WP 1.3a: Probiotics for term infants

1. Related WPs, MG contact person: Synergy with WP 1.1, 1.2a, 1.3b, 1.4b, 1.6, 2.2, 2.4, 4.3. MG: Per Sangild

2. Key involved personnel, their institution and mail address (project leader + main study site underlined):
Bo Lönnerdal, Prof., Univ. of California, Davies, US, bllonnerdal@ucdavis.edu (5%)
Olle Hernell, Prof., Umeå University, Olle.Hernell@pediatri.umu.se (5%)
Britt Christensen, Arla Foods amba, Britt.Christensen@arlafoods.com (50%)
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Xiaonan Li, Phys., Nanjing Medical Univ., Affiliated Children's Hosp., Nanjing, xiaonan6189@yahoo.com (20%)
Yongmei Peng, Physician, Children's Hospital of Fudan University, Shanghai, ympeng99@yahoo.com.cn (20%)
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Yanqi Li, post doc., Comparative Pediatrics and Nutrition, Univ. Copenhagen, yli@life.ku.dk (5%)

3. Main aim and sub-aims:
To evaluate the sensitivity to infections after feeding with an infant formula containing probiotics as compared to an infant formula without probiotics.
Target population for intervention and control groups: Healthy full-term infants of mothers who could not or resigned completely from breast-feeding at age 21 ±7 days. Breast-fed term infants act as reference group. All groups, intervention, control and breast fed, are n = 200.

4. Background and a central hypothesis:
The main goal of infant formula development is to approach the composition and functionality of breast milk to give formula-fed infants as small a disadvantage as possible compared to breast-fed infants. Breast-fed infants have been shown to have a gut microbiota more dominated by bifidobacteria and lactobacilli compared to formula-fed infants, who have a more diverse microbiotia, containing *Bacteroides*, bifidobacteria, staphylococci, *Escherichia coli* and clostridia. These observed differences have been suggested to contribute to the lower incidence of infections, allergies and gastrointestinal disturbances in breast-fed compared with formula-fed infants, probably via a maturational effect on the gut and systemic immune systems. If this is the case, it seems reasonable to develop infant formulas to support the establishment of a microbiota, which resembles that of breast-fed infants, for example by adding probiotics.
We hypothesize that addition of probiotics will reduce infections in formula-fed infants, via improved composition of their gut microbiotia and immunity and in this way make them more similar to breast-fed infants.

5. Key analyses and methods:
The study is a randomized, double-blind, controlled trial with clinical recording of infections episodes (gastrointestinal and upper and lower respiratory infections).

6. Expected results:
Reduced incidence of infectious episodes (gastrointestinal and upper and lower respiratory infections) in infants fed with infant formula containing probiotics compared with standard formula.

7. Estimated time frame

Task	2013				2014				2015				2016				2017				2018			
Planning, protocol																								
Sample collection	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x						
Clinical data analysis																		x	x					
Possible microbiota analyses																		x	x	x				
Possible immunity biomarkers																x	x	x						
Publication(s)																						x		

8. Estimated budget from NEOMUNE:
5.0 mio DKK (financed entirely by ARLA Foods, no funds from DSF)

9. Estimated budget from elsewhere:
2.0 mio DKK (local doctors and hospital infrastructure). 1.0 mio DKK from synergy with NEOMUNE partners (fecal and plasma sample analyses)

10. Additional comments:

- The study outline is published at ClinicalTrials.com. The exact nature of the intervention and the details of the recorded endpoints are kept confidential to the public and to NEOMUNE partners not involved in the study until the results of the study will be published.
- This project is run entirely by the sponsoring industry partner but association with the NEOMUNE network is aimed to provide win-win at many levels. Scientific synergy with other NEOMUNE projects (see point 1) can be reached by sharing/collaborating on:
  1) Protocol formation for nutritional studies in Chinese hospital settings (WP 1.6a).
  2) Experience in performing clinical studies in China (WP 1.6a, 1.6b, 1.4b).
  3) Experience with Danish-Chinese partnerships, scientific, legal, ethical etc. (WP 1.6b, 1.4b, 4.3).
  4) Evidence for use of probiotics in newborn infants across the world (WP 1.5, 1.6b).
  5) Synergy and information from animal probiotic studies (WP 2.2, WP3.2).
  6) Possible shared analytical capacity for gut microbiota analyses (WP 1.1, BGI Shenzhen).
  7) Possible shared capacity for blood immunity analyses (WP 1.2a, SDU Denmark).
  8) Increased networking with Chinese partner institutions and stakeholders (WP 4.3).
  9) Joining the NEOMUNE scientific meetings for science and partnerships (WP 4.2).

