A COLLABORATIVE EUROPEAN NETWORK ON RABBIT GENOME BIOLOGY: RGB-NET

Garreau H.[1], Bosze Z.[2], Curik I.[3], Piles M.[4], Rogel-Gaillard C.[5], Thulin C.-G. [6], Fontanesi L.[7] and the RGB-Net consortium

[1]INRA, UR631 SAGA, F-31326, Castanet-Tolosan, France
[2]Agricultural Biotechnology Center, 4. Szentgyörgyi A. Gödöllő, Hungary
[3]University of Zagreb, Faculty of Agriculture, Department of Animal Science, Svetosimunska 25,10.000 Zagreb, Croatia
[4]IRTA, Torre Marimon s/n, E-08140 Caldes de Montbuí, Spain
[5]INRA, UMR1313 Laboratory of Animal Genetics and Integrative Biology, 78 352 Jouy en Josas Cedex, France
[6]Swedish University of Agricultural Sciences, SE-901 83 Umeå, Sweden
[7]University of Bologna, Dept. of Agro-Food Science and Technology, Viale Fanin 48, 40127 Bologna, Italy
*Corresponding author: garreau@toulouse.inra.fr

ABSTRACT

COST Action TD1101 "Rabbit Genome Biology-Net" is an action granted by COST in the domain of Biomedicine and Molecular Biosciences. Chaired by the University of Bologna and INRA, it will last for 4 years from November 2011, and gather 94 experts from 20 European countries and from USA, China, Japan, Taiwan and South Africa. Rabbit Genome Biology-Net (RGB-Net) aims at building an open international network of research organizations, associations and companies in all rabbit research areas and in other complementary research fields (breeders, geneticists, bioinformaticians, physiologists, evolutionists, embryologists, immunologists, physicians, industry experts, etc.) in order to facilitate the transfer of rabbit genomic information from experimental data into usable benefits and applications. Four Working Groups are focused on i) the refinement of the European rabbit genome resources and the development of genome-based platforms, ii) genetic aspects in meat, fur and pet rabbits and biodiversity resources, iii) the rabbit as a model in basic biology and human diseases and as a tool for biotechnology applications, and iv) genetic and comparative genomic aspects for the study, exploitation and management of wild lagomorphs. The outcome is a coordination of rabbit research activities and a transfer of knowledge, that will produce a strong European added value across a broad spectrum of biology research fields.

Key words: European rabbit, lagomorphs, genome biology, translational research, networking expertise

INTRODUCTION

The order *Lagomorpha* includes several species of relevant interest in different fields of applied biology. The most important species is the European rabbit (*Oryctolagus cuniculus*) that is considered not only as livestock (for meat and fur production), but also as an animal model used to address many biological questions, a pest or a wild resource species in several regions, and a fancy animal. The recent sequencing of the European rabbit genome, carried out by the Broad Institute (USA) in collaboration with the INRA (France), opens new perspectives in these different research areas and paves the way to an "omic" vision of rabbit biology. The European network "Rabbit Genome Biology-Net (RGB-Net)" granted by COST since November 2011, will facilitate close cooperation among groups working in different research areas and with complementary expertise maximizing possibilities for translational applications of rabbit genome information. The objective of this paper is to shed information on the Collaborative European Network on Rabbit Genome Biology: RGB-NET.

OBJECTIVES AND BENEFITS

The aim of this Action is to establish a multidisciplinary and cooperating network of experts in different research and applied fields interested in developing new scientific and commercial opportunities, resources and tools from the European rabbit genome and to strengthen and consolidate Europe as a leader in the scientific and economic exploitation of the European rabbit and related species.

As a first step, coordinated activities and additional contributions are needed to refine the rabbit genome sequence, by improving assembly and annotation, as well as to develop and exchange genomic tools. Then, many specialized research and applied fields will benefit from this resource in more advanced studies and applications. For meat rabbit industry, the network will explore the possibility of using genomic selection to improve relevant traits such as disease resistance or feed efficiency. New approaches in rabbit breeding using genomic information will be developed, with the aim to renew breeding schemes. The network will investigate the potential of the European rabbit as a model for human diseases based on the exploitation of genomic information. A better definition of the role of the European rabbit in biotechnology applications and exploration of new avenues in this area are expected. New genomic resources will be used in population genomic studies of wild lagomorph for a better understanding of the current status of wild population spread all over Europe and for conservation and management plans. Comparative genomics will provide additional clues about the domestication process and its consequences on the modification of domesticated rabbit biology.

The final objectives of the network will be to stimulate collaborative research activities among complementary research fields and to promote the rapid transfer of innovations to end-users.

SCIENTIFIC PROGRAMME

Four Working Groups (WG) divided into several tasks have been implemented to meet the scientific objectives defined in RGB-Net (Figure 1).

