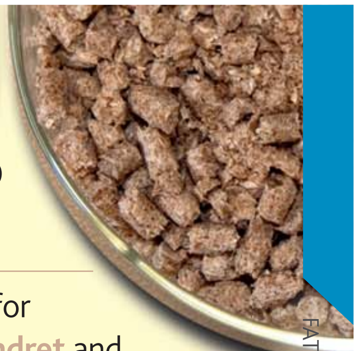


Farm feed findings

Optimising animal feeds and nutritional supplements are vital goals for improving food production in Europe. Against this context, **Dr Florence Gondret** and **Professor Sandrine Lagarrigue** lead a consortium exploring the way feed energy affects animal tissues

Can you briefly outline how the FatInteger project emerged?

FatInteger was proposed to gain scientific knowledge around lipid metabolism, which regulates fat storage and its partition between animal tissues, taking into account genotypes and diets as sources of flexibility.

What are the primary scientific objectives of the project?

First, we aim to better understand the cellular actors and master elements controlling variations in body adiposity and lipid content in the tissues of growing animals, where diets of differing feed energy sources are used.

Second, our approach is unique in our comparative use of two farm species: pigs and chickens. Working with the same approaches and methods for avian and mammal species and carefully coordinating the dietary trials will reveal specific and generic clues for prospective feeding and genetic schemes within these species.

Lastly, because FatInteger will generate large datasets on animal tissues, the final objective is the development of software tools for gathering, summarising and mining biological information that could serve a wide scientific community.

Are you using any novel approaches to analyse tissues and reveal the key actors?

We propose gathering physiological, genetic, phylogenetic, statistical and bio-informatics skills. FatInteger aims to acquire transcriptional and biochemical data relevant to tissue function and so it is important for us to consider key tissues serving as energy reserves (adipose tissues) and using energy (liver and muscle), as well as the way they communicate with one another via blood circulation.

Statistical methods are also required to analyse the differences induced by experimental conditions and to find the genes that work together (networks). In additon, the upstream regulators of these networks will be proposed by searching common motifs of response on the promoters (the 'driving licence' of expression) of the genes and analysing the influences between genes by automatic reasoning informatics.

Finally, the similarities and specificities in these actors are observed by gene evolution between mammals and other vertebrates. This last overview will be very helpful in choosing the best candidates to be modulated in forthcoming genetic schemes.

How significant is the application of genomics to these investigations?

At least 300 molecular players in lipid metabolism have been discovered when considering nutrition challenges, physio-pathological conditions, pharmacological modulations and genetics in laboratory rodents. Most pathways converge to transcription factors (the 'master elements'), which sense stimuli and modulate the expression of panels of genes. However, specificities may limit the translation of rodent data into actionable technologies in animal production. Most studies have been conducted on only one kind of tissue or one type of isolated cells. Functional genomics has emerged during the past 10 years as a way of revisiting the multiplicity of cellular actors and crossroads of different functional pathways.

What benefits are afforded by this approach?

Collecting large datasets simultaneously in various organs and without any a priori knowledge on their modulations has the main benefit of providing complete answers and novel hypotheses to evaluate the global animal response. Both transcriptomics (the molecular messages within cells) and metabolomics (the circulating metabolites in blood) are associated in this project to reveal organ-related specificities and their concerted actions in regulating lipid metabolism and body fat.

How does working collaboratively on such a project enhance your research?

The five partners comprising around 30 people across associated institutions and disciplines are highly dependent on each other, so collaboration in the project is effective and fruitful. The benefits will be seen for informatics as well as biological science, with the development of computational tools and approaches in association with data producers.

Have you had any positive responses from policy makers and industry experts so far?

This work has the potential to interest a wide range of service companies committed to animal feeds and nutritional supplements, and industries connected to animal breeding. The results of the project will be disseminated through professional congress talks.

Because FatInteger also aims to provide application tools in bioinformatics, interventions in academic and vocational training sessions dedicated to data integration will also be realised, and a statistics forum will be organised by one of the project partners.

Optimising animal intake

The **FatInteger** project addresses the physiological bases of feed efficiency, body composition and growth. The study will refine nutritional recommendations for farm animals and predict outcomes on other phenotypic traits

MODERN FARM ANIMAL producers are forced to juggle numerous economic, environmental and social concerns. Key considerations include the efficiency of feed conversion into meat, egg or milk products; the composition of animal products themselves; and the environmental waste associated with their production.

Fatty animals tend to be less feed efficient and the producer is paid on carcass yield with a lower grade for excessive amounts of fat in the carcass. However, higher fat content in meat products is often associated with better quality in terms of taste. For this reason, it is vital that producers consider the body fat content of the animals and the way this fat is distributed among tissues.

