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Preface

Lactation and the process of breastfeeding has been integral to the survival and long-term well-being of neonates and infants of most mammalian species. Mothers' milk has been considered as a complete source of nutrition for the suckling infant from times immemorial, often with many magical healing powers. It is only in the past 2 centuries that significant scientific information has become available about the evolution of the mammary glands and the development of lactation and its impact on the suckling mammalian neonate. Since the observations of Paul Ehrlich over 120 years ago, it is now clear that mammalian breastfeeding is associated with significant reduction in infant mortality, protection against enteric, respiratory, and other mucosal and systemic infections, and protection against the development of allergic disorders. Recent observations have demonstrated that breastfeeding has a profound impact on the development and function of the neonatal immune system, mucosal microbiological homeostasis, and long-term protection against autoimmune and other inflammatory disease states and malignancy. The nutritional and immunobiological benefits attributed to breastfeeding are related to the diverse spectrum of specific cellular and soluble products present in the early colostrum and milk. It is now clear that the immunologic activity in the products of lactation represents the effector functional elements of the common mucosal immune system. The discovery of the secretory IgA (SIgA) immunoglobulin isotype in the milk, followed by the identification of antibacterial, antiviral, and antiparasitic activity in the milk associated with SIgA and demonstration of important elements of cellular immunity in the milk represent crucial milestones in the understanding of lactation as the single most important element of neonatal health in most mammalian species.

The 94th Nestlé Nutrition Institute workshop is dedicated to Prof. *Lars A. Hanson*, who was the first investigator to identify SIgA in the colostrum and milk. He has been one of the most devoted scholars to the study of mammalian lactation and breastfeeding, and has also been instrumental in a global

effort to foster breastfeeding in the developing world and for undernourished infants.

He is rightfully considered as the “father of modern breastfeeding.”

This workshop was designed to develop a comprehensive perspective about available information on the evolution of lactation in most mammalian species, and to examine in some detail the origin, composition, and functional characteristics of different nutritional and immunologic components in mammalian milk and other lactation products. Specifically, the workshop focused on the following areas: (1) the evolution of mammalian lactation and breast feeding; (2) immunologic aspects of cellular and soluble products in milk; (3) the microbial composition of human milk and its effects on the development of the mucosal microbiome in the suckling infant, and (4) the role of oligosaccharides, antimicrobial peptides, and other important soluble compounds in the products of lactation, especially in the human milk.

The evolution of mammary glands and lactation has been the subject of deep interest and considerable speculation since Darwin. More recently, it has been possible to compare the evolutionary development of mammary glands across diverse taxa. The workshop began with a comprehensive discussion of the genetic origins and functions of different components of lactation across the evolutionary tree. The keynote addressed by *Olav T. Oftedal* introduced the prevailing concepts about the evolution of mammary glands and different constituents in the products of lactation. It was suggested that appearance of a milk protein across monotremes, marsupials, and eutherians, the 3 major mammalian taxa, may indicate that the protein evolved before these groups diverged and is inherited from the ancestral taxa. Milk constituents of evolutionary interest are lactalbumin, caseins, milk fat globules, several proteins, including antimicrobial peptides, butrophilin 1A1, and xanthine, which will also be discussed in the context of their immunologic functions and host defense. The workshop program was designed to provide a historical perspective of the immunology of milk and its impact on the breastfeeding infant. During subsequent presentations in session I by *Pearay L. Ogra*, *Jiri Mestecky*, *Helena Tlaskalová-Hogenová et al.*, and *Valerie Verhasselt*, we aimed to elucidate the recent observations on the common mucosal immune system and the maternal contribution to the development of immunity in the neonate in some detail. Subsequently, the immunomodulatory components of human milk, influence of breastfeeding on long-term health, and the role of breastfeeding in preventing allergy and infection will be explored in some detail.

Session II of the workshop was designed to examine the importance of microbiota and their metabolic products in breast milk, and the breast milk microbiome with regard to neonatal colonization was discussed. Although there is no direct proof that the breast milk microbiome contributes significantly to coloni-

zation, the combination of the breast milk microbiome and factors in breast milk which facilitate growth of health-producing bacteria was emphasized. We know that the microbiome of milk comes from various sources (skin, baby's oral cavity, and the maternal gut). Since the newborn encounters breast milk (colostrum) at the beginning of life, breastfeeding is important as an initial colonizer. Maternal gut microbiota gain access to the breast milk through hormonal alterations in the gut barrier and uptake by macrophages which travel to the breast. When we consider microorganisms in breast milk, we often overlook the virome. However, new evidence suggests that breast milk contains a considerable viral component. This viral component is being considered more relevant to infant health and to the microbiome composition. The dynamic composition of breast milk with regard to microbes and their metabolites and the molecules such as IgA which affect colonization collectively provides important defense to the newborn infant. A new observation regarding breast milk is that it supplies substrates for bacterial metabolism which allow anti-inflammatory metabolites to form. The topics of specific consideration include an overview of the milk, microbiome, and neonatal colonization; the origin of the milk microbiome and its potential utility; the current status of the milk virome; gut microbiota, host gene expression, and cell traffic via breastfeeding; and protection from necrotizing enterocolitis and breastfeeding and microbiota. These areas are discussed by *Samuli Rautava, Leónides Fernández and Juan M. Rodríguez, Sindhu Mohandas and Pia S. Pannaraj, Josef Neu, and W. Allan Walker and Di Meng*, respectively.

Finally, we considered to examine in some detail other important protective factors in human milk. The objective of session III was to explore the structure and function of milk oligosaccharides, the role of select oligosaccharides in viral infection, milk fat globules, and their effects on the mucosal microbiome. Other presentations explore the effects of lactoferrin, osteopontin, and effects of other proteins and antibodies on the mucosal microflora in breastfed infants. These areas of milk protective factors will be discussed by *Lars Bode, Franz-Georg Hanisch and Cem Aydogan, Olle Hernell et al., Nicholas D. Embleton and Jannet E. Berrington, Rulan Jiang and Bo Lönnerdal, and Vanessa P. Dunne-Castagna et al.*, respectively.

The organizers of this workshop have made every attempt to provide a balanced state-of-the-art update on the current knowledge of milk, mucosal immunity, and the microbiome as well as their impact on breastfeeding in mammalian neonates. We hope the readership of the NNI workshop series will find this information helpful in their own endeavors in specific areas discussed during this workshop.

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