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Epo and EpoR signaling dynamic in hematopoietic and tumor context

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Lung carcinoma is the most frequent cause of death in cancer. The current therapeutic approaches cause anemia, reducing the therapeutic response and the quality of life in patients. In order to correct this, recombinant human erythropoietin (rhEpo) has been widely used to reestablish normal levels of erythrocytes. But, EpoR expression has been found in tumor cell lines and primary cancers. Furthermore, several clinical trials have associated Epo treatments with cancer progression. Due to the referred studies, the administration of Epo to the cancer patients is still under discussion.

In order to clarify the potential role of Epo in a tumor context, we combined mathematical modeling with quantitative data from NSCLC (non Small Cell Line Carcinoma) and hematopoietic cells. For this purpose we firstly screened NSCLC cells for significant levels of EpoR mRNA (by RT-PCR) and EpoR protein expression (by quantitative IB and MS). Later on, we characterized the dynamic of EpoR activation, Epo depletion and the subsequent signaling of JAK-STAT pathway in NSCLC cells (by quantitative IB and ELISA). Two ordinary differential equation models have been calibrated with the EpoR-transduced Baf3 (mouse hematopoietic cell line) and with the CFU-E (mouse Colony Forming Unit Erythroid). The first model describes the EpoR dynamic, and the second model describes the JAK2-STAT5 signaling upon Epo stimulation. These two models enable us to compare and define the dynamic of Epo/EpoR interaction and signaling activation, in hematopoietic and tumor context. Based on model predictions, we hypothesize sensitive and safe range of Epo concentrations that induce erythropoiesis but do not activate the NSCLC cells.