

Innovative management of animal genetic resources (IMAGE): an EU project aimed at enhancing the value of gene banks.

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Summary

Are gene banks just a set of freezers or liquid nitrogen tanks, holding biological material for uncertain use? How representative of the genetic diversity of domestic species are collections in gene banks? How can they contribute to address the challenges facing the livestock sector? The IMAGE H2020 research project has been funded in 2016 to address these issues. The consortium of 28 partners undertakes a multi-disciplinary approach to evaluate resources from gene banks and facilitate their exploitation by combining genomics, bio-informatics, reproductive biotechnologies and social sciences. An inclusive approach is set up to analyse stakeholders' expectations. Knowledge gaps and organisational constraints are analysed before presenting the project organisation and first actions regarding molecular characterisation, data integration, reproductive physiology and gene bank operations.

Keywords: gene bank, Europe, genetic diversity, genomics, reproduction

Introduction

Animal genetic resources provide the basis for selection and improvement of livestock, as well as for research projects aimed at characterising the genome diversity and the relationships between genotype and phenotype. A large diversity of local and commercial breeds as well as experimental lines has been obtained as a result of domestication and selection of the main domestic animal species: cattle, sheep, goats, horses, donkeys, pigs, rabbits, poultry (chickens, turkeys, ducks, quails, guinea-fowls) fishes and shellfish. This variety ensures the capability and adaptability of livestock to fulfil its role in food production under different circumstances, now and in the future.

Yet, as a result of intensification and specialization of livestock systems, one third of domestic breeds are now considered to be at risk of extinction (FAO 2015). Many countries have set up cryobanks to store reproductive material of domestic animals, and FAO has provided guidelines for that aim (FAO, 2012). This represents an important investment for countries, so that cryobanks are both a heritage and a resource for the future.

At the same time, genotyping and sequencing technologies are boosting genomic studies which require an easy access to high-quality biological samples. Molecular analyses provide estimates of genetic diversity, contribute to reconstructing breeds history and to guide sampling for conservation. DNA collections have been set up as a follow-up of several projects aiming at characterising genetic diversity, as for example in chickens (Hillel et al., 2003).

The objectives of the IMAGE H2020 research project are to better evaluate the resource provided by gene banks and to facilitate the exploitation of these collections of biological samples in order to improve resilience of farming systems by increasing the range of diversity available to farmers.

Knowledge gaps

The level of information available on the collections currently stored in cryobanks is very variable according to species. The comparison of collections of Holstein Friesian, the main breed of dairy cattle, from France, Netherlands and USA, showed that gene bank collections have captured substantial amounts of genetic variability of this breed (Danchin-Burge et al., 2011). However, this is one of the most well-known breeds and such an evaluation is generally not available for other breeds or species.

The challenge is to evaluate the representativeness of gene bank collections relative to the diversity at the species level: which part is unique to gene banks (B area on Figure 1) which part is shared between gene banks and on-farm populations (C area on Figure 1) and which part of the on-farm variability is missing in the gene banks (A area on Figure 1). If B is empty, the strategic interest of the gene bank is limited to long term conservation, because all the variability is still available on-farm. If B is not empty, then the challenge is to determine whether original variants may be extracted from the gene banks to reintroduce lost traits or reorient breeding scheme. This will be all the more relevant than the gene bank collections are genetically distant from the on-farm gene pool, and that new production conditions call for a shift in desired genotypes. Using high density SNP chips now make possible to evaluate distance according to chromosomal regions (Engelsma et al., 2012).

Reintroducing distantly related sires (such as old sires) into a small population may help to decrease inbreeding level. Reorienting a breeding scheme generally requires new phenotypic information, unless phenotype may be inferred from genotype, thanks to data integration. Previous results obtained by a simulation study in Holstein suggested that a major shift in selection objectives would be needed (Leroy et al., 2011) to warrant reintroduction of a genotype showing extreme values for a trait previously considered with a low priority. If the reorientation of a breeding scheme is motivated by adaptation to new environmental conditions, the main gap is the insufficient knowledge of which genotypes may be suitable to these conditions.

Another major limitation to use gene bank collections is the unpredictability of fertility following the use of frozen semen or embryos. Except for cattle, the use of frozen semen is not a routine practice, and is hampered by the uncertainty in the number of progeny obtained, as for example in chickens (Blesbois et al., 2007) or donkeys (Vidament et al., 2009).

