Here we report that administration of neutralizing antibody to the p75 neurotrophin receptor (p75NTR) prevents the hyperalgesia without affecting inflammation itself. Thus the p75NTR is acting directly on the peripheral terminal to produce thermal neuritis. NGF plays an important role in inflammatory pain cytokine-like functions, modifying mast cell, macrophage and neuron responses to that an elevation in NGF levels which may itself have role of p75NTR during inflammatory condition has not been clarified. Here we report that administration of neutralizing antibody to the neurotrophin receptor p75NTR blocks hyperalgesia that develops with intra-planar injection of NGF or with complete Freund’s adjuvant (CFA)-induced inflammation.

Materials and Methods:

Male ICR mice were used in this study. Hyperalgesia was induced by intraplantar injection of NGF (Sigma, 1 µg/paw, n=10). The inflammation models were prepared by intraplantar injection of complete Freund’s adjuvant (CFA; Calbiochem, 10µl/paw, n=12). In each group, anti-p75NTR antibody (Advanced Targeting System, 5µl/paw for NGF injected group, n=5, 10µl/paw for CFA injected group, n=6) was injected at the same sites 30 minutes before the injection of NGF and CFA. Nociceptive assay was measured in response to noxious thermal stimulus by paw withdrawal latencies. The degree of inflammation induced by CFA was assessed by changes in paw thickness. L5 DRGs were obtained 24 hours after CFA injection, and inflammation induced by CFA was assessed by changes in paw thickness. Nociceptive assay was measured in response to noxious thermal stimulus by paw withdrawal latencies. The degree of inflammation induced by CFA was assessed by changes in paw thickness. The degree of inflammation induced by CFA was assessed by changes in paw thickness. NGF plays an important role in inflammatory hyperalgesia by acting as a cytokine-like function. Mast cells express trkA receptor and degranulate their contents in response to NGF stimulation. In this study, the blockade of exogenous and endogenous NGF to bind with p75NTR prevents the hyperalgesia without affecting inflammation itself. Thus the hypothesis underline here is: the p75NTR may modulate the function of trkA receptors by forming the complex and modulates its trophic signals.

In an inflammatory condition, unprocessed pro-neurotrophin represents abundant which has high affinity to p75NTR. Thus the pro-NGF can activate p75NTR regardless of the presence of TrkA, and the ratio of pro-NGF to mature NGF emerges as a regulatory factor for the balance between neuronal plasticity and pain.

Present study demonstrated that the role of p75NTR and activation of its signaling pathways are considered to be major contributors for the induction of inflammation related pain. It is conceivable that neutralizing antibody to p75NTR could be a new therapeutic strategy for the treatment of inflammation related pain. Although we show that p75NTR is necessary for the inflammation-induced hyperalgesia, further investigation is needed to elucidate the precise actions of trkA and p75NTR in the inflammatory hypersensitivity.

Materials and Methods:

Male ICR mice were used in this study. Hyperalgesia was induced by intraplantar injection of NGF-B (Sigma, 1 µg/paw, n=10). The inflammation models were prepared by intraplantar injection of complete Freund’s adjuvant (CFA; Calbiochem, 10µl/paw, n=12). In each group, anti-p75NTR antibody (Advanced Targeting System, 5µl/paw for NGF injected group, n=5, 10µl/paw for CFA injected group, n=6) was injected at the same sites 30 minutes before the injection of NGF and CFA. Nociceptive assay was measured in response to noxious thermal stimulus by paw withdrawal latencies. The degree of inflammation induced by CFA was assessed by changes in paw thickness. L5 DRGs were obtained 24 hours after CFA injection, and inflammation induced by CFA was assessed by changes in paw thickness. NGF plays an important role in inflammatory hyperalgesia by acting as a cytokine-like function. Mast cells express trkA receptor and degranulate their contents in response to NGF stimulation. In this study, the blockade of exogenous and endogenous NGF to bind with p75NTR prevents the hyperalgesia without affecting inflammation itself. Thus the hypothesis underline here is: the p75NTR may modulate the function of trkA receptors by forming the complex and modulates its trophic signals.