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(54) Title: INTRACELLULAR KINASE ASSOCIATED WITH RESISTANCE AGAINST T-CELL MEDIATED CYTOTOXICITY, AND USES THEREOF

(57) Abstract: The invention is based on the identification of the intracellular kinase calcium / calmodulin-dependent protein kinase ID (CAMKID) as a key checkpoint inhibitor in tumour cells mediating resistance against cytotoxic T lymphocytes (CTL). CAMKID was identified in PD-L1 refractory tumours to impair CTL-induced death receptor signalling and apoptosis via caspase inhibition. The invention offers therapeutic approaches involving impairing CAMKID immune checkpoint function by various CAMKID inhibitors, especially nucleic acid or small molecule inhibitors of CAMKID and/or treatments involving CAMKID inhibitors with death receptor agonists. The medical approaches of the invention are useful for treating subjects suffering from various proliferative disorders; preferably such proliferative disorders that are characterized by a resistance to CTL mediated immune responses, or which are refractory or resistant to treatments with other immune checkpoint therapies, such as PD1-PDL1 antagonistic treatments. Provided are the medical applications and corresponding diagnostic approaches, kits, CAMKID inhibitors and screening methods for the identification of new therapeutic agents for the treatment of proliferative disorders.



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