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ACCEPTED MANUSCRIPT

ER-localized protein-Herpud1 is a new mediator of

IL-4-induced macrophage polarization and migration

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Abstract:

ER-localized proteins have been reported function in endoplasmic reticulum, unfolded protein degradation and destruction of misfolded proteins by the ER-associated protein degradation (ERAD) system, but their function in the chemotaxis of macrophage cells remained un-addressed. Here, we showed that ER protein with ubiquitin like domain 1(Herpud1) was upregulated in IL-4-treated M2 macrophage cells and its expression pattern was similar with macrophage polarization markers, such as Arg1, Mrc1 and Fizz1. Inhibition of Herpud1 by using specific target shRNA decreased these marker's expression at mRNA and protein level in IL-4-treated or -untreated M2 macrophage cells. IL-4 treatment promoted M2 macrophage cell migration and polarization, but this promotion was weakened by Herpud1 depletion and we got similar results by inhibition of ER stress response with chemical molecule 4-phenylbutyric acid (4-PBA) in IL-4-treated or untreated-M2 macrophage cells with Herpud1 overexpression. These results indicated that depending on ER-associated protein degradation (ERAD) to help unfolded protein degradation or destruction is not the only function of Herpud1 and acting as a mediator of IL-4 induced

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