CARBO-CLICK

CARbohydrate BOosted ControL of Intestinal Immunity in ChicKens

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Background

Early-life coccidiosis in broiler chickens, caused by protozoan parasites *Eimeria*, causes intestinal disease, and predisposes for overgrowth by harmful gut bacteria (such as *Clostridium*) which can result in severe gut inflammation. Prebiotic carbohydrates have a great potential as alternatives for preventive and therapeutic use of antimicrobials in broilers against these intestinal infections.
The *Eimeria*/*Clostridium* infection model in broilers is very suitable to be used in the development of an *in-vitro* workflow to test effects of carbobiotics on early-life intestinal barrier and immune functions for chickens and can serve as a basis for translation of this tool to humans (and other animals).

Main objectives

Carbobiotic induced increased broiler health reduces use of antimicrobials/ antimicrobial resistance, improves food safety, and is beneficial for both broiler and human health.

- Acquire in-depth knowledge and tools for assessment of in-feed carbobiotics that improve early-life gut and immune health in broilers.
- The human tool will enable preclinical analyses to assess beneficial effects of carbobiotics on early-life human health and immune-fitness.

Approach

1. Design a translational *in-vitro* workflow to evaluate anti-infective, immuno-modulating effects of carbobiotics in the broiler chicken gut. This workflow consists of:
   - The Chicken ALIMEntary tRact mOdel (CALIMERO, WP-1)
   - Co-cultures of broiler gut-organoids with innate immune cells and microbiota or fecal waters (WP-2)
2. The *in-vitro* broiler workflow will be translated into an *in-vitro* workflow for humans (WP-3).

Deliverables

WP1 Deliverables

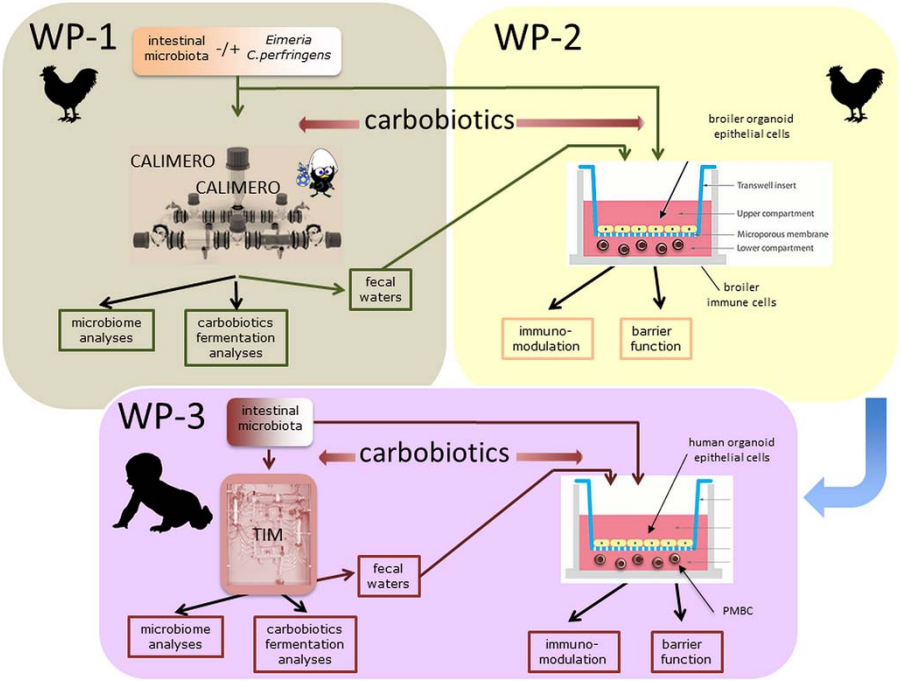
1. A protocol for reproducible establishment of a standardized broiler microbiota that can be exposed to *Eimeria* or/and *C. perfringens* (months 0-6)
2. A protocol for fermentation of carbobiotics by microbiota from broilers in CALIMERO (months 6-24)
3. A protocol for collection of 'fecal water' from CALIMERO (months 0-24)
4. A list of selected intermediate carbohydrate structures to be used in WP2 (months 6-30)
5. A description of concentration-dependent effects of various carbobiotics on microbiota composition and activity (incl. during *Eimeria* and *C. perfringens* infection) (months 12-36)

WP2 Deliverables

1. A protocol to culture broiler-organoids in a transwell system using broiler-specific growth factors (months 0-12)
2. A protocol to co-culture broiler-organoids with innate immune cells (months 12-24)
3. Protocols to co-culture organoids with (infected) broiler microbiota and fecal waters (months 12-24)
4. Concentration-dependent effects of oligosaccharides on broiler organoid system (months 0-36)

WP3 Deliverables

1. A new advanced human *in-vitro* workflow consisting of co-cultures of organoids with intestinal microbiota and epithelial and immune cells, based on WP2 (months 30-40)
2. A selection of relevant carbobiotics will be tested in this model (months 39-45)



Overall project deliverables

1. Strategic mechanistic and applicable knowledge on effects of specific carbobiotics and their fermentation products on gut microbiota, immune responsiveness, and gut function
2. A protocol for an innovative translational *in-vitro* workflow, consisting of CALIMERO and innovative stem cell-derived broiler gut-organoids, co-cultured with gut microbiota and innate immune cells
3. A list of potential carbobiotic-products suitable for further development and application as in-feed alternatives for antimicrobials
4. First steps in translating the newly developed *in-vitro* workflow for broilers to human and other (young) animals

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Logo: Jean Paul ten Klooster

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