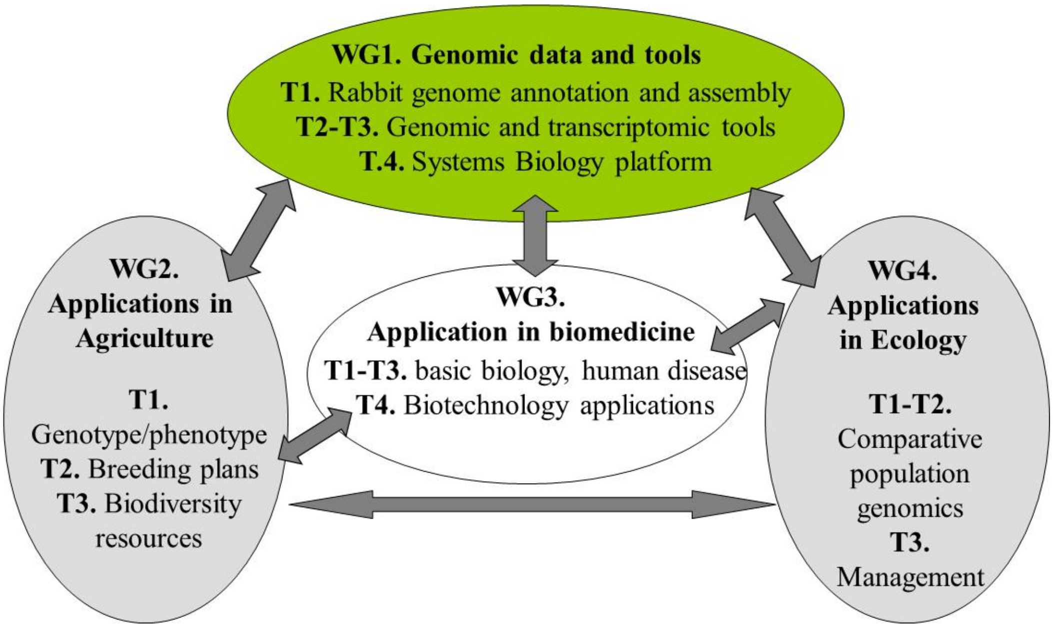

Figure 1: Working groups (WG), tasks (Tn) and interactions between working groups of the COST action rabbit genome biology-net.

Working Group 1: Refinement of the European rabbit genome resources and development of genome-based platforms

Task 1. Improvement of the annotation and assembly of the European rabbit genome

Groups working in comparative genomics, bioinformatics and computational biology will devote resources and platforms to this task. Targeted analysis of candidate regions, discovery of single nucleotide polymorphisms (SNP) by high throughtput resequencing of genomic DNA from various rabbit breeds together with transcriptomic analyses and systems biology approaches will be provided by Action groups. These data will contribute to improve knowledge on the rabbit genome.

Task 2. Sharing and development of genomic tools and information

Resources already available within the Action members (e.g. large DNA fragment libraries) will be shared and/or screened in a coordinated way upon request for the needs of the different groups. SNPs and other information on structural variations will be used to improve annotation of the rabbit genome and to develop high throughput genotyping tools for this species. Platforms for copy number variation analysis (based on array comparative genome hybridization, aCGH) and results of these studies will be shared or produced and developed *ex novo*.

Task 3. Sharing and development of transcriptomic tools and expertise

WG1 will coordinate the acquisition of needed expertise and will explore the use of RNA-seq for practical applications in targeted experiments. According to the needs of the other WG, WG1 will provide coordination for the design of a DNA chip based on the improved annotated European rabbit genome, adding features that may be useful in several applications, including interspecies analysis.

Task 4. Systems biology platform

Task 4 will develop dedicated analysis platforms and a relational database collecting data from several experiments provided by the Action members (e.g. transcriptomic data) and derived from public databases. The platform will include tools for the construction of gene coexpression networks and for their integration with interactomic and regulatory networks, and with metabolic and signaling pathways.

Working Group 2: Genetics in meat, fur and pet rabbits and biodiversity resources

Task 1. Genetics of phenotypic and production traits

This Task will explore the possibility of linking production traits and/or massive phenotypes (phenomics) in rabbits to genotypes based on genomic tools already available or that will be developed in the framework of WG1. Particular attention will be given for traits like disease resistance, feed efficiency and reproduction performances.

Task 2. New breeding programs

The aim of Task 2 is to simulate and theoretically design applications of new breeding schemes in rabbits using genomic information. Designs and practical results will provide useful information for application of genomic selection programmes in other species.

