510 A PD-L1 REPORTER CELL LINE BASED ON THE IMMUNE CHECKPOINT PROTEIN PROFILING OF ATCC CELL LINES FACILITATES CANCER IMMUNOTHERAPY DRUG SCREENING

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Background The success of immune checkpoint inhibitors in the treatment of various types of cancers and their continued growth in the market have driven burgeoning interests in developing more drugs in this category. However, the intrinsic complexity of the immunological models and the variable drug responses among different cancer types have become the most prominent challenges.

Methods To facilitate large scale research projects and drug discovery of immune checkpoint inhibitors, we conducted a comprehensive protein profiling of ATCC's vast portfolio of human tumor and immune cell lines for several established and novel immune checkpoint molecules. Based on this protein profiling data, we generated an immune checkpoint reporter cancer cell line with high expression of endogenous programmed death-ligand 1 (PD-L1), a highly validated target for immune checkpoint inhibitor therapeutics. The reporter system contains a gamma interferon activation site (GAS)-response element upstream of the luciferase gene, preventing luciferase expression when PD-L1 binds to programmed death-1 (PD-1) that suppresses T cell-mediated antitumor activity. In the presence of a PD-1/PD-L1 inhibitor, a luciferase expression based bioluminescent signal is produced, which can be readily detected and quantitated to evaluate the efficacy, potency, and dynamics of the inhibitor.

Results Our data showed that the bioluminescence in the reporter cancer cells increased ~ 250 folds in a dose-dependent manner in response to interferon gamma stimulation, which mimics the signaling from activated CD8+ cytotoxic T cells. The bioluminescence increased ~100 folds in response to CD8+ primary T cell-conditioned media stimulation, and up to 5 folds in response to co-culture with CD8+ primary T cells in the presence of an anti-PD-L1 blocking antibody in a dose-dependent manner. The luciferase expression and endogenous PD-L1 expression were well maintained after the cell line had reached >30 population doubling level. These results highlight the robustness and responsiveness of the reporter system for the assessment of T cell-mediated immune responses triggered by PD-1/PD-L1 checkpoint inhibitors.

Conclusions This PD-L1 immune checkpoint reporter cancer cell line yields exceptional in vitro and ex vivo assay sensitivity and reproducibility, while simplifies the complex immunological model by providing physiologically relevant expression of PD-L1, in comparison to similar assays on the market with an artificial PD-L1 overexpression system.

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