

Thalidomide affects macrophage activation and Leshmania

Z Zhanzak¹ and Y.Goto²

¹Nazarbayev University, Kazakhstan

² University of Tokyo, Kazakhstan

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Introduction: Leishmania parasites are the causative agents of LEISHMANIASIS, group of vector-borne parasitic diseases endemic worldwide. Once inoculated into the organism, Leishmania parasites are rapidly uptaken by macrophages. Macrophages are primary resident cells for their proliferation: they can either phagocyte or allow parasite growth. That is why proper activation of macrophages is crucial in disease fate. Macrophage activation is divided into two classes: classical (M1) and alternative (M2) that induce parasite killing and its survival, respectively. Classical activation is mediated by pro-inflammatory cytokines which cause macrophages to produce toxic molecules to kill intracellular parasites. In contrast, alternative activation is induced by anti-inflammatory cytokines that lead to parasite survival in infected cells. Thalidomide is reported to stimulate immune response and enhance cellular phagocytotic activity by selectively inhibiting M2 pathway. Here, thalidomide was examined as potential drug to have suppressive effect on intracellular replication of L.major within infected macrophages in-vitro.

Methods: To observe macrophage activation, Raw264.7 cells were cultured. After 24hr incubation of cells in 370°C, 5% CO₂ incubator, thalidomide treatment of different concentration

was done. Supernatant and pellet were collected for ELISA, RT-PCR, qPCR and WB tests. To observe pathogen survival, Raw 264.7 cells were cultured in chamber slides and infected with L. major at 1:10 ratio. After 24hr incubation, thalidomide treatment was done. Giemsa staining was applied to slides and intracellular amastigote forms of L.major were counted.

Results: In this study thalidomide's effect on proper macrophage activation and parasite survival was analyzed. It was found that thalidomide can a) up-regulate pro-inflammatory M1 macrophages (IFN- γ , TNF- α , iNOS); b) down-regulate anti-inflammatory M2 macrophages (IL-10 and Arg-1); c) decrease intracellular amastigotes of L. major. Thalidomide shows inhibitory effect on alternative activation of macrophages and induces M1 polarization of macrophages, thus making them resistant to L. major infection.

Conclusion: Results highlight thalidomide's potential contribution to a new drug development towards Leishmaniasis in the future.

Speaker Biography

Z Zhanzak is an undergraduate student in School of Science and Technology, Nazarbayev University, Kazakhstan.

e: zhuldyZ Zhanzak@nu.edu.kz

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