ENDOTHELIAL NITRIC OXIDE SYNTHASE (e-NOS) IS HIGHLY EXPRESSED IN BROWN ADIPOSE TISSUE

K. Kikuchi-Utsumi, B. Gao and A. Kuroshima, Department of Physiology 1, Asahikawa Medical University, Asahikawa 078-8510, Japan.

Brown adipose tissue (BAT) is the unique organ that specializes in heat production in the body and is the major site of nonshivering thermogenesis during cold acclimation. Blood flow through BAT is directly related to its thermogenic state and high rate of blood flow is required for heat production in BAT to provide oxygen and to transfer heat. Noradrenaline released from sympathetic nerve terminals in BAT is involved in the regulation of BAT blood flow, however, the mechanism of vasodilatation by noradrenaline in BAT has not been well elucidated. Concerning this regulatory mechanism, we have previously shown that noradrenaline may induce a production of nitric oxide (NO) in BAT, resulting in an increase in its blood flow. NO is produced by NO synthase (NOS), constitutive and inducible isoforms, both of which have been identified. However, it has not been determined which NOS isoform is involved in the control of BAT blood flow. Since noradrenaline increases BAT blood flow within a minute, it is likely that constitutive NOS-produced NO regulates the blood flow through BAT. To ascertain this possibility, we studied the expression of two constitutive NOS (e-, b-NOS) in BAT. Further, we examined the effect of cold exposure for 24 hours on the expression of these genes. Male Wistar rats were killed by decapitation and interscaplar BAT was excised quickly, and then total RNA and protein were prepared. Reverse transcriptase-polymerase chain reaction (RT-PCR), Northern and Western blot analyses were performed to identify the isoforms of constitutive NOS. In control rats, e-NOS mRNA was highly detected, while b-NOS mRNA was not in BAT. The high level of e-NOS mRNA was also detected in isolated brown adipocytes. Similar results for protein level of NOS were obtained by Western blot analysis. Cold exposure led to an increase in e-NOS mRNA expression. Intraperitoneal injection of beta3-adrenoceptor agonist, which is responsible for BAT thermogenesis, also elevated the level of e-NOS gene expression. These results suggest that NO produced by e-NOS in BAT may regulate BAT blood flow, and activity as well as expression of e-NOS are controlled by an activation of sympathetic nervous system. Furthermore, NO derived from brown adipocytes may be involved directly in metabolic activity of this tissue, since we have previously reported that the administration of NOS inhibitor depressed the in vitro oxygen consumption of BAT. Thus, NO might be one of the essential regulators involving in BAT thermogenesis. However, neither localization site for e-NOS nor signaling pathway for activating e-NOS in BAT has been clarified. To understand the physiological role of NO in BAT, further studies are warranted to elucidate these points.

utsumi@asahikawa-med.ac.jp