Interferon gamma

Interferon gamma (IFNγ) is a dimerized soluble cytokine that is the only member of the type II class of interferons.

Mainly produced by T lymphocytes, activates its corresponding receptor and plays important roles under both homeostatic and inflammatory conditions.

The existence of this interferon, which early in its history was known as immune interferon, was described by E. F. Wheelock as a product of human leukocytes stimulated with phytohemagglutinin, and by others as a product of antigen-stimulated lymphocytes or tuberculin-sensitized mouse peritoneal lymphocytes challenged with PPD; the resulting supernatants were shown to inhibit growth of vesicular stomatitis virus. Those reports also contained the basic observation underlying the now widely employed interferon gamma release assay used to test for tuberculosis. In humans, the IFNγ protein is encoded by the IFNG gene.

Oncolytic herpes simplex virus stimulate immune cells to release cytokines such as Interferon gamma (IFN-γ) during oncolysis, further improve tumor microenvironment (TME) and enhance therapeutic efficacy. IFN-γ plays vital role in the apoptosis of tumor cells and recruitment of tumor-infiltrating T cells. Zhu et al. hypothesized that oncolytic herpes simplex virus-1 (oHSV-1) enhanced the antitumor efficacy of novel CD70-specific chimeric antigen receptor (CAR) T cells by T cell infiltration and IFN-γ release. In this study, oHSV-1 has the potential to stimulate IFN-γ secretion of tumor cells rather than T cell secretion and lead to an increase of T cell activity, as well as CD70-specific CAR T cells can specifically recognize and kill tumor cells in vitro. Specifically, combinational therapy with CD70-specific CAR T and oHSV-1 promotes tumor degradation by enhancing pro-inflammatory circumstances and reducing anti-inflammatory factors in vitro. More importantly, combined therapy generated potent antitumor efficacy, increased the proportion of T cells and natural killer cells in TME, and reduced regulatory T cells and transformed growth factor-β1 expression in orthotopic xenotransplanted animal model of Glioblastoma. In summary, they revealed that oHSV-1 enhance the therapeutic efficacy of CD70-spefific CAR T cells by intratumoral T cell infiltration and IFN-γ release, supporting the use of CAR T therapy in Glioblastoma therapeutic strategies [1)].

The impact of IFN-γ on the γ-aminobutyric acid (GABA)-mediated currents in the hippocampus, a major brain region involved in the cognitive function, has not been investigated. Here we detected abundant expression of both IFN-γ receptor subunit gene transcripts (Ifngr1 and Ifngr2) in the rat hippocampus by quantitative PCR. In addition, we pre-incubated rat hippocampal slices with IFN-γ (100 ng/ml) and recorded GABA-activated spontaneous and miniature postsynaptic inhibitory currents (sIPSCs and mIPSCs) and tonic currents in hippocampal CA1 pyramidal neurons by the whole-cell patch-clamp method. The pre-incubation with IFN-γ increased the frequency but not the mean amplitude, rise time or decay time of both sIPSCs and mIPSCs in hippocampal CA1 pyramidal neurons, suggesting a presynaptic effect of IFN-γ. Moreover, the GABA-activated tonic currents were enhanced by IFN-γ. In conclusion, the potentiation of GABAergic currents in hippocampal neurons by IFN-γ may contribute to the disturbed neuronal excitability and cognitive dysfunction during neuroinflammation [2)].

1)

Zhu G, Zhang J, Zhang Q, Jin G, Su X, Liu S, Liu F. Enhancement of CD70-specific CAR T treatment by IFN-γ released from oHSV-1-infected glioblastoma. Cancer Immunol Immunother. 2022 Mar 6. doi: 10.1007/s00262-022-03172-x. Epub ahead of print. PMID: 35249119.
2)
Flood L, Korol SV, Ekselius L, Birnir B, Jin Z. Interferon-γ potentiates GABA(A) receptor-mediated inhibitory currents in rat hippocampal CA1 pyramidal neurons. J Neuroimmunol. 2019 Sep 3;337:577050. doi: 10.1016/j.jneuroim.2019.577050. [Epub ahead of print] PubMed PMID: 31505410.