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Delivery of functional RNA cargos by dietary exosomes from cow's milk in C57BL/6J mice

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Various species of RNA, including microRNAs and mRNAs are encapsulated in exosomes from dietary sources, including cow's milk. Encapsulation confers protection against degradation and provides a vehicle for intestinal uptake of exosomes and their RNA cargos by endocytosis. In previous studies we challenged the paradigm that microRNAs and mRNAs are derived solely from endogenous sources. We demonstrated that milk consumption causes a postprandial increase in plasma microRNAs (including bovine-specific microRNAs), endogenous microRNA synthesis is insufficient to compensate for dietary microRNA depletion and dietary microRNA are delivered to circulating cells and tissues to regulate gene expression in host organisms. Here we assessed the bioavailability and distribution of milk exosomes endogenously and exogenously labeled with fluorophores, phenotypes of exosome depletion and the functionality of milk exosome cargos in wild-type and transgenic mice. Dose-response studies of milk exosomes were conducted using a live mouse imaging system. Our data suggest that mice absorb milk exosomes and that a fraction of these exosomes escapes re-packaging in the intestinal mucosa and reaches tissues in intact form; the majority of exosomes accumulates in macrophages. Exosome feeding studies suggest that dietary depletion elicits a substantial decrease in fertility, intrauterine growth and postnatal survival; Exosome depletion also caused aberrant purine metabolism. Ongoing studies suggest that dietary exosomes extend the life span of tamoxifen-inducible Drosha conditional knockout mice and that mRNA cargo in milk exosomes can be translated into proteins.

Biography

Janos Zempleni has obtained his PhD in Nutrition Science from the University of Giessen, Germany and received Postdoctoral training at Innsbruck University Medical School, Austria, Emory University School of Medicine, USA and the University of Arkansas for Medical Sciences, USA. He is the Willa Cather Professor of Molecular Nutrition at the University of Nebraska-Lincoln, USA, where he directs an NIH-funded obesity prevention and nutrient signaling center. He has published more than 200 papers and has been continuously funded by federal agencies and foundations for 15 years and is a Fellow of the American Association for the Advancement of Sciences.

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