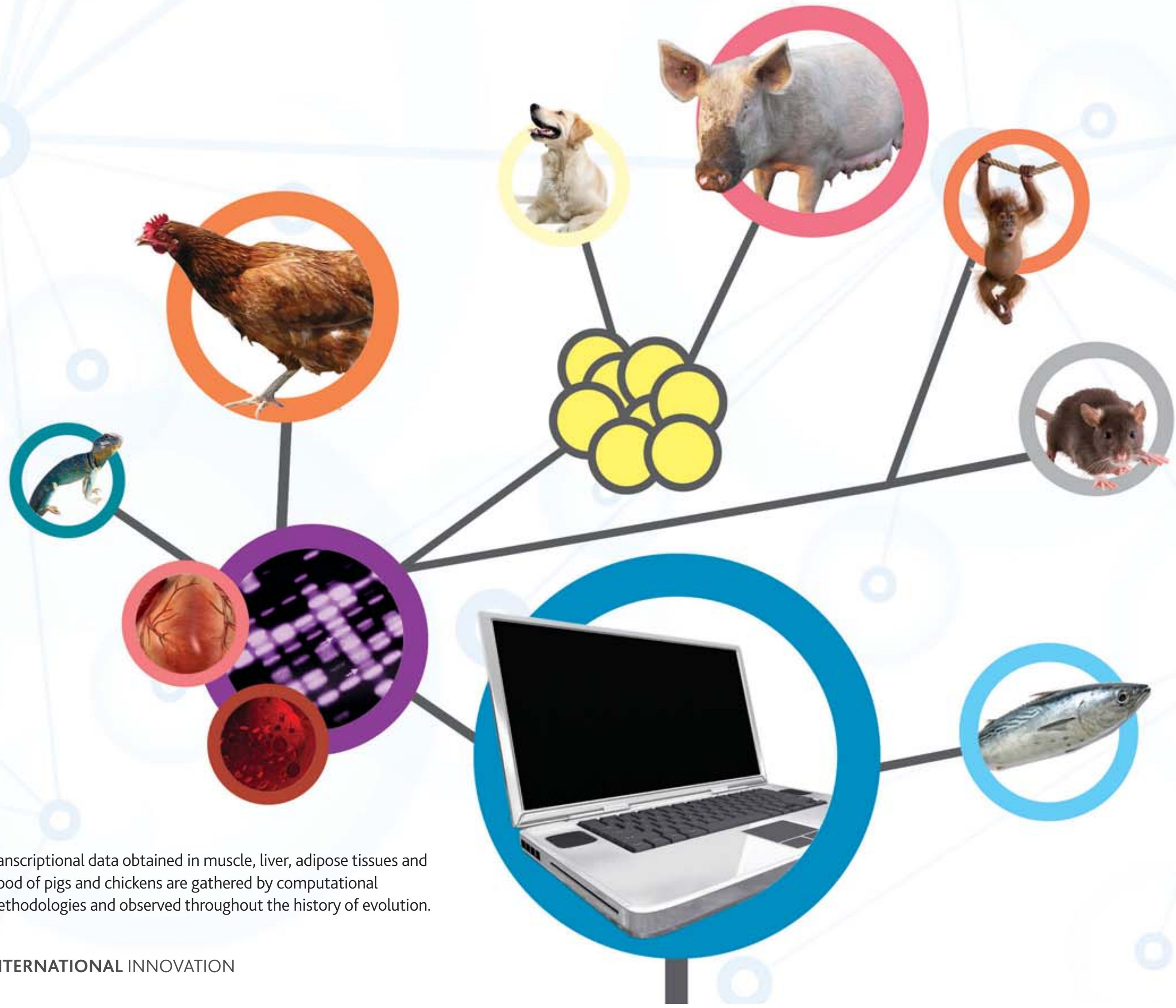
The link between genetics and feeding concerns is key. Diet is chosen based on issues such as cost of ingredients and nutritional values; however, the animals' genotypes have a significant impact on the way feed is utilised and how it benefits growth and the subsequent quality of meat.

Meat production is increasing worldwide and one way for farms and producers to maintain profitability is to enhance feed efficiency – the feed to gain. It is also important to consider the availability and fluctuating costs of feed resources. Cereals, for example, have risen in price and are in much greater demand as they have become increasingly integral to human diets. In these instances, it is vital that producers find other diet sources; but their impacts on the efficiency and quality of meat production must be considered.

LIPID STORAGE AND ENERGY USE

To assist in this, the FatInteger project is exploring the adaptation of genotypes to diets containing different feed energy sources, using starch from cereals compared with lipids from vegetable oils. The project, which began in March 2012 and is coordinated at the French National Institute for Agricultural Research (INRA), is evaluating responses in terms of growth, body composition and tissue lipid features.

By studying the flexibility of lipid metabolism, researchers Dr Florence Gondret and Professor Sandrine Lagarrigue believe they will be able to highlight the ways in which phylogenetically distant farm species – pigs and chickens – adapt to their environment, including changes in diet: "In growing animals, feed energy is used primarily for cellular functions (survival) and tissue construction (growth)," explains Gondret. "It is also stored in various organs as lipids. These lipids serve as a remobilised energy reserve to cope with meal intervals and situations of stress inherent to fluctuations of the environment



Transcriptional data obtained in muscle, liver, adipose tissues and blood of pigs and chickens are gathered by computational methodologies and observed throughout the history of evolution.

