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Review

The mammary gland in domestic ruminants: A systems biology perspective

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ABSTRACT

Milk and dairy products are central elements in the human diet. It is estimated that 108 kg of milk per year are consumed per person worldwide. Therefore, dairy production represents a relevant fraction of the economies of many countries, being cattle, sheep, goat, water buffalo, and other ruminants the main species used worldwide. An adequate management of dairy farming cannot be achieved without the knowledge on the biological mechanisms behind lactation in ruminants. Thus, understanding the morphology, development and regulation of the mammary gland in health, disease and production is crucial. Presently, innovative and high-throughput technologies such as genomics, transcriptomics, proteomics and metabolomics allow a much broader and detailed knowledge on such issues. Additionally, the application of a systems biology approach to animal science is vastly growing, as new advances in one field of specialization or animal species lead to new lines of research in other areas or/and are expanded to other species. This article addresses how modern research approaches may help us understand long-known issues in mammary development, lactation biology and dairy production.

Biological significance
Dairy production depends upon the knowledge of the morphology and regulation of the mammary gland and lactation. High-throughput technologies allow a much broader and detailed knowledge on the biology of the mammary gland. This paper reviews the major contributions that genomics, transcriptomics, metabolomics and proteomics approaches have provided to understand the regulation of the mammary gland in health, disease and production. In the context of mammary gland "omics"-based research, the integration of results using a Systems Biology Approach is of key importance.

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Contents

1. Introduction

Milk production represents an important sector of agriculture, in which several ruminant species are used for the production of milk and dairy products, such as butter, cheese, cream, etc. In 2010, the world milk production stood at nearly 700 million tonnes [1], from which cow (*Bos taurus* and *Bos indicus*) milk production represents approximately 84% of the total world milk production, with its production decreasing in some countries (e.g. USA, South Africa) and increasing in others (e.g. New Zealand, Denmark). Water Buffalo (*Bubalus bubalis*) milk production, although only produced in a few countries, is increasing and it constitutes 13% of the world milk production, essentially in Asia. Finally, goat (*Capra hircus*), sheep (*Ovis aries*) and camel (*Camelus dromedarius*) milk represent the remainder small fraction of the world milk production [2].

In ruminants, as in all mammals, the mammary gland is the milk secreting anatomical structure in females. Mammary glands are modified sudoriferous glands that produce milk for offspring nourishment [3]. In ruminants, mammary glands are located in the udder, a complex organ made up of a series of systems, which includes: a supportive system; a secretory system composed of epithelial cells; a duct system for storage and conveyance of milk; blood, lymph, and nerve systems. In cattle, the udder consists of four separate mammary glands (also called quarters). Each gland has one teat and each teat has one opening. The pattern of development in ovine and bovine mammary glands is similar, although sheep and goats have two glands and two teats.

The interior structure of the mammary gland consists of connective and secretory tissues and a ductular system. The secretory tissue contains lobes and each lobe consists of several *lobules*; each lobule contains clusters of *alveoli*, sac-like structures where milk is synthesized and secreted to the ductular system. This system starts at the alveolus and ends at the streak canal, the only orifice of the gland between the internal milk secretory system and the external environment. Milk is then drained into larger ducts until it enters the primary (mammary) ducts attached to the gland cistern which is then linked to the teat cistern. Milk in the teat cistern is prevented from escaping to the outside by a sphincter muscle which contracts around the teat canal through which milk is drawn to the outside. The teat canal is also lined with cells that produce a bacteriostatic secretion [4].

The proportion of secretory to connective tissue in the mammary gland is regulated by hormones and, during lactation, secretory tissue increases in volume; after the end of lactation this tissue regresses, and connective tissue assumes a high percentage of the gland [3]. In fact, the endocrine system plays a major role in the mammary development (mammogenesis), in the onset of lactation (lactogenesis) and maintenance of milk secretion (galactopoiesis) [5]. In order to synchronize mammary development with the reproductive stages and the needs of the offspring for milk, the endocrine system must have its regulating role active, through the intervention of three types of hormones which have their levels varying from phase to phase: reproductive (estrogen, progesterone, placental lactogen, prolactin and oxytocin), metabolic (growth hormone, corticosteroids, thyroid hormone and insulin) and mammary hormones (growth hormone, prolactin, parathyroid hormone-related peptide and leptin) [6]. In a very simplistic way, progesterone withdrawal triggers lactogenesis and glucocorticoids and prolactin are essential for this process. Progesterone is additionally responsible for maintaining pregnancy [7].

This hormonal regulation as well as nutritional and genetic factors involved in the mammary gland development and lactation processes have been largely studied for many years not only in cattle but also in other farm animals [8–10]. However, genomics, transcriptomics, metabolomics and proteomics approaches, which have recently started being applied to Animal Science [10–16], already proved to contribute with new advances to understand in great detail mammary and lactation biology in ruminants, both in health and