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Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Protocol Number: **H-43692**
Status: Approved
Initial Submit Date: 8/21/2018
Approval Period: 1/2/2022 - 1/11/2027

Section Aa: Title & PI

A1. Main Title

NON-INVASIVE MARKER OF INFANT FRUIT AND VEGETABLE INTAKE

A2. Principal Investigator

Name:	NANCY MORAN	Phone:	713-798-0520
Id:	[redacted]	Fax:	
Department:	PEDIATRICS: NUTRITION	Email:	nemoran@bcm.tmc.edu
Center:		Mail Stn:	BCM320

A3. Administrative Contact

None

A3a. Financial Conflict of Interest

Does any member of study personnel (Investigator (including investigatorâ€™s spouse and/or dependent children)) that are involved in the design, conduct, or reporting of the research have a Significant Financial Interest (SFI) that would reasonably appear to be affected by the research for which funding is sought and/or associated with an entity/business that would reasonably appear to be affected by the research?

No

Section Ab: General Information

A4. Co-Investigators

Name:	TERESIA O'CONNOR	Phone:	713-798-6782
Id:	[redacted]	Fax:	713-798-7098
Department:	PEDIATRICS: NUTRITION	Email:	teresiao@bcm.tmc.edu
Center:		Mail Stn:	BCM320
Name:	JOCELYN CHANG	Phone:	713-798-0517
Id:	[redacted]	Fax:	
Department:	PEDIATRICS: NUTRITION	Email:	jocelync@bcm.tmc.edu
Center:		Mail Stn:	BCM320
Name:	FIDA BACHA	Phone:	713 7987166
Id:	[redacted]	Fax:	
Department:	PEDIATRICS: NUTRITION	Email:	fbacha@bcm.edu
Center:		Mail Stn:	BCM320

Name: YUSUF ZAIDI
Id: [redacted]
Department: PEDIATRICS: NUTRITION
Center:
Phone: 713 7980519
Fax:
Email: yzaidi@bcm.edu
Mail Stn: BCM320

Name: RACHEL STROH
Id: [redacted]
Department: GRADUATE MEDICAL EDUCATION
Center:
Phone:
Fax:
Email: u234960@bcm.edu
Mail Stn:

A5. Funding Source:

Baylor College of Medicine (Internal Funding Only)

A6a. Institution(s) where work will be performed:

TCH: Texas Children's Hospital
Texas Children's Health plan: Center for Children and Women
Texas Children's Hospital- Women's Pavilion
Texas Children's Pediatric Associates (TCPA)

A6b. Research conducted outside of the United States:

Country:
Facility/Institution:
Contact/Investigator:
Phone Number:

If documentation of assurances has not been sent to the Office of Research, please explain:

A7. Research Category:

A8. Therapeutic Intent

Does this trial have therapeutic intent?
No

A9. ClinicalTrials.gov Registration

Does this protocol/trial require registration on ClinicalTrials.gov due to it: meeting the definition of an Applicable Clinical Trial, being required under the terms and conditions of an award, or being proposed to be published in ICMJE journals?
No, this clinical is not a clinical trial, or does not meet the definition of an Applicable Clinical Trial, or does not need to be registered under the terms and conditions of an award, or is not a clinical trial with results intended to be reported in an journal belonging to the ICMJE. Registration is not required.

Section B: Exempt Request

B. Exempt From IRB Review

Not Applicable

Section C: Background Information

Blood carotenoid concentrations are a widely accepted objective biomarker of fruit and vegetable intake (1,2), which has been used in countless national surveys and epidemiological and clinical studies for over 4 decades. Nonetheless, blood carotenoid concentration measures require specialized chromatographic analysis and venipuncture for sample collection, impeding the more widespread, field use of this measure for monitoring pediatric fruit and vegetable intake. Dermal carotenoid intensity is a promising biomarker of fruit and vegetable intake in adults and children, with most research using a non-commercial Raman spectroscopy technology. Raman spectroscopic measures of skin carotenoids, however, are confounded by the presence of hemoglobin and melanin, so a newer, commercially-available technology utilizing reflectance spectroscopy (RS; Veggie Meter, Longevity Link, Corp., UT) which corrects for these confounding signals is now available (3). Non-invasive estimation of pediatric fruit and vegetable intake is an exciting prospect and is more likely to be pursued with the availability of the new RS device. Infanthood and the period

of complementary food introduction is a particularly important time during which fruit and vegetable intake should be monitored in children. This time in life may be a critical window during which infants can experience new flavors and textures, indeed leading to greater acceptance later in childhood and into adulthood (4,5). However, infant fruit and vegetable intake is difficult to objectively assess because of parental reticence about infant blood sampling and because of imprecision inherent with rapid food intake recall tools used to query caregivers. However, use of RS-measured dermal carotenoid intensity as a non-invasive biomarker of fruit and vegetable intake must be validated on a number of parameters before it can be reliably deployed for research, clinical use, or community monitoring.

