

Thesis offering "Genetic determinism of vaccine response and caecal microbiota composition in free-range chickens."



This thesis will contribute to the production of knowledge that will make it possible to support the change of practices, in particular in terms of integrated management of health and well-being in free-range poultry farms.

Supervision

- Marie-Hélène Pinard-van der Laan (DR, HDR; thesis director)
- Fanny Calenge (CR, team leader; co-supervisor)

Location of the thesis

- UMR GABI, INRAE, Centre de Jouy-en-Josas, Domaine de Vilvert
- Team GeMS : " Genetics, Microbiota, Health

Funding

- 50% INRAE (Holoflux metaprogram) and 50% NOVOGEN. INRAE contract.

Abstract

Vaccination is one of the most efficient preventive methods to fight against infectious diseases in livestock. However, genetic variations and variations in the gut microbiota

influence the effectiveness of the vaccine response. In addition, genetic variations of the host impact those of the microbiota. Finally, little is known about the influence of free-range animal husbandry on the vaccine response. However, it is in full expansion, especially for its supposed effect on the improvement of animal welfare. Combining genetic selection and modulation of the microbiota to improve and homogenize the vaccine response in free-range livestock would be an innovative approach, responding to a strong societal and sanitary challenge.

To better understand how the complex interactions between microbiota and genetics impact the vaccine response, the PhD student will study the genetic control of the vaccine response and the gut microbiota in a cohort of 400 free-range laying hens under experimental conditions. Measurements of immune parameters, vaccine response, gut microbiota composition and behavior will be performed with the support of immunologists and behaviorists. Individual genotyping data will be used to conduct GWAS to identify genomic regions involved in the genetic control of these traits. The comparison of the genetic architectures of the different traits will allow a better understanding of the interactions between traits, and a first evaluation of the feasibility of a genetic selection for a better vaccine response. In parallel, an association study between caecal microbiota variability and phenotypes will be conducted (MWAS). It will allow to understand the part of the variability of the vaccine response explained by the microbiota and to evaluate the interest of an approach based on the modulation of the microbiota.

Background

Vaccination is the most effective strategy for the prevention of infectious diseases. However, its effectiveness could be improved, as most vaccines show variable efficacy at the individual level. In animal husbandry, genetic variability of the response to vaccines has been demonstrated, either by successful selection of this response or by estimating its heritability. On the other hand, variability of the gut microbiota probably influences the vaccine response, but this has not been clearly demonstrated in chickens. The gut microbiota interacts with the host in a close symbiotic relationship. Variations in the gut microbiota influence many traits in farm animals, including health traits. In an integrated health management approach, combining the effect of genetics on immunocompetence with that of the gut microbiota with the use of pharmaceuticals and management to improve vaccine response could be an innovative strategy, taking into account the new holobiont concept.

The project responds to increasingly important socio-economic issues. Improving the immunocompetence of animals is crucial to prevent the spread of infectious pathogens and to reduce the use of drugs. Moreover, the market for veterinary vaccines is huge; improving the efficacy of vaccines by adopting a more personalized veterinary medicine is of direct interest to this market. Secondly, the efficiency of genetic improvement programs is essential to the competitiveness of the livestock industry. The discovery of predictive markers for better health and the identification of the underlying genetic variability, combined with nutritional advice to modulate a favorable microbiota, would allow the design of innovative breeding programs integrating improved health and robustness. Finally, societal expectations are calling for more responsible production channels, particularly with the development of "organic" channels. Research must contribute to this evolution, and this thesis will contribute to the production of knowledge that will allow to accompany the change of

practices, in particular in terms of integrated management of health and well-being in free-range poultry farms.

Scientific state of the art - originality of the project

It has been established that host genetic variations control part of the vaccine response, in particular by work carried out in the host team on experimental chicken lines genetically selected for their strong response to the Newcastle disease virus (NDV) vaccine (Minozzi et al. 2007, 2008). On the other hand, the effect of gut microbiota on vaccine response is likely in hens, but not yet clearly demonstrated. In the hen, health is the result of complex interactions between the gut microbiota and host immunity (Broom and Kogut 2018). The gut microbiota has long been identified for its protective effect against *Salmonella* colonization through a competitive exclusion phenomenon. Its involvement has since been shown for the control of several other pathogens, not all intestinal (Clavijo et al. 2018). In addition, numerous works in hens show that the gut microbiota influences the immune response (Broom and Kogut, 2018; Kogut et al 2020). The impact of gut microbiota composition on vaccine response is beginning to be established in humans but remains to be demonstrated in chickens. Results obtained in the host team show that vaccination has an effect on the composition of the hen microbiota (Borey et al, 2022), thus showing the probable existence of a functional link between vaccination and microbiota in an infectious context (infectious bronchitis virus). The existence of an effect of the composition of the microbiota on the vaccine response in a non-infectious context remains to be demonstrated.

