6th International Conference on
CARDIOLOGY HEART DISEASE AND HEART FAILURE

September 19, 2022 | Webinar

Submitted Date: 02-05-2022 | Accepted Date: 04-05-2022 | Published Date: 15-10-2022

Down regulation of interferon gamma activation by macrophage antioxidant 7,8-Dihydroneopterin

Siddarth Raajasekar[1] and Steven Gieseg[2]
[1]University of Canterbury, New Zealand
[2]University of Otago, New Zealand

Human macrophages produce neopterin and 7,8-Dihydroneopterin in response to interferon gamma (IFN-γ) stimulation as a part of their inflammatory process. IFN-γ upregulates cyclohydrolase II to convert GTP to 7,8-Dihydroneopterin and upregulates IDO enzyme to breakdown tryptophan to kynurenine. 7,8-Dihydroneopterin reacts with and neutralises the oxidants superoxide and hyperchlorite with neopterin being the product. Neopterin is extensively used as a marker of inflammation in a range of clinical conditions. 7,8-Dihydroneopterin also down regulates CD36, the receptor responsible for macrophage uptake of the oxidised low-density lipoprotein. On this basis we have examined whether 7,8-Dihydroneopterin has an anti-inflammatory effect by altering the balance of various cytokines within inflammatory sites such as atherosclerotic plaques. Peripheral blood mononuclear cells (PBMCs) were prepared from whole blood by centrifugation over a lymph prep cushion. Cells were incubated in RPMI1640 with 10% human serum and the media was analysed by HPLC for neopterin, 7,8-Dihydroneopterin and Kynurenine.

The addition of IFN-γ to PBMCs caused a significant increase in total neopterin and neopterin formation. PBMCs pre-treated with 7,8-dihydroneopterin showed 70% reduction in neopterin levels in response to IFN-γ stimulation. Kynurenine production was also reduced by 33% after pre-treatment with 7,8-Dihydroneopterin. Neopterin, the oxidation product of 7,8-Dihydroneopterin had no effect on the interferon-γ induced neopterin production but did reduce kynurenine levels by 80%.

7,8-Dihydroneopterin synthesis in response to interferon-γ is controlled by a feedback mechanism limiting the levels of 7,8-dihydroneopterin release by PBMC. This mechanism may provide an important control mechanism preventing over stimulation of the cells during inflammation.

References

1. Prebble, H., Cross, S., Marks, E., Healy, J., Searle, E., Aamir, R., ... & Gieseg, S. P. (2018). Induced macrophage activation in live excised atherosclerotic plaque. Immunobiology, 223(8-9), 526-535.

2. Baxter-Parker, G., Chu, A., Petocz, P., Samman, S., & Gieseg, S. P. (2019). Simultaneous analysis of neopterin, kynurenine and tryptophan by amine-HPLC shows minor oxidative stress from short-term exhaustion exercise. Pteridines, 30(1), 21-32.

Biography

Siddarth is currently in his final year of his PhD. His research is on the inflammatory basis of cardiovascular disease. He has completed his masters in biotechnology from VIT university, Vellore, India.

siddarth.raajasekar@pg.canterbury.ac.nz