To definitively develop dermal carotenoid intensity as a biomarker of infant fruit and vegetable intake, we ultimately must conduct controlled feeding studies. In controlled studies, the dietary carotenoid inputs and dermal carotenoid responses will be carefully quantitated and can be correlated to develop predictive models relating the two, along with relevant covariates. However, before proposing controlled feeding studies in infants, we must address the following questions specific to this pediatric population: 1) Is skin carotenoid measurement feasible in infants at the finger and heel? 2) How do replicate measurements effect measurement reliability? 3) What are the mean skin carotenoid scores observed across infancy? 4) What are the mean carotenoid intakes and plasma carotenoid concentrations observed in infancy. 5) Are plasma carotenoid concentrations and carotenoid intakes associated with skin carotenoid scores in infants? Primary analyses will focus on 4 month olds.

REFERENCES

1. Mayne ST, Cartmel B, Scarmo S, Jahns L, Ermakov IV, Gellermann W. Resonance Raman Spectroscopic Evaluation of Skin Carotenoids as a Biomarker of Carotenoid Status for Human Studies. Arch Biochem Biophys. 2013;539:163-70. 2. Institute of Medicine (U.S.), Panel on Micronutrients. DRI: dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc [Internet]. Washington, D.C.: National Academy Press; 2002 [cited 2018 Mar 6]. Available from: http://public.eblib.com /choice/publicfullrecord.aspx?p=3375262 3. Ermakov IV, Ermakova M, Sharifzadeh M, Gorusupudi A, Farnsworth K, Bernstein PS, Stookey J, Evans J, Arana T, Tao-Lew L, et al. Optical assessment of skin carotenoid status as a biomarker of vegetable and fruit intake. Archives of Biochemistry and Biophysics. 2018;646:46-54. 4. Grimm KA, Kim SA, Yaroch AL, Scanlon KS. Fruit and Vegetable Intake During Infancy and Early Childhood. Pediatrics. 2014;134:S63-9. 5. Mikkilä V, Räsänen L, Raitakari OT, Pietinen P, Viikari J. Consistent dietary patterns identified from childhood to adulthood: the cardiovascular risk in Young Finns Study. Br J Nutr. 2005;93:923-31. 6. Chan GM, Chan MM, Gellermann W, Ermakov I, Ermakova M, Bhosale P, Bernstein P, Rau C. Resonance Raman Spectroscopy and the Preterm Infant Carotenoid Status: Journal of Pediatric Gastroenterology and Nutrition. 2013;56:556-9.

Section D: Purpose and Objectives

Aim 1: To determine the feasibility and reliability of skin carotenoid measurement in infants.

Aim 2: To determine the mean carotenoid intakes and mean plasma carotenoid concentrations in infants.

Aim 3: To assess the validity of skin carotenoid scores as a correlate of plasma carotenoid concentrations and carotenoid intake in infants.

Aim 4. To determine the relative validity of different infant dietary assessment tools for estimating infant carotenoid intake, energy intake, and food group intake at 4, 6, and 8 months of age.

Section E: Protocol Risks/Subjects

E1. Risk Category

Category 1: Research not involving greater than minimum risk.

E2. Subjects

Gender:
Both

Age:
Adult (18-64 yrs), Geriatric (65+ yrs), Infant/Toddler (0-36 mos)

Ethnicity:
All Ethnicities

Primary Language:
English

Groups to be recruited will include:
Healthy, non-patient, normals

Which if any of the following vulnerable populations will be recruited as subjects?
Children, Women of child bearing potential

Vulnerable populations require special protections. How will you obtain informed consent, protect subject confidentiality, and prevent undue coercion?
The subjects in this study will be healthy, post-partum women of childbearing age along with their healthy infants. Informed, written consent will be obtained from all women participating in the study. The adult participants will be healthy subjects with decisional capacity. During the informed consent process we will inform the adult participants that there is no direct benefit to them or their infants for participating in the study. The infants are too young to provide assent, so informed consent will be obtained from their parents on their behalf.

E3. Pregnant woman/fetus

Will pregnant women and/or fetuses (as described in 45 CFR 46 Subpart B) be enrolled in the research?
No

E4. Neonates

Will neonates of uncertain viability or nonviable neonates (as described in 45 CFR 46 Subpart B) be enrolled in the research?
No

E5. Children

Will children be enrolled in the research?
Yes

Section F: Design/Procedure

F1. Design

Select one category that most adequately describes your research:
z.s) Biomarker/Gene Association Study

Discuss the research design including but not limited to such issues as: probability of group assignment, potential for subject to be randomized to placebo group, use of control subjects, etc.
This is a prospective observational study of the associations between a non-invasive biomarker of fruit and vegetable intake, dermal reflectance, with reported dietary fruit and vegetable intakes and blood biomarkers of fruit and vegetable intake (blood carotenoid concentrations). There are no placebo or control groups.