Main constraints

A variety of constraints may take place either at the entry into collection or at the distribution stage. Regulatory issues are here the main constraints. Typically, local breeds cannot afford heavy monitoring programmes for a number of diseases, and they are often located in remote areas, far from licenced AI centers. Ignoring these specific issues leads to a possible antagonism between the animal health policy and the plan of action for animal genetic resources.

At the distribution stage, the constraints may be technical, since well-trained people are needed for species where frozen semen is not used routinely, but they may also deal to intellectual property rights, and particularly to the ownership of the stored reproductive material. Legal constraints could be enhanced by the recent entry into force of the Nagoya protocol for Access to genetic resources and Benefit Sharing following their use.

Approaches developed in IMAGE

In order to fill these gaps and overcome these constraints, the IMAGE project is gathering 28 partners from 14 European countries and 4 third countries (Argentina, Columbia, Egypt and Morocco). Third countries were chosen in order to address the challenge of climate adaptation worldwide; the presence of a gene bank as well as previous collaborations played a great role for the final choice. IMAGE also includes FAO and the European Forum of farm animal breeders, EFFAB, as full partners. It is organised with 6 research and innovation workpackages (WP), one dissemination WP and the coordination WP (Figure 2):

WP1 will involve stakeholders all along the project and will design methods and tools to account for their needs. A multi-actor dialogue forum has been set up with a yearly meeting that national coordinators of animal genetic resources generally attend.

WP2 aims at improving the functioning and networking of animal gene banks, in terms of standards and protocols, information dissemination, transparency of rules and procedures

WP3 will develop and implement methods and tools to improve the cryoconservation and reproductive efficiency of biological samples.

WP4 will develop comprehensive genome information for a more precise and meaningful evaluation of animal genetic resources, which will be particularly novel for local or non-commercial rare breeds.

WP5 will develop a European web portal to integrate genotype and phenotype data, up to the integration with geographic information.

WP6 will develop methods to enhance the contribution of genetic collections to diversity restoration and will demonstrate in real size the introduction of a rare allele from a local breed into a commercial chicken line, in partnership with a breeding company.

WP7 aims to enhance the effective use of research results achieved by all stakeholders and to ensure dialogue and exchange of procedures with third countries. A training strategy has been established with workshops and courses to be held in Europe and in third countries.

Filling the gaps

Work planned under WP4 and WP5 aims at improving the knowledge of the genetic diversity of gene bank collections, relative to the gene pool of a domestic species. The inventory of available molecular data among the partners and in public databases revealed major issues in this respect:

- the use of different genotyping tools is a technical limitation for data sharing; whereas SNP chips are rather well standardised and shared in ruminants, it is not the case in chickens for which sequencing data are needed to merge SNP data sets.
- The inclusion of gene bank material into major molecular surveys is low to moderate according to species and country, with an average of 20%, except for cattle, but very few bulls of the 1000 genome project are found in gene banks; more generally, DNA banks should be better connected with
- HD SNP chip data are lacking for local sheep breeds in Central and Eastern Europe.
- Access to data is conditioned by various agreements, 20 different modalities were counted for cattle and sheep data.

To fill these gaps, nearly 300 chickens, 110 pigs and 100 sheep have been chosen for whole genome sequencing, and 350 sheep are chosen for HD genotyping to cover a large geographic range in Europe. These data will be made available at first publication. Other targeted sequences and genotyping are on the way for case studies aimed at illustrating the usefulness of gene banks in cattle and chickens. Cases with long time-series are a priority in order to use gene banks to gauge genetic changes over time.

WP5 has now defined a model for data integration (see Stella A. et al., this congress). Connecting genetic and phenotypic information with information associated to the geographic origin of the genetic materials (socio-economic, climatic) will greatly improve our knowledge of the resources available in gene banks.

Work done under WP3 shows a great variability of biology of reproduction among species and among breeds within a species, so that procedures have to be tested on more than one breed for a species. New approaches are developed to better understand individual variability in semen fertility, such as miRNA in cattle semen (Capra et al., 2017) and semen proteomics in chicken (Labas et al., 2015). To overcome the impossibility to freeze embryos in birds, two alternative strategies are under development: gonad transfer and conservation of Primordial Germ Cells for restoring the whole genome.

