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USING COMPUTATIONAL APPROACH FOR OPTIMIZING THROMBOPOIETIN TREATMENT EFFECTS - PROOF OF CONCEPT IN MURINE EXPERIMENTS

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Until recently, drug schedules have been selected by a method of "trial and error" alone. Aiming to replace this method by a more formal approach a mathematical model of murine thrombopoiesis was constructed, which was then implemented in computer simulations. This model succeeds in reproducing bone marrow dynamics and platelet count changes in the periphery. The effects of Thrombopoietin administration were introduced into this model, which proved to be capable of retrieving published experimental results of TPO. With the aid of this biomathematical tool, Thrombopoietin administration protocols have been identified, yielding efficacious clinical results with a significant reduction in the total dose.

The current work aims at prospectively validating the concept of using mathematical methodologies for selecting improved drug protocols and, in particular, those of hemopoietic growth factors such as thrombopoietin. In the present experiments mice treated by a previously tested recombinant-murine-Thrombopoietin administration protocol received a single dose of Thrombpoietin, which is reported in literature to yield a significant rise in platelet counts. In the model recommended schedule mice received 45% of the previous total dose, under different dosage and timing regimen. The results, whose averages are displayed in the figure below, show that the two groups of mice achieved statistically similar platelet profiles, with essentially identical peaks.Our results pinpoint the role of rational and quantitative methods in protocol selection, thus saving time and money, and leading to improved and inexpensive patient care.

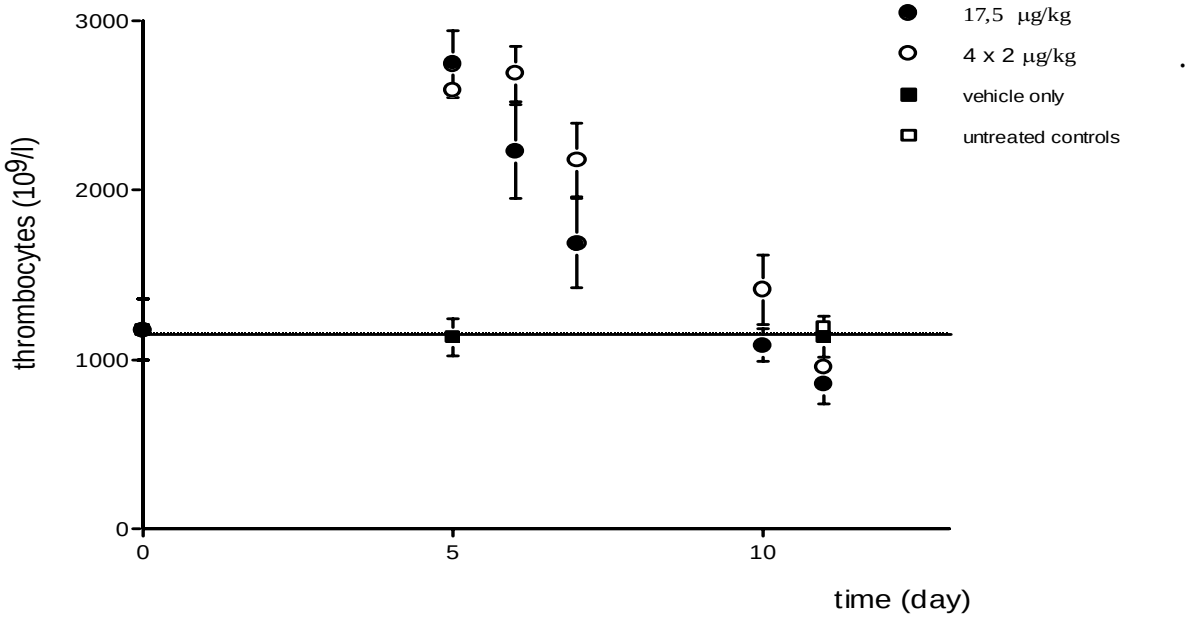

Figure: Thrombocyte counts of the study groups.