Inclusion Criteria:
Inclusion: infant is 4-4.5 months old at baseline; was born at term (>/=37 weeks gestation); is within the 5th-95th weight-for-age percentile (inclusive); primary caregiver can speak, read, and understand English; infants are exclusively breast- and/or formula-feeding at baseline. Exceptions to exclusive breast and formula feeding can be made if the infant has been fed a single-grain infant cereal, as is customary in some ethnic populations in Houston, or has consumed equal to or less than 1 teaspoon of solid food per week. Consenting parent or caregiver must be 18 years old or older.

Exclusion Criteria:
Exclusion: If infant has a sibling enrolled in the trial they are not eligible to participate. Infants will be excluded if the infant has a metabolic, digestive, or malabsorptive disorders; has a known bleeding or clotting disorder; requires a special diet; is exposed to tobacco smoke in the home; is currently taking any isolated carotenoid supplements; is using medications or complementary or alternative medications that interfere with dietary fat absorption; and/or has a history of endocrine disorders requiring hormone administration.

F2. Procedure

Overall Study Design: Caregivers will be phone pre-screened to review subject eligibility. Pre-screened subjects and the primary caregiver will be invited to the Children's Nutrition Research Center (CNRC) Metabolic Research Unit (MRU) for on-site screening, consent, and baseline 4-month-old assessments between 4 and 4.5 months of age. Subjects and their primary caregiver will return between 6-6.5 and again between 8-8.5 months of age. At each visit,

caregivers will complete a 7 day food frequency questionnaire (FFQ) on behalf of the infant, an optional infant blood sample will be drawn, infant dermal carotenoid intensity, length, weight, and body fatness will be measured. One week prior to the 6- and 8-month-old visits, the primary caregiver will complete an online secure food intake questionnaire for 3 separate days to provide a 24-hour dietary recall for the infant. A research staff member may contact the caregiver the next day about any questions regarding the 24 hour dietary recall. Lactating mothers will be asked to provide an optional breast milk sample at study visits if they are currently breastfeeding.

Contact 1: Recruitment (less than 1 hour): Subjects will be recruited in-person, by posted flyers, or be social media advertising. For details on recruitment locations, see the attachment "H-43692 Recruitment Sites".

Contact 2: Pre-screening phone/secure video call or in-person interview (less than 1 hour): Review of eligibility and invitation for consent and enrollment will be accomplished by e-mail, phone call, or with the participant's permission, in-person at the point of recruitment. The interested adult will be pre-screened to assess general availability and eligibility for the study. If deemed potentially eligible, they will be invited to the CNRC or secure video call for Contact 3a. If too young, we will waitlist and phone/text/email to confirm eligibility/interest.

Contact 3a: Screening, consent, and enrollment (virtual or in-person) (2 hours): Eligible volunteers will be invited to the CNRC MRU or secure video call for advanced screening of inclusion/exclusion criteria. Eligibility will be reviewed with the research staff by a questionnaire and anthropometric measures taken by nursing or research staff or parent-reported infant weight if by video-call. Parent-reported infant weight will be confirmed during in-person visit 1. Those meeting the inclusion criteria will be invited to consent and enroll. The informed consent will be reviewed by video call, and subjects will be asked to sign an electronic PDF and/or paper copy of the consent forms and return the signed electronic consent or picture of the signed paper consent by e-mail. Alternatively, secure electronic consent forms on RedCap may be used which both parties. Upon receipt, the staff will move forward with virtual education and orientation, query infant demographics (race/ethnicity and sex), and parent contact information. In order to provide financial compensation via the ClinCard (debit card) we are required to collect their social security number. We will not use this number for subject tracking or elsewhere in our records.

Contact 3b: Visit 1 (1 hour): If consent was conducted virtually, wet-signed consent forms will be received upon arrival to the CNRC for in-person visit 1. At the CNRC, infant length, weight, and skinfold thickness will be measured. Those that consent and enroll will complete a food frequency questionnaire for their infant, will provide an optional 10 mL breastmilk sample (if they are currently lactating) for baseline carotenoid and vitamin A status analysis, and an optional blood sample will be provided by the infant (4-8 mL) for baseline blood carotenoid and vitamin A status. Infant dermal carotenoids will be measured at the finger and heel.

Anthropometry: Infant height and weight will be measured visits using standard procedures (measured 3x). Infant fat mass will be estimated from skinfold thickness by validated equation (1) at the 4, 6, and 8 month visits. Trained staff will collect the data.

