

GAS-LUC2 REPORTER CELL LINES FOR IMMUNE CHECKPOINT DRUG SCREENING IN SOLID TUMORS

¹Hyeyoun Chang, ²Kevin M Tyo*, ¹John G Foulke, ²Fang Tian, ²Luping Chen, ²Zhizhan Gu. ¹ATCC (American Type Culture Collection), Manassas, VA, USA; ²ATCC (American Type Culture Collection), Gaithersburg, MD, USA

Background Cancer immunotherapies that target immune checkpoints, such as immune checkpoint inhibitors (ICIs), antibody-dependent cellular cytotoxicity (ADCC), and antibody-drug conjugates (ADCs), have shown tremendous success in the treatment of solid tumors, including skin, lung, breast, renal, and liver cancers. However, the built-in complexity of immunological models and the variable drug responses among different cancer types have challenged the development and application of these novel immunotherapies.

Methods To facilitate large-scale drug discovery for this growing class of immunomodulators, we conducted a comprehensive cell surface protein profiling of ATCC's vast portfolio of human tumor and immune cell lines for established and novel immune checkpoint molecules as well as their binding ligands. Based on this protein profiling data, we generated three immune checkpoint reporter cell lines HCC827-GAS-Luc2 (CRL-2868-GAS-LUC2™), MG-63-GAS-Luc2 (CRL-1427-GAS-LUC2™), and NCI-H1650-GAS-Luc2 (CRL-5883-GAS-LUC2™), which endogenously express high levels of programmed death-ligand 1 (PD-L1), cluster of differentiation 155 (CD155), and B7 homolog 3 protein (B7-H3/CD276), respectively.

Results These reporter cell lines were engineered to contain a gamma interferon activation site (GAS)-response element upstream of a luciferase gene. The luciferase expression is suppressed when the relevant immune checkpoint marker on the cancer cells binds to the corresponding checkpoint protein on T cells. In the presence of a relevant immune checkpoint inhibitor, the GAS-Luc2 reporter cell senses the IFN γ from the activated T cells to produce a luciferase expression-based bioluminescent signal.

Conclusions This signal can be readily detected and quantified to evaluate the efficacy, potency, and dynamics of the checkpoint inhibitor. In addition to drug screening for immune checkpoint inhibitors, these GAS-Luc2 reporter tumor cell lines have also been demonstrated to be effective in detecting paracrine IFN γ signaling for immune checkpoint targeted ADCC drug development.

<http://dx.doi.org/10.1136/jitc-2023-SITC2023.0496>