In vitro models for screening of immune modulating properties of drug candidates under immunosuppressed conditions seen in cancer

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In vitro models are important tools in cancer research, enabling development of new drug candidates. In order to select immunological active drug candidates more efficiently, and with a strong predictive value to human studies, we have at Bioneer designed different immune in vitro models which simulate immune suppressive conditions as seen in a tumor microenvironment. These models include tolerogenic IL-10 producing dendritic cells (DC10s), dendritic cells (DCs) treated with different tumor conditioned media and M2 type macrophages. The models are optimized to induce relevant surface markers or cytokine profiles and are validated by clinically relevant reference drugs. Bioneer develops human monocyte derived DC/T cell models mimicking different disease conditions, which now includes a cancer related pathway for prediction of the in vivo effects of e.g. immune checkpoint inhibitors. DCs are key regulators of the specific responses of the immune system under both homeostasis and pathological conditions. For these reasons, DCs are attractive targets for immunomodulatory drugs. We report here that the tolerogenic DC10 model can be used to validate the effect of Pembrolizumab (targeting PD1) which activates T-cells in the presence of allogenic DC10s. Immunosuppressive conditions simulating the tumor microenvironment can also be obtained by addition of tumor conditioned media to DCs which may lead to reduced IL-12 secretion and lower stimulatory capacity of allogenic T-cells. In conclusion, the assays are relevant in pharmacological screening and discovery in relation to e.g. immune-oncology drug development.

Keywords :
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