

Mathematical modelling of the CD8⁺ T cell immune response to heterogeneous tumours

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The number of sub-populations generating a tumour, as well as the immunogenicity of tumour cells are two major components of intra-tumour heterogeneity (ITH) and play a key role in the immune response against solid tumours ([2, 3]). Mathematical models allow to separate these two components and investigate their effects on tumour aggressiveness independently or together, evaluating their influence on anti-tumour immunity in a controlled manner. We present a spatially individual-based model that takes into account different degrees of tumour heterogeneity, and effectively captures the way it affects the anti-tumour immune response, [1]. Tumour cells are characterized by different antigen profiles and a level of antigen presentation. In our model, ITH can vary with the number of antigens (*i.e.* the number of sub-populations) and with the level of antigen presentation (*i.e.* the immunogenicity of the cells). Computational simulations show that both components play a role in the anti-tumour immune response. First, the number of sub-populations generating the tumour correlates with the ability of the immune system to produce an efficient response. Then, the fraction of non-immunogenic cells within the tumour can significantly reduce the effectiveness of the immune response.

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- [3] Y. Wolf, et al. *Uvb-induced tumor heterogeneity diminishes immune response in melanoma*. *Cell*, **179**(1), 219–235, 2019.