WP 1.3b: Bioactive milk formula for term infants

1. Related WPs, MG contact person: Synergy to WP1.2a,1.3a,1.4b,1.6a,2.4,4.3. MG contact: Per Sangild

2. Key involved personnel, their institution and mail address (project leader + main study site underlined):
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Yongmei Peng, Physician, Children's Hospital of Fudan University, Shanghai, ympeng99@yahoo.com.cn (20%)
Zailing Li, Peking University Third Hospital, Department of Paediatrics, Beijing, topbj163@sina.com (20%)
Yanqi Li, post doc., Comparative Pediatrics and Nutrition, Univ. Copenhagen, yli@life.ku.dk (5%)

3. Main aim and sub-aims:
To evaluate effects on the immune system after feeding with an infant formula containing an improved Whey Protein Concentrate (WPC). Target population for intervention and control groups: Healthy full-term infants of mothers who could not or resigned completely from breast-feeding at infant age 21 ±7 days. Breast-fed term infants act as reference group. All groups, intervention, control and breast fed, are n = 200.

4. Background and a central hypothesis:
Specific milk proteins have been demonstrated to have antimicrobial activities and can prevent diarrhea in small children. It has also been shown that infants fed with formula with added WPC have reduced frequency of acute otitis media compared with infants fed with a standard formula.
We hypothesize that addition of an improved WPC will reduce infections in formula-fed infants, improve their health and make them more similar to breast-fed infants.

5. Key analyses and methods:
The study is a randomized, double-blind, controlled trial with clinical recording of infection episodes (gastrointestinal and upper and lower respiratory infections).

6. Expected results:
Reduce incidence of infectious episodes (gastrointestinal and upper and lower respiratory infections) in infants fed with infant formula containing an improved WPC compared to standard formula.

7. Estimated time frame

Task	2013				2014				2015				2016				2017				2018			
Planning, protocol																								
Sample collection	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x						
Clinical data analysis																		x	x					
Possible microbiota analyses																		x	x	x				
Possible immunity biomarkers																x	x	x						
Publication(s)																						x		

8. Estimated budget from NEOMUNE: 5.0 mio DKK
Financed entirely by ARLA Foods, no funds from DSF.

9. Estimated budget from elsewhere:
2.0 mio DKK (local doctors and hospital infrastructure). 1.0 mio DKK from synergy with NEOMUNE partners (faecal and plasma sample analyses).

10. Additional comments:

- The study outline is published at ClinicalTrials.com. The exact nature of the intervention and the details of the recorded endpoints are kept confidential to the public and to NEOMUNE partners not involved in the study until the results of the study will be published.
- This project is run entirely by the sponsoring industry partner but association with the NEOMUNE network is aimed to provide win-win at many levels. Scientific synergy with other NEOMUNE projects (see point 1) can be reached by sharing/collaborating on:
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  2) Experience in performing clinical studies in China (WP 1.6a, 1.6b, 1.4b).
  3) Experience with Danish-Chinese partnerships, scientific, legal, ethical etc. (WP 1.6b, 1.4b, 4.3).
  4) Evidence for use of probiotics in newborn infants across the world (WP 1.5, 1.6b).
  5) Synergy and information from animal probiotic studies (WP 2.2, 3.2).
  6) Possible shared analytical capacity for gut microbiota analyses (WP 1.1, BGI Shenzhen).
  7) Possible shared capacity for blood immunity analyses (WP 1.2a, SDU Denmark).
  8) Increased networking with Chinese partner institutions and stakeholders (WP 4.3).
  9) Joining the NEOMUNE scientific meetings for science and partnerships (WP 4.2).