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Physiological modelling of neutrophil development guides regimen optimisation during chemotherapy

Chemotherapeutic regimens are toxicity-limited due to the uncontrolled anti-mitotic effects on healthy cells, including the blood cells. Acute neutropenia, brought on by the destruction of neutrophils by chemotherapy, necessitates future lower doses and/or complete cessation of the protocol until the absolute neutrophil count (ANC) returns to acceptable levels. To counteract declining ANCs, granulocyte colony-stimulating factor (G-CSF) is administered following chemotherapeutic agents to recover neutrophils by stimulating their differentiation from the hematopoietic stem cells (HSCs), their proliferation, and the speed of their maturation. Through mathematical modelling and analysis, several authors have proposed dose-adaptation regimens for the concurrent administration of chemotherapeutic agents and G-CSF. In this talk, I will discuss a completely physiological model for granulopoiesis which is used to study the concomittant administration of Zalypsis and G-CSF and the optimisation of chemotherapeutic regimens resulting from our work. Further, I will demonstrate how this DDE model, derived from an age-structured PDE model with variable aging rate, also serves as the basis of the refinement of the pharmacokinetic model of G-CSF.