The composition of the intestinal microbiota is very dynamic under the influence of numerous factors of variation, all of which are likely to influence through the microbiota the expression of the numerous traits that it regulates. Among them, the diet is one of the most important, as well as the use of various feed additives (probiotics, prebiotics, post-biotics, essential oils, etc.). The farming system (Chen et al 2019) and host genetics (Calenge et al, 2020a; 2020b) also have a role to play. Finally one can experimentally change the microbiota of chickens by administering high doses of antibiotics (e.g. Schokker et al, 2017; Wisselink et al, 2017).

In the first phase of the Vaccibiota project, we demonstrated the impact of genetic lineage and rearing mode (indoor vs. outdoor) on microbiota and vaccine response (Lecoeur et al, Journées de la Recherche Avicole, Tours, 2022; Lecoeur et al, WC-GALP, Rotterdam, 2022). This thesis focuses on the second phase of the Vaccibiota project, which aims to further our understanding of the role of genetics and caecal microbiota in variations in vaccine response, behavior and immune parameters.

This thesis project is original and innovative in many aspects, including three main ones:

- (1) It studies the holobiont, not just the animal. Until now, the interest of genetics and microbiota as levers on vaccine responses have been studied as individual factors, but never in combination to our knowledge.
- (2) This interaction between genetics and microbiota will be studied in a free-range farm, whose effect on the vaccine response and all other measured parameters (behavior, immune parameters) is unknown.
- (3) The project will take into account animal welfare, which will allow the identification of levers for improving the vaccine response that are compatible with animal welfare and will allow the establishment of possible links with the composition of the gut microbiota.

Research questions

The PhD student will mainly answer the following questions:

- What is the genetic architecture of vaccine response, microbiota composition, and behavior in the chicken population studied?
- Are there common genomic regions between these traits?
- What portions of the phenotypic variability can be attributed for each trait to a) genetic variation and b) variations in the caecal microbiota?

Material and methods

The analyses carried out during the thesis will be based on data mainly acquired before the beginning of the thesis thanks to an experiment carried out within the framework of the France Futur Elevage Vaccibiota2 project. A cohort of 400 hens from a commercial line provided by the company Novogen will have been reared at the INRAE PEAT unit (Nouzilly), on the floor and with free-range access from twelve weeks of age. At the beginning of the thesis, the sequences of the 16S V3-V4 amplicons of the hen caecal microbiota DNA will have been obtained. The animals will have been genotyped. Vaccine response measurements will have been acquired for the most part before the start of the thesis but a contribution to their acquisition would be desirable. Behavioral measurements will have been acquired by the expert partners of the Vaccibiota project (UMR PRC and Institut Technique d'Aviculture). The person recruited for the thesis will link genotyping data with phenotypic data (vaccine response and microbiota first, immune parameters and behavior second) in order to conduct association analyses (GWAS) in the cohort and thus understand how host genetic variations control phenotypes. In addition, she will conduct association studies between variation in gut microbiota components and the same phenotypes, to understand the role of gut microbiota in phenotypic variation.

Skills needed to start the thesis

These analyses will require skills in bioinformatics, biostatistics and quantitative genetics. A background in quantitative genetics is preferred.

The candidate is expected to be curious and open-minded in the context of an interdisciplinary thesis.

Work environment

This thesis will allow the PhD student to train in association analyses used in both quantitative genetics (GWAS) and microbiology (MWAS), in a highly interdisciplinary context. The PhD student will acquire skills in immuno-phenotyping; microbiology; bioinformatics and biostatistical analysis of microbiota sequencing data; welfare measures; biostatistics. This thesis will be financed for half by the company Novogen, which will ensure the recruit a visibility in the business world of the poultry industry and will allow him to better understand the current practices in poultry breeding. The thesis work will be carried out within the GeMS team of the GABI unit, in Jouy-en-Josas, under the supervision of Marie-Hélène Pinard-van der Laan and Fanny Calenge. The recruit will be provided with all the necessary equipment and will be able to rely on the team's expertise in immunogenetics, bioinformatics, genetics and biostatistics. Support outside the team will be possible for the other disciplines with the partners of the Vaccibiota project, and training in bioinformatics and biostatistics will be possible (R, 16S analysis). The person recruited will be invited to participate in

meetings and networks in which this work is included (in particular the Sanba and Holoflux metaprograms). + presentations/participation in relevant conferences

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See also

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