ROLE OF THE NEUTROPHIL IN TNFα-INDUCED THERMAL HYPERALGESIA

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Thermal hyperalgesia is the heightened sensitivity to heat and occurs during inflammation. NGF-induced thermal hyperalgesia is neutrophil-dependent (Foster et al., 2003). This group previously found that the TRPV1 receptor mediates a bilateral thermal hyperalgesia in TNFα-induced inflammation (Russell et al., 2005), but it is not yet known how TNFα mediates the response. The aim of this study was to deplete circulating neutrophils in a mouse model of TNFα-induced inflammation to elucidate the role of the neutrophil in the thermal hyperalgesia.

Female C57BL6 mice (20-30g) were pretreated with either rabbit anti-mouse neutrophil serum (ANS) or normal rabbit serum as control (Accurate Chemicals; diluted 1:10 in saline, 20mg/ml i.p.; Boyer et al., 2005). Total leukocyte counts and differential cell counts were carried out before treatment and 24h post treatment (Pitchford et al., 2003). At 24h mice were isoflurane (2%) anaesthetised and given intraplantar injections (i.pl) of TNFα (10pmol/50µl) and Tyrode (contralateral paw; 50µl). Thermal nociceptive thresholds were measured using the Hargreaves technique before injection and over a 4h time period after injection (Hargreaves et al., 1988). The mean of triplicate values was taken as paw withdrawal latency. Results are expressed as mean of group ± s.e.m and statistical analysis performed using Student’s t-test.

ANS caused a >90% depletion of circulating neutrophils. Vehicle-treated mice that received TNFα into the ipsilateral paw exhibited significant hyperalgesia, that was also observed in the Tyrode-injected contralateral paw (Figure 1), evidence of a bilateral hyperalgesia, as previously described (Russell et al., 2005).

However, ANS-treated mice exhibited hyperalgesia only in the TNFα-injected paw (Figure 1). Thus neutrophils, whilst not appearing to be important for mediating the thermal hyperalgesia, may play a role in influencing nociception information relevant to the bilateral hyperalgesia. However, the total leukocyte cell counts in ANS-treated mice decreased by >50% 24h post treatment, despite neutrophils accounting for only ~10% of all leukocytes. This implies that ANS at this dose is also depleting other cell types that may influence the bilateral hyperalgesia response. Further studies will be aimed at determining a more selective depletion of neutrophils.

Foster, P.A. et al. (2003). FASEB J, 17, 1703-05

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