Dietary Assessment: At each study visit, usual infant consumption of breast milk and/or formula intake (including brand), fruits and vegetables, and other carotenoid-rich foods (e.g. eggs) will be assessed by 7 day recall using a validated infant food frequency questionnaire (FFQ) (2). This FFQ is analyzed using Nutrient Data System for Research (Univ Minnesota) software by the MRU registered dietician (Ann McMeans, RD) and yields food group and nutrient intake data including carotenoids. Dietary intake will be assessed during the 1 week prior to the 6- and 8-month-old study visits through 3x24 hour dietary recalls (2 weekdays and 1 weekend day) using ASA24 (NIH/NCI), a confidential, online tool. In order to assist caregivers in remembering and finding out about what their infant ate each day, they will be given an Infant Food Diary in which to record everything their infant ate during the queried 7 day period. The Food Diaries will be collected at visits 2 & 3 for our records. Research staff will follow-up with the subjects by phone to clarify any food responses as needed. These 24 hour recalls will be analyzed for energy intake, fruit and vegetable servings, and carotenoid intake. If the participants cannot access the ASA24 food survey using their device, the research staff will call them by phone and ask the ASA24 questions in order to complete the recall.

Dermal Carotenoid Assessment: Pressure-mediated RS ("Veggie Meter") will measure dermal carotenoid intensity. Before use, the device is calibrated. The same index finger of the infant is cleaned with an alcohol wipe and placed on the device's lens for 10 s at each visit. Triplicate readings are recorded electronically. Because some infants' fingers may be too small to obtain a reproducible reading, we will also collect a back-up measurement of the infant's heel using the same procedure as for the finger. This device will not diagnose or treat a disease or condition, so will not require FDA Investigational Device Exemption.

Plasma and Breast Milk Sample Collection: All samples will be collected and handled in low light to prevent carotenoid degradation. Infants' blood (4-8 mL, no more than 3 mL/kg body mass) will be collected by venipuncture into evacuated tubes by nursing staff. If venipuncture is unsuccessful, a heel (at 4 months) or toe prick (at 6 or 8 months) by lancet can be used for capillary sampling (up to 2 mL). Plasma will be aliquoted immediately after collection and stored at -80 ℃ for carotenoid analysis and inflammatory cytokine analysis. Lactating mothers have the option to pump total breast milk from one breast (the first breast from which the infant fed at the prior feeding, >1 h prior) manually (Harmony Breast Pump, Medela, IL), total volume recorded, and a 10 mL sample will be collected, lipid content analyzed by the creamatocrit method (3), and the remainder stored at -80 ℃ for carotenoid analysis and inflammatory cytokine analysis. Milk lipids are measured for descriptive purposes as milk carotenoids correlate with milk lipids (4). Remaining

expressed milk can be offered to the infant.

Contact 4, 5, 6, 7: 3 x 24 hour recalls of infant dietary intakes (45 min each): During the 1 week period after the 4-4.5 month old visit, the research coordinator will call/text/email the primary caregiver to notify them that they should begin recording their infant's food and drink in the food diary, and complete an online 24 hour dietary intake recall using ASA24 for the infant from two weekdays and one weekend day. If needed, research staff will place a follow-up call to clarify any information needed from the online dietary recall. Contact 8: Reminder of upcoming visit and 24 hour recall phone calls (5 min): The primary caregiver will be contacted by phone/text/email to confirm subject availability and instructions for preparing for their 24 hour dietary recalls. They will be asked to provide contact information for any additional caregivers that should be interviewed about the dietary intake of the child.

Contacts 9, 10, 11, 12: 3 x 24 hour recalls of infant dietary intakes (45 min each): During the 1 week period before the 6-6.5 month old visit, the research coordinator will instruct the caregiver as described for Contacts 4-7.

Contact 13: Reminder of upcoming visit (5 min): The primary caregiver will be reminded of the date and time of the 6 month study visit.

Contact 14: 6-month study visit (2 hours): The primary caregiver and infant will come to the CNRC MRU between the ages of 6-6.5 months old. Caregivers will complete a semi-quantitative FFQ reflecting on the dietary intakes of their infant during the past 7 days. Infant dermal carotenoids will be measured by pressure-mediated reflectance spectroscopy, infants will provide an optional blood sample (4-8 mL) for carotenoid and vitamin A analysis, and lactating mothers will be asked to provide an optional breast milk sample (10 mL). Infant length, weight, and skinfold thickness will be measured.

Contacts 15, 16, 17, 18: 3 x 24 hour recalls of infant dietary intakes (45 min each): During the 1 week period before the 8-8.5 month old visit, the research coordinator will instruct the caregiver as described for Contacts 4-7.

Contact 19: Reminder of upcoming visit (5 min): The primary caregiver will be reminded of the date and time of the 8 month study visit.

