WP 2.4: Bioactive formula diets for preterm pigs

1. Related WPs, MG contact person: Synergy with WPs 1.3b, 1.4a, 2.1-2.3. MG contact: Thomas Thymann

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

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3. Main aim and sub-aims:

The benefits of breast-feeding may be explained by absorption of milk bioactives present in natural milk. We aim to use the established preterm pig model (WP 2.0), coupled with the experience from WPs 2.1-2.3, to test the effects of selected compounds and milk diets provided by the NEOMUNE partners ARLA FI and Danone. The compounds will be selected based on their potential effects on immunity, gut and brain endpoints.

4. Background and a central hypothesis:

While specific milk components have long been hypothesized to have important immune effects, firm evidence of effects in sensitive newborn infants is not available. Using diet- and microbiota-sensitive preterm pigs, we investigate how milk formulas enriched with selected milk bioactives affect immune, gut and brain maturation. It is not possible to investigate all relevant milk bioactive components in pigs. The choice and number of interventions will rely on further discussions with our partners, as guided by both scientific rationale, the model development phase (as described in WP2.0) and financial constraints. Specifically, for the brain functional and structural endpoints, the exact nature/timing of the functional tests and their structural correlates will be defined in WP2.0 studies (the model development phase).

We hypothesize that feeding milk formula diets containing specific bioactive components will improve immunity, gut and brain maturation, as tested in the preterm piglet model.

5. Key analyses and methods:

Preterm pigs are derived by cesarean section and provided parenteral nutrition and minimal enteral nutrition with either formula or formula enriched with bioactive compounds. Following 5-10 days they are gradually weaned off parenteral support. After transition to full enteral nutrition both groups are bolus-fed up until day 22. On postpartum days 4 and 9, all pigs are subjected to an open field test to document motor skills and explorative behavior. Additionally, cognitive function is assessed in a T-maze system during the last week of the experiment. The extent, to which microbial composition and other endpoints related to gastrointestinal function will be studied, depends on the nature of the selected bioactive compounds. Likewise, the exact choice of endpoints related to brain function will be determined when the model development phase (WP2.0) has been completed.

6. Expected results:

We expect to test the effect of one or two bioactive compounds/diets from each of the partners ARLA FI and

Danone. The results will provide the best available evidence for the effects of these selected compounds/diets in a preterm neonatal animal model. We expect to produce three to four scientific manuscripts, one for each of the tested compounds.

7. Estimated time frame

Task	2013				2014				2015				2016				2017			
Planning, protocol							x	x												
Sample collection									x	x	x	x								
Open field test									x	x	x	x								
Cognitive test									x	x	x	x								
Clinical assessment									x	x	x	x								
Blood brain barrier													x	x	x	x				
Brain and gut histology													x	x	x	x				
Gut microbiota													x	x	x	x				
SCFA													x	x	x	x				
Cytokines													x	x	x	x				
Gut digestive function													x	x	x	x				
Publication(s)																	x	x	x	x

8. Estimated budget from NEOMUNE: 3.2 mio DKK

- The budget for WP2.4 is mainly derived from our industrial partners (ARLA FI and Danone)
- Remaining parts will be derived from the DSF funds of NEOMUNE (Thomas Thymann).

9. Estimated budget from elsewhere:

0.6 mio DKK is supplied as university self-financing, 1.7 mio DKK from industrial sources (e.g. ARLA Foods amba), 1.0 mio DKK from personnel and product resources supplied by our industrial partners. ARLA Foods Ingredients have provided 1.5 mio DKK extra (2015) for additional WPC study within NEOMUNE.

10. Additional comments:

- The exact choice of endpoints in WP 2.4 will have to await the results of the model development phase in WP 2.0. The industrial partners will be given priority for further use of the preterm pig brain model beyond the described project phase, according to separate contracts.
- While brain endpoints are the main priority in this WP, also gut and immunity endpoints will be recorded if this is relevant and economically feasible. Contribution from ARLA Foods FI will in part support these analyses for interventions of interest for this company.
- This WP may expand over the course of NEOMUNE as new ingredients/products become relevant for tests from new/existing university/industrial partners.