The T-cell repertoire as a biomarker for response to anti PD-1 immunotherapy in a GBM mouse model

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The prediction of patients' response to checkpoint immunotherapy is currently imprecise. Here, we show that a measurement of the T-cell repertoire, from peripheral blood of mice, is enough to predict which mice would or would not respond to anti-PD1 treatment. To show this, we used a syngeneic orthotopically implanted CL261 glioma-bearing mouse model. We followed the mice over the timeline of tumor implantation and checkpoint immunotherapy, with blood samples on days 0, 7, 21, 35, 49, and 63. Since the (syngeneic) implanted tumor is bioluminescent, we were able to monitor tumor size using bioluminescence imaging (up to 9 measures, 1 measure per week), up to day 63 post-tumor inoculation. We then produced more than 130 T-cell receptor libraries for the alpha and beta chains and sequenced the libraries to produce a data set of the dynamics of the T-cell repertoire during tumor progression and during response to treatment. In this model, only 30% of animals respond to treatment, which allowed us to look at the repertoires of two distinct groups: responders and nonresponders. Using machine learning, we were able to build a model that allows us to tag, in a validation set, responders and nonresponders, thereby predicting response.