WP 1.5: Probiotics, feeding and NEC in preterm infants

1. WP (related WPs, MG contact): WPs 1.4b, 1.6a, 1.7; 2.2, 3.1, 3.2. MG contact: Gorm Greisen

2. Key involved personnel, institutions, mail address (project leader + main study site underlined):

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3. Main aim and sub-aims:

1. To examine the periodicity of the NEC rate at Copenhagen University Hospital
2. To describe the epidemiology of NEC at the national level
3. To describe the association between gut microbiota and NEC
4. To examine the effect of routine use of probiotics on a) rate of NEC and b) fecal microbiota
5. To evaluate the importance of naso-gastric tube biofilm on early upper GI colonization in preterm infants
6. To reexamine the Bell staging of necrotizing enterocolitis

4. Background and a central hypothesis:

NEC is one of the four major neonatal morbidities in preterm infants. NEC has high mortality and carries a high risk of long term consequences in the form of short bowel syndrome and neurological deficit. NEC is probably caused partly by too aggressive enteral feeding and bacterial overgrowth. Clinically, it is difficult to balance the risk of NEC with the nutritional needs of the small, preterm infant.

We hypothesize that:

a) The incidence and mortality of NEC is stable in absolute terms but decreasing when corrected for gestational age and weight at birth

b) The use of probiotics is associated with lower risk of NEC and probably with a 'better' gut microflora

c) The clinical staging system of Bell is suboptimal in describing the clinical presentations of NEC.

5. Key analyses and methods:

Collection of routinely recorded clinical data. Re-assessment of clinical X-rays. Access to local and national databases. Statistical analysis. DNA analysis of stool from cohorts of preterm infants from Copenhagen and Newcastle. Prospective study of preterm infants at high risk of NEC.

6. Expected results:

Confirmation or rejection of hypotheses (a-c)

7. Estimated time frame

Task	2013				2014				2015				2016				2017				2018			
1+2+4a. Data analysis				x	x	x																		
1+2+4a Publication													x											
3+4b DNA analysis														x										
3+4b Data analysis															x									
3+4b Publication														x		x								
5. Data collection					x	x	x																	
5. Data analysis								x																
5. Publication														x										
6. Analysis											x	x	x	x										
6. Publication															x		x							
Publication(s)											1		1	1	1	1	1							

8. Estimated budget from NEOMUNE:

0.8 mio DKK (0.33 MD PhD + tuition + annum), ressources moved to 1.6a.

9. Estimated budget from elsewhere:

0.7 mio DKK (analytical costs 0.3, contribution from senior researchers 0.4). Additional funds will be required to perform all the indicated tasks and further support will be applied for (e.g. task 5).

10. Additional comments:

- This work package has synergies with ongoing projects at Copenhagen University Hospital and Statens Serum Institute, as well as collects new data from patients at Copenhagen University Hospital.
- The depth of the gut microbiota analyses (various levels of conventional and/or molecular techniques) will be decided upon depending on the quality of the samples collected in relation to the hypothesis and the funding available at the time of sample collection. Collaboration with other partners will be added as judged appropriate (BGI Shenzhen, Newcastle, Univ. Copenhagen). Work not started initially due to lack of supplementary funding and now due to difficulties in getting permission from the data protection board. March16: still not started
- The data collected may influence the possible choice and the mode of probiotic interventions for preterm infants in WP 1.6b. No longer relevant.
- The key institution is part of WP 1.4b (data base project) and part of this WP will relate to observations collected for the overall international data base (NEC, probiotics use, antibiotics).