【Grant-in-Aid for Scientific Research (S)】

Animal Lipid Bio-Technology: The Science of Lipids that Shape, Move, and Disease the Animal Body

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Purpose and Background of the Research

1. Research Background

Animals adapt to different environments while consuming food, growing, being active, and aging. Cows ferment grass to synthesize lipids and secrete large amounts of milk from mammary gland cells. Dogs, being omnivorous, have highly developed brains that support social behavior, while fish incorporate large amounts of ω3 fatty acids to maintain cell membranes, enabling them to remain active in cold seas (Figure 1, left).

Fats from food are digested and absorbed, then incorporated into the phospholipids of cell membranes as fatty acids. This composition determines cell flexibility, division, and movement. When exposed to stress, fatty acids within phospholipids are metabolized, generating bioactive lipids such as prostaglandins, which protect tissues.

Phospholipids in cell membranes exist in various forms depending on the type and combination of alcohols and fatty acids they contain, as well as the positions where they are attached. These qualitative and quantitative differences in phospholipids regulate cellular functions, meaning that fatty acid uptake and metabolism play a crucial role in the unique tissue formation and function maintenance of animals (Figure 1, center and right). Disruptions in this balance can impair productivity and health. For instance, in undernourished cows, altered fatty acid metabolism leads to decreased milk quality. Additionally, dogs have different requirements for both the quality and quantity of fatty acids compared to humans, and an imbalance in intake can cause dermatitis.

Recently, research has increasingly shown that tissues and cells selectively absorb specific fatty acids via blood vessels, but the underlying mechanisms remain unclear. The intake of ω3 fatty acids such as EPA and DHA, known for their health benefits, has expanded beyond humans to include pets and livestock. However, an unbalanced intake of fatty acids places significant stress on cells. Understanding how fatty acids are absorbed and metabolized through the blood vessels of animal tissues, as well as the mechanisms of their disruption, could enable the targeted delivery of essential fatty acids to specific tissues, supporting health without stress and improving productivity.

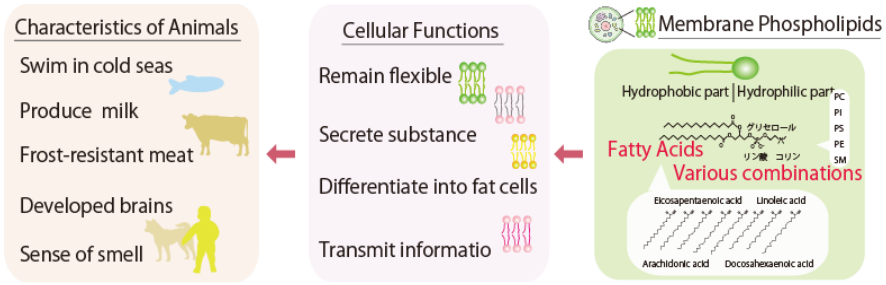

Figure 1 Phospholipids in various animals

2. Research Objectives

This study aims to establish “Animal Lipid Biology” by investigating how animals sustain life through their diet, fatty acid synthesis, absorption, and utilization from the perspective of phospholipid composition in cell membranes. Furthermore, we will develop technologies to stably deliver essential fatty acids to specific tissues and apply these advancements to livestock production and veterinary medicine. Through this approach, we seek to contribute to the realization of One Health, promoting the well-being of the environment, animals, and humans alike.

Expected Research Achievements

Summary:

This study aims to 1. Identify differences in the quality of phospholipids in cell membranes that support distinctive tissue functions in various animal species. 2. Elucidate the mechanisms underlying these differences. 3. Investigate how cell functions depend on phospholipid composition. 4. Assess the risks that disrupt phospholipid homeostasis. 5. Develop and apply technologies to deliver essential fatty acids to target tissues, improving productivity in livestock farming and enhancing the quality of veterinary medicine.

Description of Each Research Component:

Construction of the Cell Membrane Phospholipid Atlas: Using mass spectrometry techniques, a comprehensive phospholipid atlas will be created for various tissues in different animal species. Additionally, the effects of fatty acid transporter deficiencies or inhibitors—whether previously reported or newly discovered—on phospholipid composition and function will be evaluated.

Elucidation of Phospholipid Metabolism Mechanisms: Gene expression and protein analyses will be conducted for target tissues and cells to construct fatty acid metabolism models for different animal cells. These models will be used to develop fatty acid regulation technologies.

Evaluation of the Impact of Phospholipid Dysregulation on Tissue Function: The effects of genetic defects or stress that disrupt phospholipid metabolism will be assessed in terms of tissue and cellular functions. The mechanisms underlying these abnormalities will be clarified, and potential compensatory strategies will be developed. This study will incorporate AI-based phenotype analysis techniques using image data obtained from model animals.

Development of Technologies to Improve Cattle Productivity: The unique fatty acid synthesis and uptake mechanisms in ruminants, as well as the phospholipid composition and function in reproductive and muscle tissues, will be analyzed. The findings will contribute to enhancing cattle reproduction, lactation, and fattening efficiency, as well as disease prevention strategies through fatty acid regulation.

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