THE CELL-SIGNALING OF LEUKEMIA INHIBITORY FACTOR IN HIPPOCAMPAL NEURON REGENERATION

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Abstract

PURPOSE: Leukemia inhibitory factor (LIF-1) is a multifunctional cytokine protein with a variety of roles, including neural development. Previous literature has found that LIF is involved in cerebral development in rats. More specifically, it was found that after injecting LIF into the rodent's cerebrum increased the number of neurons. This could imply that LIF-1 may have some kind of neuro-regeneration role, however said mechanism has not yet elucidated. Our goal is to deduce the role of LIF-1 in neuro-regeneration and derive the mechanism of action of LIF-1 in neuro-regeneration. With the end to possibly utilized LIF-1 as a possible therapeutic agent to treat patients suffering from HIV-associated neurocognitive disorders (HAND).

METHODS: To study the effects of LIF-1 on HIV cytotoxic neurons in an in vitro rat model, we utilized 18-day Sprague Dawley (SD)fetus hippocampal neuron cells. SD neuron cells were treated with LIF-1, gp120, or LIF-1 + gp120 for 1hr or 24 hrs and left to incubate. The controls used were naïve and LPS. Cell viability and cell proliferation were measured to determine the effect of LIF-1 on neurons. Apoptosis and necrosis assays were performed to determine cell death pathway.

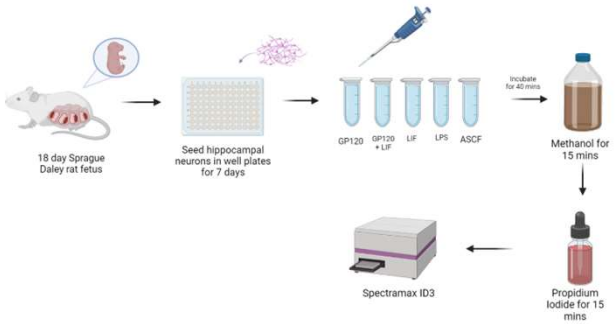
RESULTS: Suggesting that LIF promotes neurogenesis after exposure to HIV-gp120 protein. An increased expression of microtubule-associated proteins (MAPs), a marker of mature neurons was found. The presence of neurites (NeuN) increased when treated with LIF-1.

CONCLUSIONS: These results demonstrate that LIF-1 has neural regeneration potential. Suggesting the used of LIF-1 as a potential drug for future HIV treatments.

Purpose

- Leukemia inhibitory factor (LIF-1) is a pleiotropic cytokine that plays a role in various physiological processes, including embryonic development, hematopoiesis, neuroprotection, inflammation, and immune response. (Zhang et al., 2021)
- HIV-associated neurocognitive disorder (HAND) is a group of cognitive, motor, and behavioral symptoms that can affect people living with HIV. (Irollo et al., 2021)
- A subclassification of these disorders is HIV-associated dementia (HAD) (Mohammed et al., 2020) which can be accompanied by mild neurocognitive disorder. (Cornea et al., 2023).
- It has been found that LIF-1 contributes to neuroprotection of neural stem cells after ischemic stroke. (Tian et al., 2019)
- Our goal is to deduce the role of LIF-1 in neuro-regeneration and derive the mechanism of action of LIF-1 in neuro-regeneration.

Methods



Results

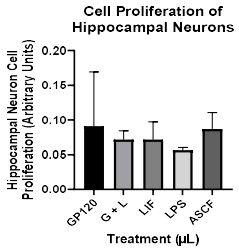


FIG. 1 Cell Proliferation of Hippocampal Neurons. Sprague Dawley 18-day rat fetus hippocampus was dissected and seeded in a 96 well cell culture plate for 7 - 9 days. Followed by treatment with GP120 (2 uL), LIF (40 uL), LPS (5 uL), and ASCF (5 uL). The plate was left to incubate for 40 minutes at 37 C. After treatment, cells were fixed with methanol, stained with propidium iodine, and visualized using the Spactramax ID3 at 450 nm.

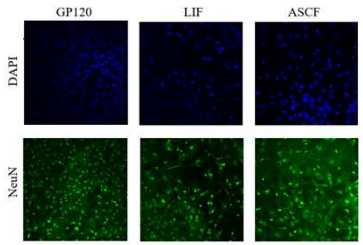


FIG. 2 Expression of NeuN in presence of GP120 or L.
Confocal microscopy studies of expression (NeuN) in the culture of primary hippocampal neurons in the presence of gp120 or LIF (20 ng / mL). Cultures of primary hippocampal neurons cells were induced to mature neurons in the presence of gp120 or LIF (20 ng/mL). Neurites immunostaining in primary hippocampal neuronal cells treated for 40 mins and analyzed.

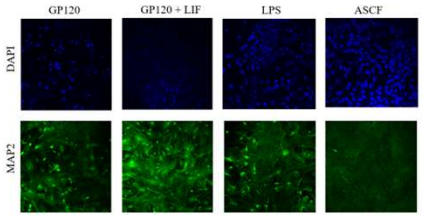


FIG. 3 Expression of MAP2 in the presence of GP120 and in combination with LIF.
Confocal microscopy studies of expression microtubule associated protein 2 (MAP2) in culture of primary hippocampal neurons in the presence of gp120 and in combination with LIF (20 ng / mL). Cultures of primary hippocampal neurons cells were induced to mature neurons in the presence of gp120 and in combination with LIF (20 ng/mL). MAP2 immunostaining in primary hippocampal neuronal cells treated for 40 mins and analyzed.

Conclusions

- Preliminary data suggests that LIF has some kind of neuroprotective or neuroregenerative action on primary hippocampal neurons.
- Primary hippocampal neurons treated with GP120 in combination with LIF reduced cell proliferation in comparison with primary hippocampal neurons treated with GP120.
- Primary hippocampal neurons treated with LIF demonstrated the same reduction in cell proliferation as cells treated with GP120 + LIF in comparison with primary hippocampal neurons treated with GP120.
- More investigation needs to be done on how the LIF protein affects the primary hippocampal neurons infected with GP120.

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