

The effects of Histidine-Rich Glycoprotein(HRG) on neutrophil-like differentiated cell lines

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Background: Our previous study revealed that HRG treatment ameliorated the survival rate of septic mice due to suppressing the excess immunothrombus formation. These results suggested that HRG may be one of the most useful drug for sepsis. However, it is difficult to obtain the stable experiment system for standardization of HRG drug product using neutrophils because of the short survival time and individual differences. In the present study, we examined whether the differentiated neutrophil-like cell lines showed the similar responses by HRG compared with human purified neutrophils. **Method:** All trans retinoic acid (ATRA) induces differentiation of the human myeloid leukemia cell lines HL-60 and NB-4. These cells were treated with Hank's Balanced Salt Solution (HBSS), human serum albumin (HSA), or HRG. The effects of HRG on these cells were evaluated on the basis of cell shape, microcapillary passage, ROS production, NETs formation, expression of activated CD11b and the cell viability. **Result:** HRG treatment kept the rounding shape of differentiated neutrophil-like cells, decreased the cells passage time through microcapillaries, inhibited the ROS production, NETs formation and expression of activated CD11b on the cells surface. Moreover, the cells could survive longer in presence of HRG than control groups. **Conclusion:** We showed that the ATRA-induced differentiated cell lines could be used as the alternative cells to investigate the effect of HRG on neutrophils. This method can be used for standardization tests essential for pharmaceutical development.