Contact 20: 8-month study visit (2 hours): The primary caregiver and infant will come to the CNRC MRU between the ages of 8-8.5 months old. Caregivers will complete a semi-quantitative FFQ reflecting on the dietary intakes of their infant during the past 7 days. Infant dermal carotenoids will be measured by pressure-mediated reflectance spectroscopy, infants will provide an optional blood sample (4-8 mL) for carotenoid and vitamin A analysis, and lactating mothers will be asked to provide an optional breast milk sample (10 mL). Infant length, weight, and skinfold thickness will be measured.

1. Schmelzle HR, Fusch C. Body fat in neonates and young infants: validation of skinfold thickness versus dual-energy X-ray absorptiometry. The American Journal of Clinical Nutrition. 2002;76:1096¿100. 2. Palacios C, Rivas-Tumanyan S, Santiago-Rodríguez EJ, Sinigaglia O, Ríos EM, Campos M, Diaz B, Willett W. A Semi-Quantitative Food Frequency Questionnaire Validated in Hispanic Infants and Toddlers Aged 0 to 24 Months. Journal of the Academy of Nutrition and Dietetics. 2017;117:526-535.e9. 3. Lucas A, Gibbs JA, Lyster RL, Baum JD. Creamatocrit: simple clinical technique for estimating fat concentration and energy value of human milk. Br Med J. 1978;1:1018 20. 4. Tanumihardjo SA, Russell RM, Stephensen CB, Gannon BM, Craft NE, Haskell MJ, Lietz G, Schulze K, Raiten DJ. Biomarkers of Nutrition for Development (BOND) Vitamin A Review. J Nutr. 2016;146:1816S-1848S.

Section G: Sample Size/Data Analysis

G1. Sample Size

How many subjects (or specimens, or charts) will be used in this study?

Local: 21 Worldwide: 21

Please indicate why you chose the sample size proposed:

A final n=21 is sufficient to estimate the mean time required to measure skin carotenoid concentrations in 4 month olds, to estimate the reliability of skin carotenoid score measurements in 4 month olds, obtain estimates for mean and SD skin carotenoid scores in 4 month olds, and examine the correlation between skin carotenoid scores and plasma carotenoid concentrations and carotenoid intake in 4 month olds.

G2. Data Analysis

Provide a description of your plan for data analysis. State the types of comparisons you plan (e.g. comparison of means, comparison of proportions, regressions, analysis of variance). Which is the PRIMARY comparison/analysis? How will the analyses proposed relate to the primary purposes of your study?

Experimental Question 1: Assess the feasibility of triplicate skin carotenoid measurements in infants by calculating the mean time required for measurement.

Approach - mean time to measure skin carotenoid scores in triplicate at the finger and heel were calculated in 4, 6, and 8 month olds (primary endpoint is 4 month old measurements).

Experimental Question 2: The effect of replicate measurements (3 versus up to 6 replicates) on measurement reliability in 4, 6, and 8 month olds.

Approach: Calculate the intraclass correlation coefficients and 95% confidence intervals using generalized linear mixed models with restricted maximum likelihood. Models specify a random replicate effect with nesting of replicates within infant and no covariates. ICC is calculated by dividing the variance effect for replicate by the total variance.

Experimental Question 3: Calculate the mean skin carotenoid scores, plasma carotenoid concentrations, and carotenoid intakes in infants.

Approach: Mean and standard deviation skin carotenoid scores, plasma carotenoid concentrations, and carotenoid intakes are calculated for 4, 6, and 8 month old infants.

Exploratory Questions: The correlation between skin carotenoid scores, at the finger or heel, with dietary carotenoid intake and total plasma carotenoid concentrations in 4, 6, and 8 month olds.

Approach: Generalized linear mixed models controlled for age, skin measurement location, and their interaction, with either plasma carotenoids or dietary carotenoid intake as predictors of the outcome skin carotenoid scores.

Section H: Potential Risks/Discomforts

H1. Potential Risks/Discomforts

Describe and assess any potential risks/discomforts; (physical, psychological, social, legal, or other) and assess the likelihood and seriousness of such risks:

Potential risks or discomforts may result from phlebotomy such as discomfort, bruising, or infection at the venipuncture site. Subjects may experience dizziness or dehydration or fainting. Risks of breast milk collection by manual breast pumping are discomfort of the breast. There is a risk of loss of confidentiality.

H2. Data and safety monitoring plan

Do the study activities impart greater than minimal risk to subjects?

No

H3. Coordination of information among sites for multi-site research

Is the BCM Principal Investigator acting as the SPONSOR-INVESTIGATOR for this multi-site research?

No or Not Applicable

Is BCM the COORDINATING CENTER for this multi-site research?

No or Not Applicable

Section I: Potential Benefits

Describe potential benefit(s) to be gained by the individual subject as a result of participating in the planned work.

