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Autophagy protects monocytes from *Wolbachia* heat shock protein 60 (rWmhsp60) induced apoptosis and senescence

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Monocyte dysfunctions by filarial antigens have been postulated as major mechanism underlying immune evasion following hypo responsiveness during patent lymphatic filariasis. Recent studies have initiated a paradigm shift to comprehend the immunological interactions of *Wolbachia* and its antigens in inflammation, apoptosis in monocytes, lymphocyte energy, etc. Here we showed that rWmhsp60 (recombinant *Wolbachia* heat shock protein 60) interacts with TLR-4 and induces apoptosis in monocytes of endemic normal, but not in chronic patients. Higher levels of reactive oxygen species (ROS) induced following TLR-4 stimulation resulted in loss of mitochondrial membrane potential and caspase cascade activation, which are the plausible reason for apoptosis. Furthermore, release in ROS owing to TLR-4 signalling resulted in the activation of NF- κ B p65 nuclear translocation which lead to inflammation and apoptosis via TNF-receptor pathway following the increase in IL-6 and TNF- α levels. Here for the first time, we report that in addition to apoptosis, rWmhsp60 a possible antigen in filarial pathogenesis also induce molecular senescence in monocytes. Targeting TLR-4 therefore presents a promising candidate for treating rWmhsp60 induced apoptosis and senescence. Strikingly, induction of autophagy by rapamycin, detains TLR-4 in late endosomes and subverts TLR-4-rWmhsp60 interaction thus protecting TLR-4 mediated apoptosis and senescence. Also, rapamycin induced monocytes were unresponsive to rWmhsp60 and triggered lymphocyte activation and proliferation following PHA stimulation. With the perspective of the evidences put forward, targeting inherent autophagic degradation pathway may provide perfect catalyst to herald a potential area of research for the development of inherent methods to treat filariasis and other inflammatory conditions.

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