Preclinical Brown Norway Rat Models for the Assessment of Infant Formulas in the Prevention and Treatment of Cow's Milk Allergy - DTU Orbit (18/10/2019)

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**Background:** Infant formulas (IFs) based on hydrolysed cow's milk proteins are central in the management of cow's milk allergy (CMA) in infants and small children. New IF compositions with improved prevention and treatment properties are needed, along with appropriate preclinical animal models, to evaluate these properties before introduction into humans.

**Objectives:** We aimed to develop preclinical models for the assessment of the primary preventive and desensitising capacity of cow's milk IF in allergy-prone, high-IgE responder Brown Norway rats. Method: Preventive capacity was assessed in cow's milk-naïve rats given a 2- or 4-week regimen of whey-based extensively hydrolysed IF (eHF), partially hydrolysed IF (pHF), or intact β-lactoglobulin (BLG) ad libitum in drinking bottles, followed by intraperitoneal (i.p.) immunisation with BLG. Desensitising capacity was assessed in orally BLG-sensitised rats after a 3- or 6-week regimen of eHF, pHF, or intact BLG administration in drinking bottles, followed by i.p. challenge with BLG. Primary preventive and desensitising capacity were analysed by serum BLG-specific IgG1 and IgE. Results: The preventive regimens did not induce detectable BLG-specific IgG1 or IgE in cow's milk-naïve rats. A preventive regimen consisting of pHF or BLG, but not eHF, induced complete tolerance to BLG, as demonstrated by the absence of BLG-specific IgE following i.p. immunisation. Desensitising regimens had a limited effect on BLG-specific IgG1 or IgE when comparing sensitised rats before and after treatment. Challenge with BLG (i.p.) increased BLG-specific IgE in all treatment regimens except for in the BLG group, suggesting a limited desensitising capacity of IF based on hydrolysates and a need for the presence of intact allergen for desensitisation. Conclusions: The presented models highlight that different mechanisms are at play in the induction of de novo tolerance to cow's milk proteins and the desensitisation of CMA. Different IF products may be needed for the primary prevention and treatment of CMA.

**General information**
- **Publication status:** Published
- **Organisations:** National Food Institute, Research group for Food Allergy, Arla Foods
- **Corresponding author:** Bøgh, K. L.
- **Pages:** 307-314
- **Publication date:** 2019
- **Peer-reviewed:** Yes

**Publication information**
- **Journal:** International Archives of Allergy and Immunology
- **Volume:** 178
- **Issue number:** 4
- **ISSN (Print):** 1018-2438
- **Ratings:**
  - BFI (2019): BFI-level 1
  - Web of Science (2019): Indexed yes
- **Original language:** English
- **Keywords:** Animal models, Food allergy, Infant formula, Milk
- **DOIs:** 10.1159/000495801
- **Source:** FindIt
- **Source ID:** 2443980248

Research output: Contribution to journal › Journal article – Annual report year: 2019 › Research › peer-review