FORMYL PEPTIDE RECEPTOR (FPR) IN PAIN TRANSMISSION AND CONTROL: A CONTRIBUTION FROM FPR$^{-/-}$ MICE

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Formyl peptide receptors (FPRs) belong to the G protein-coupled receptor family, three members of which have been cloned so far in human tissues and cells and with eight genes, at least three of which translated into protein, have been identified in mice (1). The fMLF is one of the first identified FPR agonist (1) which activates at least two FPRs, the high-affinity FPR and its low-affinity variant FPR-like1 (FPRL1) in human cells. Until recently, it has been thought that FPRs are specifically expressed in neutrophils and monocytes where they strongly modulate chemotaxis. However, the presence of FPRs was demonstrated to exist in different non-hematopoietic cells, such as hepatocytes, dendritic cells and microglial cells suggesting that FPR may influence several mechanisms other than inflammatory responses (1). In a previous study, we found fMLF able to induce anti-nociceptive effects in the formalin test both after the peripheral and central administration thus suggesting a possible involvement of FPRs in nociceptive transmission (2). In order to test this hypothesis, here we used mice lacking the high affinity FPR, created by targeted gene disruption (3). FPR $^{-/-}$ mice behaved as wild type mice in several experimental paradigms - open field, rotarod, plus maze, Porsolt's test, pentamethylentetrazole test - but had a strong susceptibility to nociceptive stimuli as observed in formalin test and tail flick test. These results further suggest a FPR role in pain transmission and control.

1) Le Y., Murphy P.M., and Ji Ming Wang J.M. (2002). Trends Immunol. 23: 541-548.
2) Pieretti S., Di Giannuario A., De Felice M., Perretti M., Cirino G. 109 (2004) Pain 109: 52–63.
3) Gao J.-L., Lee E.J., and Murphy P.M. (1999). J. Exp. Med. 189: 657–662.