of T-LBL is rather long with its total duration of 24 months in most protocols including induction, consolidation and maintenance therapy. After or during the treatment, patient can be cured or relapsed. Median time of relapse is one year after complete remission (range 0.2-5.9 years).

The aim of this study is to assess the possibility to reduce the treatment duration in order to reduce its toxicity, without increasing the number of relapses. The possible reduction is applied to pairs of virtual patients simulated with a mathematical model. One patient receive chemotherapy with a short duration and an other, a long duration. Multi-Scale hybrid model is used to simulate the ontogenesis of T cells, the disease at a cellular level and the action of medications. In this model, the fate of T cell is determined by system of ordinary differential equations (intracellular regulation) and reaction-diffusion equations (extracellular regulation). To model the individual behavior of patients, the cellular level and the whole patient must be simulated. T- cells have properties (parameters) that can be inherited from the mother cells or be randomly chosen for each new cells. Cancer cells can develop resistance to treatment due to the selection and Darwinian evolution.

In the virtual population created by the model, we obtained different responses (cured or relapsed) of patients with the same dose of drug and the same duration of maintenance treatment. The number of relapses decreases (and number of healings increases) as a function of duration of "short" treatment.

Mots-Clés: Cancer, Hybrid model, T lymphoblastic lymphoma

[*]Intervenant