Task 3. Biodiversity resources

This Task will provide an updated list of rabbit genetic resources available in Europe and in several developing countries linked to the Action members integrating all information from other databases (e.g. FAO DAD-IS, EFABIS), national breeder associations, breeding companies, local breeders, fancy breeders, laboratory animal providers and biotechnology companies. A dedicated database will be established for this purpose with a description of specific phenotypes and traits, with particular attention to fancy breeds and lines (useful for Task 1 and in WG3).

Working Group 3: The European rabbit as a model in basic biology and human diseases and as a tool for biotechnology applications

Task 1. Development of a database on the use of the rabbit as model in basic biology and in human diseases
This task will provide a broad view of the role, advantages/disadvantages of the European rabbit in basic biology studies and will address the needs for the development of genomic tools and their potential applications by the scientific community.

Task 2. Application of genomic tools and information to the study of basis biology aspects and for the exploitation of different rabbit models
Action members studying the rabbit as a model in various scientific fields (early embryo development, human diseases, neurobiology, etc) will evaluate potential applications of genomic and transcriptomic tools and information in their experiments and will provide data that could be shared with other Action member and/or used to feed the systems biology platform.

Task 3. Exploitation of rabbit genetic resources to define natural models of human diseases
The large number of fancy breeds and lines will be evaluated to identify interesting phenotypes and genetic diseases that could help to study the pathological mechanisms in human diseases. Specific experimental plans or populations will be developed and genome based tools will be applied.

Task 4. Rabbit as a model/tool for biotechnology applications
It will include activities to characterize embryonic stem cells and develop methods, protocols and resources for cloning, transgenesis, reproduction biotechnologies, production of therapeutic molecules, etc.

Working Group 4: Genetics and comparative genomic aspects for the study, exploitation and management of wild lagomorphs

Task 1. Comparative genomics
The European rabbit genome will serve to anchor and compare all genomic information and sequences that will be generated from other lagomorphs. Focus will be mainly on European hare (*Lepus europaeus*) and mountain hare (*L. timidus*) for which virtual genome maps will be produced. Analysis of sequences of wild and domesticated European rabbits will provide additional clues about the domestication process.

Task 2. Population genomics of wild lagomorphs
Comparative genomic resources will be used for the development of genomic tools and information that will be important for population genomics studies of wild lagomorphs. This would represent the basis for a thorough understanding of the current status of wild population spread all over Europe.

Task 3. Conservation and management plans
WG4 will devote resources and activities to exploit genomic information in wild European rabbit and other lagomorphs for the implementation of new conservation and management plans aimed at preserving rare genetic variants and the overall genetic diversity in a scenario of climate changes and sustainable utilization (harvest) of wild lagomorphs.

ORGANIZATION

In February 2012, the consortium included 94 experts from 64 institutions (16 from industry and associations and 48 from academia) in 20 COST Action countries, 2 international organisations (FAO and EMBL-EBI), and 5 non-COST countries (China, Japan, USA, South Africa and Taiwan). The Management Committee (MC), comprising up to two representatives from each country, supervises and coordinates the implementation of this COST Action according to "Rules and Procedures for

Implementing COST Actions" (doc. COST 4159/10). The steering committee includes the Chair, the Vice Chair, 4 work group leaders and the Short Term Scientific Mission coordinator

DISSEMINATION PLAN

The findings and results of RGB-Net will be disseminated to the varied target groups including other researchers in the field, other research frameworks, rabbit, food, biotechnology and pharmaceutical industries and the general public. A Web site will be created in order to disseminate results generated by the network and for communication and exchange of information among members of the Action. Results and activities of RGB-Net will be published in peer-reviewed scientific journals and in non-technical and trade journals. Kick-off Meeting, Final Conference and WG workshops will inform interested scientists, regulatory bodies and policy makers about the results of the project. The COST Action members will participate in international and national conferences on genetics, genomics, bioinformatics, animal production, lagomorphs and rabbit science in order to disseminate the knowledge generated by RGB-Net. Short-Term Scientific Missions will contribute to dissemination of accumulated knowledge of RGB-Net to early-stage as well as senior scientists. Training Schools will be organized for young researchers (e.g. PhD student level and early postdoctoral level). These training schools will cover multidisciplinary aspects or will be specialized in a particular field as it will defined by the MC in collaboration with the WG.

CONCLUSIONS

As part of the Mammalian Genome Project, the European rabbit was selected by the Broad Institute as a relevant species for producing a high quality draft sequence assembly, thus providing strong opportunity at research and innovation levels. Genomics and post-genomics information will be used to generate societal and economic benefits and improve the competitiveness of breeding industries, pharmaceutical companies and private or public organizations. The COST Action Rabbit Genome Biology was initiated in 2011 from the initiative of the European scientific research community working on rabbits. This network creates opportunities to bring together scientists having the European rabbit as a main interest, from a large number of research fields to create a multidisciplinary network with the necessary critical mass to translate the European rabbit genome information into practical applications.