Potential benefits to be gained by the individual subject as a result of participating in the planned work include satisfaction and accomplishment for benefiting society and supporting biomedical research on an understudied population (infants).

Describe potential benefit(s) to society of the planned work.

Development of a non-invasive biomarker of fruit and vegetable intake in infants will facilitate population monitoring as well as objective clinical assessment of dietary intake. The preliminary data gained from this study will provide the basis for proposing larger, controlled feeding studies in this population. These controlled feeding studies will be necessary to develop dermal carotenoid intensity as a quantitative biomarker of infant fruit and vegetable intake. Tools for accurately monitoring fruit and vegetable intake of infants can greatly improve the responsiveness of clinical and community programs to prevent childhood obesity and reduce long-term chronic disease risks.

Do anticipated benefits outweigh potential risks? Discuss the risk-to-benefit ratio.

The potential benefits to society outweigh the potential risks, because the potential risks to the individual are minimal.

Section J: Consent Procedures

J1. Waiver of Consent

Will any portion of this research require a waiver of consent and authorization?

No

J1a. Waiver of requirement for written documentation of Consent

Will this research require a waiver of the requirement for written documentation of informed consent?

Yes

Explain how the research involves no more than minimal risk to the participants, and the specifics demonstrating that the research does not involve procedures for which written consent is normally required outside of the research context.

Written documentation of consent will be waived for the phone call to pre-screen volunteer eligibility. We will ask them several general questions about their relationship to the infant, their availability to answer phone calls during the day and come to the CNRC over the next 4 months, the name and date of birth of the infant, and how the infant is currently being fed, and if the infant has been diagnosed with any metabolic, digestive, or allergic disorders that affect their ability to digest and process foods. The questions asked on the phone call or in person screening are for the purpose of determining their eligibility and scheduling only. If the subjects do not provide informed written consent, the screening data will not be used for subsequent published analyses, only for internal recruitment tracking analyses.

J2. Consent Procedures

Who will recruit subjects for this study?

PI
Research subject (ex - recruitment of family member into genetic studies)
PI's staff
Third Party: TCH/BCM Pediatric Clinic Staff

Describe how research population will be identified, recruitment procedures, any waiting period between informing the prospective participant and obtaining consent, steps taken to minimize the possibility of coercion or undue influence and consent procedures in detail.

Websites and volunteer databases hosted by the CNRC, BCM, University of Texas, Texas Medical Center, and other local clinical study recruitment websites and listservs.

Electronic advertisements in the TCH employee newsletter, internal BCM newsletters, and UT internal newsletters. Word of mouth recruiting. Facebook will be used to advertise the study, but advertisements will have commenting and messaging capabilities blocked to prevent PHI sharing over social media.

Paper and electronic displays of flyers on the BCM campus, the Texas Children's Health Plan Center for Women and Children clinics, the TCH/BCM pediatric, Texas Childrens Pediatrics, and the TCH/BCM obstetrics and gynecology clinics, the TMC and UT Health campuses, Texas A&M Institute of Biosciences and Technology, Texas Womans University Houston, Houston Community College Coleman College for Health Sciences, the John P. McGovern TMC Commons, the Texas TMC Library, Rice University, University of Houston, MD Anderson, TCH Duncan Neurological Research Institute, Houston Methodist, Harris Health System, TMC university libraries, and Memorial Hermann, Houston Public Libraries and coffee shops and restaurants located at the TMC.

In-person flyer distribution or flyer posting (pending the permission of the site) in the waiting rooms or exam rooms of the TCH/BCM pediatrics, Texas Childrens Pediatrics, and Texas Children's Health Plan Clinic, at regional daycare centers, museums, zoos, Women Infants and Children (WIC) clinics, lactation clinics, and breastfeeding support group meetings and forums in-person and by flyers.

We will not collect any PHI during the in-person recruitment, but if caregivers wish to be contacted about the study, we will record their name, phone number, and e-mail address so that we may set up a phone call to discuss the study further. Otherwise, we will refer subjects to e-mail the study coordinator as directed on the flyer.

Are foreign language consent forms required for this protocol?

No

J3. Privacy and Intrusiveness

Will the research involve observation or intrusion in situations where the subjects would normally have an expectation of privacy?

No

J4. Children

Will children be enrolled in the research?
Yes

J5. Neonates

Will non-viable neonates or neonates of uncertain viability be involved in research?
No

J6. Consent Capacity - Adults who lack capacity

Will Adult subjects who lack the capacity to give informed consent be enrolled in the research?
No

J7. Prisoners

Will Prisoners be enrolled in the research?
No

Section K: Research Related Health Information and Confidentiality

Will research data include identifiable subject information?
Yes

Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
No

Specific information concerning alcohol abuse:
No

Specific information concerning drug abuse:
No

Specific information concerning sickle cell anemia:
No

Specific information concerning HIV:
No

Specific information concerning psychiatry notes:
No

Demographic information (name, D.O.B., age, gender, race, etc.):
Yes

Full Social Security #:
Yes

Partial Social Security # (Last four digits):
No

Billing or financial records:
No

Photographs, videotapes, and/or audiotapes of you:
No

Identifiable biospecimens
Yes

Other:
No

At what institution will the physical research data be kept?
Baylor College of Medicine

How will such physical research data be secured?

