Lab. of Pharmacology, College of Pharmacy, Sungkyunkwan University

The thermoregulatory center located in the hypothalamus maintains physiological temperature, while fever dependens on the production of exogenous pyrogens, which induce biochemical modifications in the hypothalamus. Exogenous pyrogens can induce the release of endogenous pyrogens or cytokines (IL-1β, IL-6 and TNF-α). This in turn, leads to the production of PGE. Afterwards, PGE provokes stimulation of the neurons localized within the hypothalamus, therby triggering a reaction which culminates in the generation of fever. However, the precise mechanism by which endogenous pyrogens or cytokines increase PGE synthesis in hypothalamus is still unclear. Recently, carbon monoxide (CO) was proposed as a novel mediator of the febrile response in the central nervous system. Thus, we studied the interrelationship between heme oxygenase, a CO-producing enzyme, and IL-1β-induced febrile response. Il-1β(1.c.v. inj.) elicited the febrile response and this pyresis was significantly blocked by pretreatment with indomethacin (an inhibitor of COX), but not with ZnPP IX (an inhibitor of heme oxygenase) or ODQ (an inhibitor of soluble guanylate cyclase). IL-1β significantly induced HO-1 in hypothalamus. We couldn't find any consistent evidence that CO is a possible mediator of IL-1β-induced febrile response.

[PA1-40] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Lipopolysaccharide-induced pyresis is not related to the heme oxygenase induction

Park HJ°, Lee SH, Park HY, Lee SY

Lab. of Pharmacology, College of Pharmacy, Sungkyunkwan University

Peripheral administration of lipopolysaccharide (LPS) induced the release of circulating pyrogenic cytokines, and these cytokines elicit febrile response. Since the structural impermeability of cerebral capillaries and the low efficiency of any transport system for the cytokines across the capillary wall, it was proposed that circulating pyrogenic cytokines have their major effect on the rich vascular network close to the cluster of neurons in preoptic/anterior hypothalamus (ie., organum vasculosum laminae terminalis [OVLT]). However, the precise mechanism by which blood-borne cytokines increase PGE synthesis in hypothalamus is still unclear. In our previous study, i.c.v. injected carbon monoxide (CO) elicited pyresis and this response completely was blocked by indomethacin. Also, CO was proposed as a possible mediator of febrile response in hypothalamus. CO can be produced from heme oxygenase (HO)-catalyzed metabolism of heme. Thus, we studied the relationship of heme oxygenase to LPS-induced febrile response. LPS-induced pyresis was blocked by indomethacin, but not by ZnPP IX (an inhibitor of HO) or ODQ (an inhibitor of guanylate cyclase). LPS (i.p. inj.) did not induce HO-1 in hypothalamus. These results suggest that CO is not involved in LPS-induced pyresis.

[PA1-41] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

The role of G protein in muscarinic receptor-mediated αAPPs release in SH-SY5Y cells

Kim JH°, Kim HJ

College of Pharmacy, Center for Cell Signaling Research, Ewha Womans University