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Molecular regulation of lactation: The complex and requisite roles for zinc

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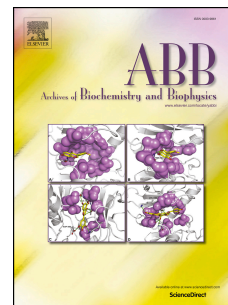
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**Molecular regulation of lactation: The complex and requisite roles for zinc**Sooyeon Lee<sup>1</sup> and Shannon L Kelleher<sup>1,2,3</sup>Departments of <sup>1</sup>Cellular and Molecular Physiology, <sup>2</sup>Pharmacology and <sup>3</sup>Surgery, Penn State Hershey College of Medicine, Hershey, PA 17033, USA

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**Abstract**

Lactation provides many health benefits to the nursing infant and breastfeeding mother. In order to successfully breastfeed, the mammary gland must expand and differentiate to activate numerous processes that regulate milk production and secretion. This involves a complex series of molecular, biochemical and cellular events driven largely by lactogenic hormones. Recent advances implicate zinc as a critical modulator of mammary gland function. Here, we provide an overview of our current understanding of the role and regulation of zinc in promoting proliferation, differentiation and secretion in the mammary gland during lactation, and highlight critical gaps in knowledge.

**Keywords:** Zinc; mammary gland; lactation; proliferation; differentiation; secretion**Introduction**

Breastfeeding provides compelling health advantages to both the growing infant and nursing mother. A recent series in Lancet concluded that the deaths of ~823,000 children and ~20,000 mothers could be averted each year through universal breastfeeding, providing a global economic savings of US\$300 billion [1]. This highlights the reasoning behind the recommendation of exclusive breastfeeding for at least the first 6 months of life supported by the American Academy of Pediatrics and The World Health Organization [2]. However, only ~16% of US infants and ~38% of infants globally are exclusively breastfed for the first 6 months [3]. The two most common reasons why ~50% of women stop breastfeeding prematurely is that they believe that they are not producing enough milk, or they are producing milk that does not meet their infant's nutritional needs [4]. Successful lactation requires a cascade of biological events that are organized into two stages, *secretory differentiation* and *secretory activation*. *Secretory differentiation* occurs during pregnancy and refers to the stage when mammary epithelial cells differentiate into milk-producing lactocytes that organize into lobulo-alveolar units and are maintained by lactocyte renewal. This process is regulated by a

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