(such as ambient temperature), the distribution of more or less appropriate diets and the presence of pathogens."

The study is closely related to nutrigenomics – the research that describes the influence of food constituents on gene expression. Nutrigenomics has the potential to reveal the mechanisms by which body fat activates and deactivates specific genes. Moreover, this approach sheds light on fat's ability to produce signal molecules to regulate appetite, homeostasis and growth when isoenergetic low-fat diets are introduced: "Both body fat content and its distribution result from an imbalance between lipid storage and energy use," Gondret explains. "Therefore, understanding flexibility in lipid metabolism is crucial in ensuring optimal growth trajectories."

By studying the flexibility of lipid metabolism, the researchers believe they will be able to highlight the ways in which phylogenetically distant farm species – pigs and chickens – adapt to their environment

DIFFERENT DIETS

So far, FatInteger has shown that the responses to diets rich in cereals or rich in lipids and by-products – each formulated with the same level of metabolisable energy and proteins – are clearly different between the two species.

According to researchers, there are no observable variations in growth performance and tissue fat contents in chickens provided with differing diets, irrespective of the genetic line considered. The study shows that chickens were thus able to synthesise and adjust the same quantity of lipids, regardless of differences in dietary fat content. On the other hand, the diets markedly altered growth, body composition and tissue lipid contents in the pigs tested. "In both species, not only lipid metabolism but also protein metabolism is affected, which underscores interconnections between the two in the use of feed energy and impact upon body composition," stipulates Gondret.

HOLISTIC APPROACH

FatInteger has adopted a multidisciplinary approach in order to obtain, record and analyse its results. A broad team of experts is required to acquire transcriptomics and lipidomics data in key tissues and from the whole blood in divergent genetic lines, and also to employ statistical, bioinformatics and phylogenetics skills to analyse the tissue- and species-specificities of the key actors. Specialists involved in the project comprise physiologists, phylo-geneticians, statisticians and bioinformaticians: "Making biological sense of numerous experimental data and identifying the hierarchy between cellular actors is the 'holy grail' of animal science," Gondret explains. The challenge is mainly conceptual and methodological, and it requires interdisciplinary skills.

The success of FatInteger is based on a constant dialogue between biologists and geneticists, who provide the experimental data, the statisticians and informaticians who integrate the data, and a synergy between both to generate and test new biological and evolutionary hypotheses. In light of this, the study will now focus on the way the information is gathered and treated to decipher the key elements by which animals responded to feeds and genetic selection in the early stages of the work. The dependence and interactions between genes within each organ will be one major consideration. To explore this further, the researchers will need to examine the network structure within the correlated genes using dedicated statistics and bioinformatics. A software tool is currently in development to search for complex patterns within genomic sequences that may be shared by the co-expressed genes.

The heterogeneity of datasets – whether molecular, metabolic, phenotypic or otherwise – is another major concern for the teams. In order to accomplish this, it is necessary to unify the biochemical transformations of proteins and the regulatory genetic effects in a way that allows an automatic interrogation of current knowledge on cell signalling pathways. This will allow upstream transcriptional regulators to be proposed.

Finally, as evolution is regarded as a branching process in which genes are born, selected or terminated, exploring phylogenetic trees of vertebrates for the key regulatory candidates will provide a signature of lipid metabolism, species by species, throughout history.

POSITIVE OUTCOMES

Although it will contribute to developing rational means of optimising nutrition with respect to the animal's genotype, the FatInteger project is still in its infancy. However, Gondret believes that understanding the hierarchy in metabolic pathways and the actors in homeostatic control could, in the future, assist in refining nutritional recommendations, finding biomarkers that help in monitoring animals in precision farming to adapt feeding regimens, and predicting the consequences of this on other phenotypic traits. This knowledge could also suggest whether or not agonists of particular metabolic pathways, such as micronutrients, should be added to the diets of animals bred for their meat. Beside nutrition, the targets will also enhance the traits recorded in support of ongoing genomic selection.

INTELLIGENCE

FatInteger

OBJECTIVES

A better knowledge of key cellular actors and their synergy of actions in controlling lipid metabolism is needed to unravel strategies aimed at controlling body fatness, a phenotypic trait of economical and sustainable importance for farm animal production.

KEY COLLABORATORS

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FLORENCE GONDRET is currently Senior Researcher at INRA-Rennes, France, where she heads a team working on the physiology and metabolisms of growth in pigs. Her research interests include the metabolic changes responsible for variation in adiposity as a driver of adaptation, with a special interest in suboptimal nutrition (early and late) as constraints. Physiology, proteomics, gene expression and computational biology in relation to tissue development and cell functions are her main areas of expertise.

SANDRINE LAGARRIGUE is Professor of Genetics and Genomics, working with agricultural engineers, MSc students, and academic and industrial professionals at AgroCampus-Ouest Faculty, France. Her research concerns the genetics of body fat and lipid metabolism in poultry, focusing on gene expression and regulation. DNA polymorphisms, transcriptomics, gene networks, cis-regulating elements in relation to lipid metabolism are her main topics.