THE HARTWELL FOUNDATION

2020 Individual Biomedical Research Award

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Harnessing Breastmilk Antibodies to Enhance Neonatal Growth and Long-Term Health

Early life is a time of profound developmental changes and rapid growth for a neonate, where proper weight gain is essential for robust health. An imbalance between nutrient absorption and a healthy body's energy requirements may, however, result in a slower than expected weight gain, known as growth faltering (previously described as 'failure to thrive'). Approximately 15% of infants born in the U.S. at full term (39-40 weeks of pregnancy) experience growth faltering but the incidence of growth failure is inversely related to gestational age and therefore can be quite high for pre-term births. Children who experience growth faltering are more likely to experience severe adverse health challenges, including heightened susceptibility to infection and chronic disease, metabolic dysfunction, behavioral problems and cognitive defects. Consequently, to avoid growth faltering and ensure optimal neonatal development it is essential to understand the factors that contribute to early life growth. Not surprisingly, breastmilk is considered the perfect 'first food' for neonatal healthy weight gain, but the breastmilk components that contribute to this beneficial effect remain unclear. In this regard, Meghan recently discovered that antibodies present in mouse breastmilk bind to beneficial (commensal) bacteria in the mouse neonatal GI tract to reinforce intestinal immunity and prevent growth faltering. The antibodies appear to coat bacteria by binding selectively to specific carbohydrate molecules. In preliminary experiments, she observed that despite equivalent birth weights, neonatal mice that did not acquire maternal antibodies during the weaning transition weighed approximately 10% less than the control group. To explain the variation, she hypothesizes that breastmilk antibodies enhance infant growth by promoting mutualism between the immune system and resident intestinal bacteria, an effect that mediates nutrient absorption and prevents growth faltering. Perturbations in the diversity of the gut microbiota (beneficial, inconsequential and detrimental microbes, consisting mostly of bacteria), as well as aberrant immune responses to the microbiota, are likely to disrupt the mutually beneficial effect. To understand how such alterations may contribute to growth faltering in neonates reared without breastmilk, she will isolate and characterize the beneficial breastmilk antibodies from mice and humans that promote host-microbiota mutualism, which ultimately will make it possible to identify and isolate the maternal B lymphocytes that produce the antibodies. If Meghan is successful, it will be possible to supplement infant formula with synthetic antibodies to prevent neonatal growth faltering and promote robust health; as well as to consider novel B cell immunization approaches to promote favorably the production of such beneficial antibodies in pregnant and breastfeeding women.