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Development of novel chemical immune checkpoint inhibitors by targeting CMTM6/PD-L1 axis in the tumor immune microenvironment for lung cancer immunotherapy

Kangwon National University

Disease Area	***Oncology***
Product Type	Chemical-Small molecule (Immunotherapy)
Indication	Solid tumors [Primary: lung cancer, Secondary: solid tumors resistant to antibody-based immune checkpoint inhibitors (ICIs) such as pembrolizumab and atezolizumab]
Target	CMTM6
Mechanism of Action	Inhibits CTMT6 binding to PD-L1 but not CD58, leading the lysosomal PD-L1 degradation in the tumor immune microenvironment. This results in a reorganization of the tumor immune microenvironment toward anti-tumor immunity.
Competitiveness	First In Class • No CMTM6-targeted immunotherapeutic agents or drugs • Can be used as an immunotherapy for lung cancer and other solid tumors by replacing antibody-based ICIs • Combination therapy with antibody-based ICIs can synergistically enhance the antitumor efficacy of antibody-based ICIs
Development Stage	***Lead***
Route of Administration	Oral or Intravenous administration

Key Data

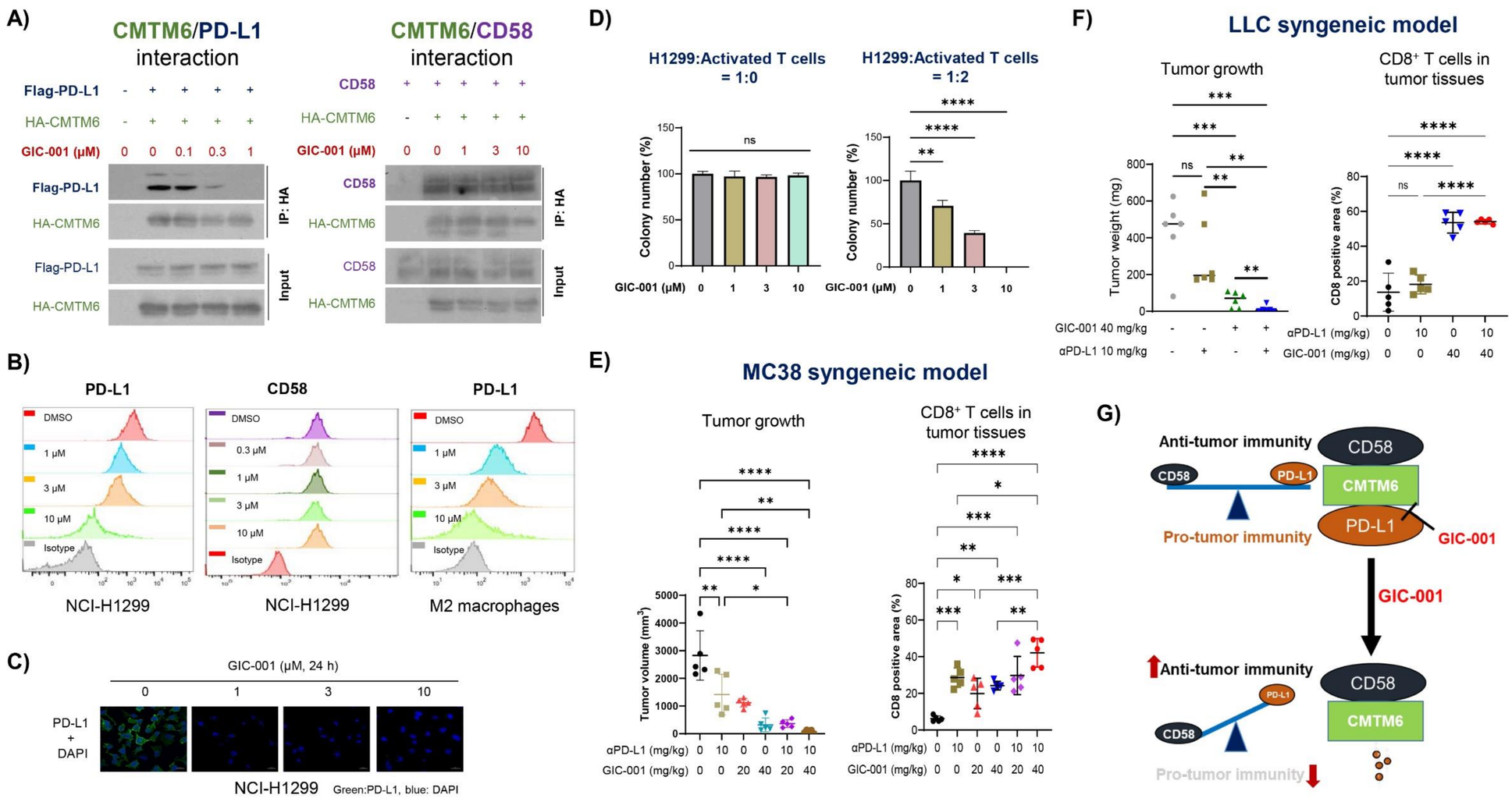

Figure legends

A) Effects of GIC-001 on the interaction of CDMT6 with PD-L1 and CD58.
B) Effects of GIC-001 on the plasma membrane expression of PD-L1 and CD58 in cancer cells and M2 macrophages (flow cytometry).
C) Effects of GIC-001 on the PD-L1 degradation (immunofluorescence)
D) GIC-001 induces CD8+ T cell-mediated cytotoxicity without exerting the cytotoxicity (colony formation assay).
E) Antitumor effects of GIC-001 on antibody-based ICB-sensitive MC38 syngeneic mouse model.