

Apolipoprotein E (ApoE) knockout mouse is an established animal model of atherosclerosis. In this study, we generated apolipoprotein E (ApoE) and Nox2 double knockout mice by crossing the Nox2^{-/-} with the ApoE^{-/-} mice on the C57BL/6J background, and characterised these mice in comparison with their littermates of wild-type, Nox2^{-/-} and ApoE^{-/-} mice. Male mice (n=6/per group) at 3 m of age were used for the study. We found that there was no significant difference in the levels of body weight, food intake, water intake, fasting serum glucose between these groups of mice. The blood pressure was measured by tail-cuff plethysmography, and we found no significant difference between these mice (mmHg: wild-type 124±5, Nox2^{-/-} 123±1, ApoE^{-/-} 123±7, ApoE^{-/-}/Nox2^{-/-} 119±5). We then examined the NADPH-dependent ROS production in different organ homogenates (heart, aorta, lung, liver, kidney, spleen, pancreas, fat, skeletal muscle, brain) by lucigenin (5 μM)-chemiluminescence, and found that lung, liver and brain tissues produce higher levels of ROS as compared to other organs in all mice examined. Compared to wild-type mice, Nox2^{-/-} mice had significantly lower levels of ROS production in all organs except the liver, and ApoE^{-/-} mice had significantly higher levels of ROS production in the heart, aorta, kidney and pancreas. Compared to ApoE^{-/-} mice, ApoE^{-/-}/Nox2^{-/-} mice reduced significantly the levels of ROS production in the heart, aorta, liver, kidney, pancreas, but significantly increased the levels of ROS production in the fat, skeletal muscle and brain tissues. In conclusion, Nox2 deletion reduced significantly the levels of ROS production in the metabolic and cardiovascular organs of ApoE^{-/-} mice. ApoE^{-/-}/Nox2^{-/-} mice serves a good animal model to study the role of Nox2-derived ROS in the pathogenesis of cardiovascular diseases associated with metabolic disorders.

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CHARACTERISATION OF ROS PRODUCTION IN DIFFERENT ORGANS OF MICE DEFICIENT OF NOX2, APOE, AND BOTH NOX2 AND APOE

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Multi-organ oxidative stress has been found to be associated with dietary obesity, insulin resistance and diabetes. Recent studies have suggested that the activation of a reactive oxygen species (ROS) generating enzyme, NADPH oxidase 2 (Nox2) is involved in the pathogenesis of cardiovascular diseases such as atherosclerosis linked to metabolic disorders. However, detailed investigation of the role of Nox2 in the development of atherosclerosis is still missing.