STRONG CHILDREN'S RESEARCH CENTER

Summer 2015 Research Scholar

Name: Houda Abdelrahman

School: University of North Dakota School of Medicine and Health Sciences

Mentor: Dr. Kirsi Jarvinen-Seppo, MD PhD

ABSTRACT

Title:
An assay for inducing APRIL production by intestinal epithelial cells to probe breastmilk's immuno-modulatory effects

Background:
Breastmilk is the infant's natural primary source of immuno-modulatory factors, such as immunoglobulin A (IgA), during the post-natal period.[1] The advent of increasingly common pediatric food allergies suggests that early immune system development and early environmental exposure determine susceptibility to allergies. IgA prevents allergies by inhibiting the excessive uptake of sensitizing food antigens through the infant's intestinal epithelium.[2] However, the infant's gut does not produce IgA due to inhibited plasma B-cell development until approximately one month after birth.[3] Normally, mucosal lamina propria B-cells convert from producing IgM to producing IgA via class switch recombination (CSR).[4] Two pathways for activating the production of IgA, T-cell dependent (TD) and T-cell independent (TI) pathways, utilize end plasma B-cell CSR but involve different upstream factors.[3] A proliferation-inducing ligand (APRIL) is a critical factor in the TI pathway for IgA production and is directly synthesized by epithelial cells upon intestinal stimulation, such as stimulation by breastmilk. APRIL binds to B-cells and activates CSR to IgA.[5] Because TD pathway factors dominate in the early gut and do not correlate with increased IgA-producing plasma B-cell densities during the one-month critical time window, the slower-forming TI pathway may be responsible for the low allergy-protecting IgA densities during early life.[3]

Objective:
Here, an assay for culturing and stimulating intestinal epithelial cells was developed to measure APRIL production in response to stimulants. This assay will be used to probe breastmilk's immuno-

Cell stimulation with media
expression compared to stim
whether the cells were grown i
-Cells that were cultured for
three or more days, elicited the
-For the experimental trials p
detecting APRIL mRNA. ELI
protein in media supernatan
development.

Conclusion:
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