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Letter to the Editor

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We read with interest the recently published paper by Amitay et al. [1] demonstrating an association of breastfeeding with protection from childhood leukemia. The authors describe some possible factors contributing to the biology underlying this protective association but highlight the need for further mechanistic investigation. We would like to bring attention to an additional potential contributor to breastfeeding-associated cancer protection, related to maternal cells acquired by the child during fetal development.

Maternal-fetal exchange during pregnancy results in transfer of maternal cells (or microchimerism, MMc) to offspring and vice versa. Functionally, tolerance to MMc can be demonstrated as the NIMA effect: specific tolerance to the noninherited maternal antigen, which has the potential to influence transplant outcomes later in life [2]. Durability and magnitude of the NIMA effect has been demonstrated to be heightened by breastfeeding. Studies demonstrate detection of soluble forms of maternal HLA antigens in breast milk [3]. Data from mouse models show that exposure to maternal antigens through breast milk appears important for persistence of MMc beyond the neonatal period and associated durable NIMA tolerance [4].

MMc is sensitized to the child's inherited paternal antigen (IPA). Such priming of MMc against IPA may confer a unique ability of MMc to perform allosurveillance against the development of cancer in the offspring. A possible graft-versus-leukemia role for MMc sensitized against specific IPAs was demonstrated indirectly in the setting of cord blood transplant [5]. These mechanisms may also have roles in cancer protection more broadly. Breastfeeding, which facilitates the durable persistence of MMc in the offspring, may provide the offspring with a specifically primed allosurveillance mechanism, thus reducing the risk of developing childhood leukemia. Further investigations of these relationships are warranted.

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