
Modèles hybrides et modèles PK-PD

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Résumé

Hybrid discrete-continuous models are widely used in the investigation of dynamics of cell populations in biological tissues and of organisms. This kind of model can be used to simulate cell growth and differentiation. The fate of cell is determined by intra and extra cellular regulation with intracellular proteins whose concentrations vary as a function of their micro-environment where growing factors (GF) and nutrients (an amino acid in our case) can be available.

Pharmacokinetic/pharmacodynamic (PKPD) models describe concentrations and effects of pharmaceutical drugs in human body taking into account ADME (Absorption, Distribution, Metabolism, and Excretion) profiles of chemical substances.

Both approaches can be complementary for development of anticancer drug. A new therapeutic approach based on starvation of cancer cells by an enzyme is developed by Erytech pharma. The enzyme encapsulated in red blood cells leads to the depletion of an amino acid. The effect of the enzyme can be controlled by supplementation with its co-factor, the B6 vitamin. PKPD modeling allows to choose doses of B6 and of the enzyme, and B6 posology. Preclinical data for mice has been provided by Erytech and allowed to assess the parameters of the model. The extrapolated to humans' model will be used to improve the design of randomized clinical trial. Simulation of a solid tumor and of its regression after the treatment will be carried out by simulation of the amino acid dependency of cancer cells.

Mots-Clés: PKPD, anticancer drugs, simulation

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