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Mathematical Modelling of Azacitidine Resistance in Myelodysplastic Syndrome Patients

Myelodysplastic syndrome (MDS) is a group of cancers in which blood cells do not fully mature. A standard chemotherapy for MDS is azacitidine, which has a poorly understood mechanism and many patients ultimately develop resistance to the drug. The dynamic interaction between MDS clones and the non-diseased hematopoietic stem cells, as well as multiple coupled feedback loops within the haematopoietic systems makes identifying the mechanism of disease progression, typically to leukemia, very difficult. We use a compartment model of the haematopoietic system, fit to each patient's blood test measurements using Kalman filtering, to understand disease progression and azacitidine's mechanism. We show how different natural histories of disease can be explained by changes in model parameters over time. This work is a collaboration with Roman Shapiro at the Dana-Farber Cancer Institute and is an excellent example of how clinical data can be used to understand a disease in-vivo.