FELLOWSHIP SUMMARY REPORTS

GIOVANNA DE MATTEIS PhD

"Evaluation of the functional significance of Interleukin-8 haplotype for anti-viral immunity"

Theme 3: **Transformational Technologies and Innovation**

Host Institution: **University College Dublin**, School of Agriculture and Food Science- Ireland

Host Collaborator: Associate Professor **Dr Kieran Meade**

Dates: **30th May 2022 to 6th August 2022**

Consensus:
I give my consent to post this report on the Co-operative Research Programme's website.

1. What were the objectives of the research project? Why is the research project important?

The aim of this project was to enhance the understanding of the molecular process that regulates immune response in bovine respiratory diseases to contribute to breeding cattle that are more resistant to diseases. Viruses, particularly respiratory viruses cause significant economic losses to the livestock industries worldwide. A key feature of disease pathogenesis is the ability of the multiple causal organisms to subvert the immune response of the host and the role of Interleukin 8 in viral infections has not been well researched, particularly in livestock. Therefore, the work focused on the cytokines Interleukin-8, a key regulator of neutrophil mobilisation and activation in response to infection.

Breeding for disease resistance in cattle requires both a more comprehensive understanding of the bovine immune response as well as the identification of genes underlying variation in immune responsiveness and disease resistance. The final objective should be to select cattle with superior immunity, thereby underpinning the sustainability of the livestock sector and reduce losses and welfare issues, such as antimicrobial resistance.

2. Were the objectives of the fellowship achieved?

The specific objectives of the proposal, relative to the assessment of *"in vitro"* experiments were only partially achieved due to the COVID-19 pandemic and due to the two-year postponement of the fellowship; therefore, the project was carried out in spring/summer 2022.
In agreement with the supervisor of the host institution, we substituted the "*in vitro"* experiments with an "*in vivo*" study that aimed to identify disease-associated immunophenotypes in cattle through the evaluation of effect of vitamin D deficiency on inflammatory cytokines and immune gene expression in cattle affected with

viral lung disease. The modified objectives of the proposal were therefore achieved resulting in contributions to on-going research which will result in a co-authored publication, training in flow cytometry, attendance at an international conference and recruitment of collaborators in Ireland for a funding call.

3. What were the major achievements of the fellowship?

The teamwork is ongoing, hence there will be more chances to continue and evolve the research project.
For now, the major experimental achievements were:

1) The set up and execution of ELISA assays for the determination of Vit D levels in bovine serum samples. Results showed significant differences in Vit D levels between calves coming from farms with different incidence of lung diseases. This has contributed to the completion of a PhD project.
2) The extraction of mRNA from whole blood samples collected in vacutainer with stabilizing solution. The mRNA samples will be run on platform FLUIDIGM to evaluate gene expression of markers involved in the immune response which includes the inflammatory cytokine interleukin 8. A 96 gene panel set will be used to evaluate cytokines, chemokines and markers of immune regulation and immune cell activation. This has contributed to the completion of a PhD project and a research paper.
3) Building a collaborative network which involved my attendance at an international meeting held in Ireland and recruitment of these collaborators to a research funding call in my home institution.

4. Will there be any follow-up work?

- **Is a publication envisaged? Will this be in a journal or a publication? When will it appear?**

  Results of this study will be part of a publication in an international peer reviewed journal in 2022-2023.

- **Is your fellowship likely to be the start of collaboration between your home institution and your host?**

  Thanks to the OECD fellowship, we expect that the collaboration started in UCD will turn into a long-term collaboration between both institutions. A Memorandum of Understanding (MoU) between UCD and CREA is being signed, therefore we also expect a possible exchange of students and postdoctoral researchers in the future.
  Therefore, we are exploring funding opportunities to support future collaboration between UCD and CREA in the immunogenetics and immune response as well as in elucidating the importance of vitamin D in genetic resistance to diseases. A new project about the evaluation of Vit D levels in water buffalo has been submitted in collaboration with the UCD.

- **Is your research likely to result in protected intellectual property, novel products or processes?**

  We did not plan to patent our findings, but we do not exclude the possibility in the future.

5. How might the results of your research project be important for helping develop regional, national or international agro-food, fisheries or forestry policies and, or practices, or be beneficial for society?

The results obtained by this project offers significant opportunities for enhanced livestock breeding which can directly address agricultural productivity constraints and the One-Health issues that involve food security, human nutrition and health. Indeed, there is urgent need for more detailed understanding of the immune response to infectious agents in livestock species in order to find alternatives to over reliance antibiotics and the emergence of antimicrobial resistance.
The innate immune system plays a critical role in the early immune response and determines outcome to bacterial and viral infections, making it an obvious starting point for the identification of immune phenotypes associated with disease susceptibility.

Success in this regard would not only reduce animal diseases, and therefore improve animal welfare but will also reduce the cost of treating infectious diseases on farm and reduce our reliance on exogenous antibiotics. Moreover, the study of the immunoregulatory role of Vit D in cattle is useful to understanding the role of this metabolite in health and disease.

6. How was this research relevant to:

- **The objectives of the CRP?**

The Co-operative Research Programme's main objectives are sustainability, food security and nutrition. Global health of humans and animals is interconnected, pointing to the need for a "One Health" perspective. Animal welfare and antibiotic resistance are important topics in consumers and citizens' expectations for the livestock sector. It is necessary to regain consumer confidence by improving practices, transparency and establishing a constructive dialogue with the society at large. Solutions can be found in a renewed animal care, improving real time monitoring of animal welfare and in enhancing natural disease resistance and robustness of animals especially at the early life stages by exploiting genetic diversity. In line with the EU strategy on Animal Health, this project will promote alternative strategies to antibiotic usage by supporting natural mechanisms of disease resistance in terrestrial livestock.

In addition, the aim of the CRP fellowship is to strengthen the international exchange of ideas and increase international mobility and co-operation among scientists working in the same areas. The common interests have favoured fruitful discussions and exchange of ideas that we put to good use with future collaborations.

- **The CRP research theme?**

This project was directly relevant for the Theme III section "Advanced breeding tools/Genetic and genomic technologies". The understanding the basis of a natural resistance to diseases though the evaluation of components of the immune system as the expression of cytokines, chemokines as well as the metabolites (Vit D) could provide an innovative approach to control cattle diseases.

The research has significant economic impacts as it focuses on increasing health and welfare and consequently the production of farm animals and income of farmers.

7. Satisfaction

- **Did your fellowship conform to your expectations?**

Yes, the fellowship exceeded my expectations in providing fruitful opportunities, knowledge increasing and research connections.

- **Will the OECD Co-operative Research Programme fellowship increase directly or indirectly your career opportunities? Please specify.**

This Co-operative research fellowship has been an excellent opportunity to improve my career and lead to new research collaboration and academic output. It allowed for me to meet scientists in similar and complementary disciplines, share experiences and methodological approaches. This will be very important for my scientific career.

- **Did you encounter any practical problems?**

I didn't encounter any problems.

- **Please suggest any improvements in the Fellowship Programme.**

My suggestion is to include in criteria of eligibility a minimum period of 12 week to spend at the host institution, for a better connection between the institutes and to have more time to complete all phases of the project.

8. Advertising the Co-operative Research Programme

- **How did you learn about the Co-operative Research Programme?**

I learned from my Research Institute.

- **What would you suggest to make it more "visible"?**

The programme needs more advertisements on different scientific platforms and social medias to get scientist's attention.

- **Are there any issues you would like to record?**

I have not faced any issues, just to thank the OECD for the support and the opportunity. The fellowship was good and successful.