Unexpected thermal modulation of microbicidal activity in macrophages

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Recent data from our laboratory have revealed that neutrophils and macrophages display opposite modulation by temperature: whereas neutrophils have their microbicidal activity increased at a fever-like temperature (38.5°C for rats), macrophages have their microbicidal activity increased at a hypothermia-like temperature (36.0°C for rats). The present study was conducted to investigate the mechanisms of the unexpected modulation of macrophages by temperature. We observed that the increased microbicidal activity of rat peritoneal macrophages in the hypothermia-like temperature was associated with heightened oxidative burst. Accordingly, inhibition of the NAPH oxidase complex by VAS2870 eliminated the inverse relationship between temperature and microbicidal activity. Next, we compared the temperature-oxidative burst relationship in macrophages activated upstream by a TLR4 agonist (LPS) and downstream by a protein kinase C activator (PMA). In both cases, oxidative burst was inversely proportional to temperature, indicating that the thermal modulation occurs downstream of protein kinase C. Because protein kinase C is known to activate NAPH oxidase by phosphorylating its regulatory subunit, p47phox, we then sought to evaluate the involvement of this subunit in the thermal modulation of macrophages. Contrary to our expectation, though, overexpression of the p47phox in RAW264.7 macrophages did not enhance the effect of the hypothermia-like temperature on oxidative burst. Therefore, the inverse thermal modulation of macrophage NADPH oxidase activity presumably involves other subunits, such as the catalytic subunit, gp91.

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