Potential sources of drug resistance during Imatinib treatment of CML

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There are various models for the interaction between Imatinib, and chronic myelogenous leukaemia (CML). However, the role of the host immune response during Imatinib treatment remains unclear. Based on experimental data from the Lee Lab at Stanford Medical School, we hypothesize that Imatinib gives rise to a brief anti-leukaemia immune response as patients enter remission.

From this hypothesis, we propose that cancer vaccinations applied at appropriate times during Imatinib treatment can boost the existing immune response and lead to a sustained remission or a potential cure. To examine this hypothesis, we take a mathematical model by Michor et al. based on the analysis of 169 patients under Imatinib and incorporate an anti-leukaemia immune response.

Using this model, we study how the effects of Imatinib resistance and immune resistance mutations of leukaemia cells may affect the dynamics and duration of leukaemia remission during treatment. We propose that Imatinib resistance mutations may be partially compensated by a persistent, low-level anti-leukaemia immune response. Thus, we hypothesize that immune resistance is the primary cause of treatment failure.

Taking into account Imatinib resistance and immune resistance mutations, we show how properly timed cancer vaccines may optimally sustain the host immune response to lessen the effects of mutation and potentially reduce or eliminate residual leukaemia cells.