Paper records will be stored in a locked filing cabinet in the Children's Nutrition Research Center at Baylor College of Medicine in a locked office.

At what institution will the electronic research data be kept?

Baylor College of Medicine

Such electronic research data will be secured via BCM IT Services- provided secured network storage of electronic research data (Non-Portable devices only):

Yes

Such electronic research data will be secured via Other:

Yes, (describe below):
Electronically stored data will be saved on a restricted access shared drive maintained by BCM IT Services.

Will there be anyone besides the PI, the study staff, the IRB and the sponsor, who will have access to identifiable research data?

Yes, identify the classes of the persons:
The samples and coded subject IDs will be transmitted to a contract lab, Labcorp, for the purpose of cholesterol concentration analysis.

Please describe the methods of transmission of any research data (including PHI, sensitive, and non-sensitive data) to sponsors and/or collaborators.

PHI and sensitive data will not be transmitted to sponsors or collaborators. Only de-identified, non-sensitive data will be shared with collaborators or sponsors.

Will you obtain a Certificate of Confidentiality for this study?

No

Please further discuss any potential confidentiality issues related to this study.

We do not anticipate any further confidentiality issues related to this study.

Section L: Cost/Payment

Delineate clinical procedures from research procedures. Will subject's insurance (or subject) be responsible for research related costs? If so state for which items subject's insurance (or subject) will be responsible (surgery, device, drugs, etc). If appropriate, discuss the availability of financial counseling.

There are no expected costs to the subjects or their insurance for the research procedures. The only cost that may arise would be if they were to have a health issue associated with phlebotomy, in which case they or their insurance would be responsible for that care cost.

If subjects will be paid (money, gift certificates, coupons, etc.) to participate in this research project, please note the total dollar amount (or dollar value amount) and distribution plan (one payment, pro-rated payment, paid upon completion, etc) of the payment.

Dollar Amount:

180

Distribution Plan:

Subjects will be eligible for up to $180 in remuneration as grocery giftcards or a prepaid credit card (ClinCard) and complimentary parking at the CNRC for study visits.

The distribution plan is based on the study visit, with a greater final payout at the end of the study for completing the study. The distribution plan is as follows:

1. Consent and baseline visit- 4-4.5 months of age: $40 for visit completion, $10 for optional blood draw, $10 for optional breast milk collection 2. 6-6.5 months of age follow-up visit: $30, $10 for optional blood draw, $10 for optional breast milk collection 3. 8-8.5 months of age follow-up visit: $50, $10 for optional blood draw, $10 for optional breast milk collection

Section M: Genetics

How would you classify your genetic study?

Discuss the potential for psychological, social, and/or physical harm subsequent to participation in this research. Please discuss, considering the following areas: risks to privacy, confidentiality, insurability, employability, immigration status, paternity status, educational opportunities, or social stigma.

Will subjects be offered any type of genetic education or counseling, and if so, who will provide the education or counseling and under what conditions will it be provided? If there is the possibility that a family's pedigree will be presented or published, please describe how you will protect family member's confidentiality?

Section N: Sample Collection

SAMPLE: Blood

What is the purpose of the sample collection?

Infant blood samples will be collected for plasma isolation. Plasma carotenoids, vitamin A, and lipids will be analyzed for each study visit.

Inflammatory cytokine concentrations will be measured in plasma samples to determine the correlation between plasma carotenoid concentrations, skin carotenoids, and and plasma markers of inflammation.

Blood glucose, insulin, and C-peptide concentrations will be measured to investigate the association between plasma carotenoids, cholesterol, and plasma cytokine concentrations with glucose and insulin metabolism.

For blood draws, specify the amount drawn, in teaspoons, at each visit and across the course of the subjects entire participation time.

Each blood draw will be for 4-8 mL (1-1.5 tsp).

1. Visit 1: Consent, Enrollment, 4-4.5 month old visit: 1-1.5 teaspoons of blood (4-8 mL) 2. Visit 2: 6-6.5 month old visit: 1-1.5 teaspoons of blood (4-8 mL) 3. Visit 2: 8-8.5 month old visit: 1-1.5 teaspoons of blood (4-8 mL)

Is there the possibility that cell lines will be developed with this sample?No

Sample will be obtained from:

Other: CNRC Metabolic Research Unit

Will the sample be stripped of identifiers?

