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Brief Summary of Research Work

This is with reference to application of **Ms. Shipra,** Ph.D. student for 'Sun Pharma Science Foundation Awards'. Ms. Shipra is a registered **Ph.D. student** under my supervision in the Department of Cardiac Biochemistry, All India Institute of Medical Sciences (AIIMS), New Delhi. Her proposed thesis work involves the understanding of intricate network of alarmins-autophagy-necroptosis in driving inflammation, immune regulation and cardiac homeostasis in doxorubicin induced model of cardiomyopathy.

Briefly, in her thesis, Ms. Shipra is working on various intervention strategies to rescue the doxorubicin induced acute and chronic cardiomyopathy (cardiotoxicity) by targeting mitochondrial biogenesis and bioenergetics, necroptosis, autophagy and alarmins. She developed a robust doxorubicin induced acute and chronic cardiac injury model in C57BL/6J mice that resembles the clinical features of (dilated) cardiomyopathy. In her thesis, one of her objectives involved targeting mitochondrial biogenesis and bioenergetics where she identified a PGC-1α (peroxisome proliferator-activated receptor gamma ((PPAR-γ) coactivator-1alpha) agonist (i.e. ZLN005) that was found to enhance the expression of PGC-1α in cardiac tissue and potentiating the mitochondrial biogenesis along with modulating the bioenergetics mechanism. PGC-1α is considered as the 'master regulator' of mitochondrial biogenesis and function. Her interventional study successfully demonstrated that the PGC1α agonist (ZLN005) mitigates cardiomyopathy phenotype by strengthening the redox balance via mitigating the DOX mediated oxidative stress, preventing the harmful tissue remodelling effects and necroptosis. Considering the global burden of cardiovascular diseases leading to heart failure, her research work demonstrated the novel therapeutic potential of PGC1α agonist and it may be translated to the clinical set-up for the management of various cardiac injury based disease conditions and/or to prevent the progression towards heart failure. However, a targeted delivery of PGC1α agonist in heart or cardiomyocyte specific overexpression of PGC1α may further improve the efficacy of PGC1α agonist.

Hope her thesis work will be appreciated and considered for the prestigious 'Sun Pharma Science Foundation Awards'. I wish her success for same.

Dr. Manoj Kumar Tembhre