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Mathematical model of lymphoma as a failure in maintanance of naïve T cell repertoire

We introduce a stochastic model of lymphoma based on the model of the competitive exclusion between different clonotypes in the maintenance of the naïve T cell repertoire [1,2]. Two clonotypes of T cells compete with each other and with other clonotypes for survival stimuli provided by professional cells (APCs) [3,4]. We assume that one of the clonotypes is normal and the other is tumorous. We model the competition as a continuous-time bivariate Markov process [5]. To model the evolution of the tumorous clonotype we introduce an augmented rate of influx of new naïve T cells, descendants of mutated stem cells, from the thymus. We obtain a deterministic approximation to the stochastic model using Van Kampen's large N expansion technique [6] and analyse four cases of competition between the two clonotypes of T cells, both analitically and numerically.

We obtain two possible scenarios, depending on the values of parameters: either both clonotypes survive in the repertoire or the clonotype of the normal T cells becomes extinct, meanwhile the clonotype of the tumorous T cells is maintained, after achieving some maximum level of growth. We show that if the income of the new T cells from the thymus is augmented, then the tumorous clonotype, which is very competitive, would never be removed from the repertoire; meanwhile the normal clonotype could become extinct if it was not specialized enough to compete effectively for survival stimuli. This result supports the hypothesis of mutated stem cells as the origin of cancer, in particular lymphoma. Any of these cells might initiate an outbreak of the illness, so as long as we do not entirely get rid of all the mutated stem cells, we can not successfully defeat lymphoma.

References

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