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MSc Agricultural Biotechnology (Animal)

**INVESTIGATION OF THE OXIDANT-ANTIOXIDANT SYSTEM IN NADPH5
KNOCK-OUT RABBITS AS A RESPONSE TO CHOLESTEROL RICH DIET**

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ABSTRACT OF THESIS

Cardiovascular diseases (CVDs) represent a serious global health burden, with oxidative stress playing a crucial role in their pathogenesis. Oxidative stress occurs due to imbalance between the production of reactive oxygen species (ROS) and antioxidant defenses which is influenced by genetic, epigenetic and environmental factors including dietary components such as the intake of cholesterol. This thesis evaluates the role of *NOX5*, a member of the NADPH oxidase family, on gene expression alterations in the brain in the context with oxidative stress in genetically modified *NOX5* knockout rabbits under dietary stress, in the form of a cholesterol-rich diet. My findings highlight the role of oxidative stress caused by a cholesterol-rich diet in the rabbit brain and point out the importance of *NOX5*. Using *NOX5* knockout rabbits on varied dietary regimens, this study investigates the association between genetic modifications, dietary factors, and cardiovascular health. The methodology comprises of a controlled experimental design with standard and cholesterol rich diets given to both wild-type and *NOX5*-deficient rabbits. Gene expression was analyzed using a Quantitative Real-Time PCR (qPCR) with a focus on significant oxidative stress-related genes. The hypothetical findings of this thesis indicate that dietary cholesterol significantly impacts the expression of essential antioxidant genes and might alter the expression of *NOX5*. *NOX5* knockout rabbits had varied antioxidant responses under various dietary conditions, highlighting the complex association between dietary influences and genetic background on oxidative pathways. The implications of these findings expand to understanding the molecular pathways through which *NOX5* and cholesterol interact and how this is manifested in the brain. By finding possible therapeutic targets within the oxidant-antioxidant system that may lower cardiovascular risk associated with dietary cholesterol, this study broadens our knowledge and opens the door for future research into the role of diet and genes in cardiovascular pathology.

Keywords: *Oxidative stress, Reactive oxygen species, NOX5, NADPH oxidase, Cholesterol, Dietary influence, Antioxidants, Knockout rabbit model*