Overcoming the constraints

In IMAGE, gene banks are considered as infrastructures aimed at collecting, storing and documenting genetic collections for research and breeding. WP1 and WP2 have analysed gene bank operations and expectations from stakeholders through 2 surveys (see Passemard et al., and Klaffenboeck et al., this congress). Ways to harmonize gene bank operations have been identified, particularly through the set-up of the European network EUGENA. Both surveys showed that most cryobanks were more active in storage than in distribution of genetic resources, and that stakeholders were not ready for new uses of gene bank material, as for example crossbreeding. However, cryobanks and DNA banks can contribute to document each other, provided that same animals have samples in both, so that coupling of collections should be encouraged. Dissemination of new information and new tools made available by IMAGE is planned in order to trigger a more innovative use of gene bank collections.

The dialogue forum set up within WP1 has clearly identified the strong limitations due to the lack of consideration of the specific features of gene banks by animal health regulations. The current revision of the Animal Health Law at the EU level is an opportunity to address these limitations. A specific survey is about to be launched for ABS regulations, the most recent legal framework likely to impact the use of gene bank collections.

Finally, sustainability of gene banks requires a funding model. Whereas WP2 survey has shown that public funding was considered the most legitimate support for gene banks, a task of WP1 is dedicated to analysing the value chain of gene bank collections.

Conclusions

Contrary to the idea that gene banks are just quiet freezers, they deserve intensive studies to better evaluate their potential. Their integration into the management of genetic variability of livestock must take into due consideration the biological differences between species and the socio-economic background. IMAGE has started to produce new data and will test methods to reintroduce diversity from gene banks into live populations. The conditions for a successful reintroduction of original variants will be studied in a range of situations:

species and breed fertility, rate of genetic trend, diversity level, selection objectives.



Figure 1- A schematic representation of the partition of genetic diversity among in situ populations and gene bank collections for a given species

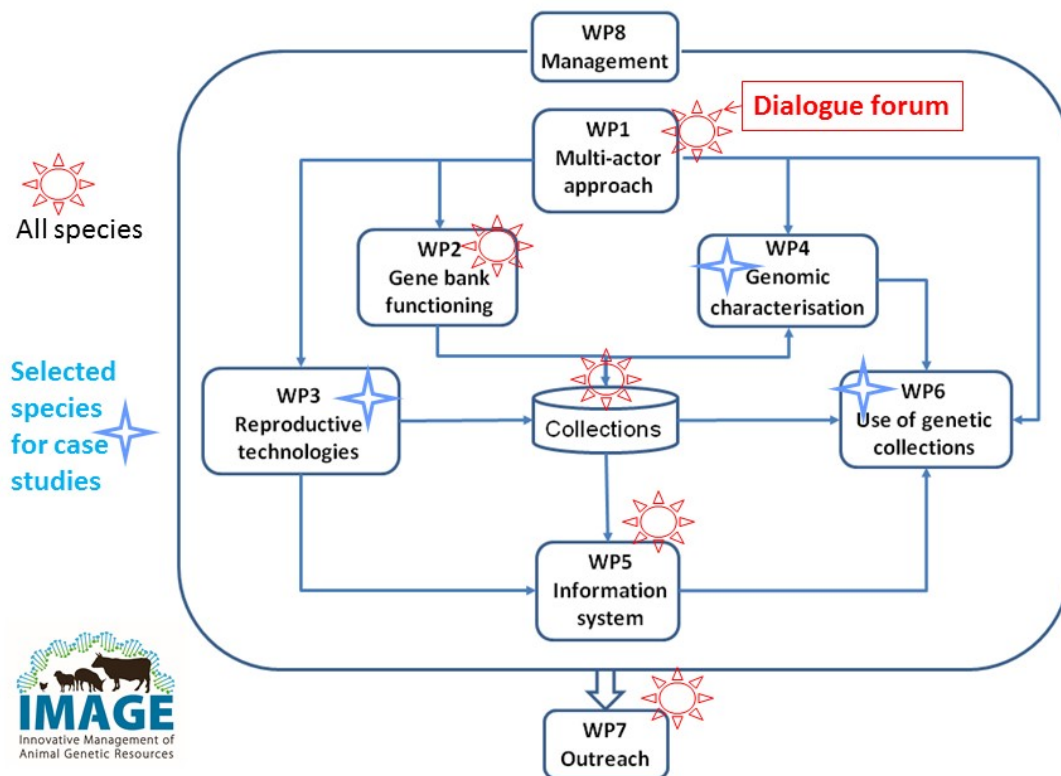


Figure 2- The WP organisation of the IMAGE H2020 project

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