No

If sample will be released outside the hospital:

Will sample be released to anyone not listed as an investigator on the protocol? Will the information be identifiable, coded or de-identified?

Yes. Coded samples transferred to LabCorp for cholesterol analysis.

Will sample material be sold or transferred to any third parties? Will the information be de-identified?

Yes. Coded samples transferred to LabCorp for cholesterol analysis.

If sample will be banked for future use:

Where will the sample be banked and for how long?

No.

Does the banking institution have an approved policy for the distribution of samples?

No.

If the entire sample will NOT be used during the course of this research study:

Will the remaining tissue be discarded? If not what will be done with the remaining sample after study completion and how long will the sample be kept?

The remaining sample will not be discarded. The remaining sample will be kept indefinitely after study completion at the CNRC/Baylor College of Medicine. If additional nutrient analyses are planned for the sample, then permission from the IRB will be obtained.

Will samples be made available to the research subject (or his/her medical doctor) for other testing?
No

If a subject withdraws from the study:

Will subject have the option to get the remaining portion of their sample back?
No

Will samples be destroyed? If not, will they be kept anonymously? What will happen to the sample if the subject revokes authorization?
If subject withdraws, samples will be retained for analysis. If subject revokes authorization for sample analysis, then samples will be disposed of.

Will data obtained from their sample be deleted? What will happen to the sample if the subject revokes authorization?
If subject withdraws, data will be retained for analysis. If subject revokes authorization for data analysis, then data will be deleted.

Will study data or test results be recorded in the subject's medical records?
No

Will results of specific tests and/or results of the overall study be revealed to the research subject and or his/her doctor?
No.

Please identify all third parties, including the subject's physician, to receive the test results.
No third parties will receive test results.

SAMPLE: Other 1: Breast Milk

What is the purpose of the sample collection?
The breast milk sample will provide a measure of carotenoids and vitamin A being provided to nursing infants from mother's milk.

Inflammatory cytokine concentrations will be measured in breast milk samples to determine the correlation between breast milk carotenoid concentrations and markers of inflammation.

For blood draws, specify the amount drawn, in teaspoons, at each visit and across the course of the subjects entire participation time.
Lactating mothers will be asked to provide a breast milk sample at each visit, for as long as they are still breastfeeding their infant.

1. Visit 1, 4-4.5 month old visit: 10 mL of breast milk or 2 teaspoons. 2. Visit 2, 6-6.5 month old visit: 10 mL of breast milk or 2 teaspoons. 3. Visit 3, 8-8.5 month old visit: 10 mL of breast milk or 2 teaspoons.

Is there the possibility that cell lines will be developed with this sample?No

Sample will be obtained from:
Other: CNRC Metabolic Research Unit

Will the sample be stripped of identifiers?
No

If sample will be released outside the hospital:

Will sample be released to anyone not listed as an investigator on the protocol? Will the information be identifiable, coded or de-identified?
No.

Will sample material be sold or transferred to any third parties? Will the information be de-identified?
No.

If sample will be banked for future use:

Where will the sample be banked and for how long?
No.

Does the banking institution have an approved policy for the distribution of samples?
No.

If the entire sample will NOT be used during the course of this research study:

Will the remaining tissue be discarded? If not what will be done with the remaining sample after study completion and how long will the sample be kept?
The remaining sample will be retained indefinitely at the CNRC. If additional analyses are planned for the sample, then permission for the IRB will be sought.

Will samples be made available to the research subject (or his/her medical doctor) for other testing?
No

If a subject withdraws from the study:

Will subject have the option to get the remaining portion of their sample back?
No

Will samples be destroyed? If not, will they be kept anonymously? What will happen to the sample if the subject revokes authorization?
If subject withdraws, samples will be retained for analysis. If subject revokes authorization for sample analysis, then samples will be disposed of.

Will data obtained from their sample be deleted? What will happen to the sample if the subject revokes authorization?
If subject withdraws, data will be retained for analysis. If subject revokes authorization for data analysis, then data will be deleted.

Will study data or test results be recorded in the subject's medical records?
No

Will results of specific tests and/or results of the overall study be revealed to the research subject and or his/her doctor?
No.

Please identify all third parties, including the subject's physician, to receive the test results.
No third parties will receive the test results.

Section O: Drug Studies

Does the research involve the use of ANY drug* or biologic? (*A drug is defined as any substance that is used to elicit a pharmacologic or physiologic response whether it is for treatment or diagnostic purposes)
No

Does the research involve the use of ANY gene transfer agent for human gene transfer research?
No

O1. Current Drugs

Is this study placebo-controlled?
No

Will the research involve a radioactive drug?
No

Section P: Device Studies

Does this research study involve the use of ANY device?
No

Section Q. Consent Form(s)

None