

OPINION

Crop archaeogenomics: A powerful resource in need of a well-defined regulation framework

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Email: laura.botigue@cragenomics.es**Societal Impact Statement**

Crop archaeogenomics has rapidly flourished in recent years, leading to a new way of understanding the past and bringing answers to important questions about human history in relation to plant management and food production. Furthermore, the knowledge derived from the analysis of ancient crops can contribute to the development of a more sustainable future. However, the extant legal framework presents a number of challenges when applied to this research field, particularly in the current scenario of disparities in scientific outcomes between countries. We expose the uncertainties of the legal framework and the factors that maintain or exacerbate these inequalities, as well as possible solutions.

Summary

Crop archaeogenomics is a flourishing field that has greatly benefited from next-generation sequencing technologies. Ancient and historical plant remains are currently considered genetic resources and as such are subject to legal frameworks like those implemented by the Nagoya Protocol. In addition to the challenges in complying with genetic resource regulations that crop archaeogenomics share with other basic plant research disciplines, there are additional difficulties specific to this interdisciplinary field that includes science and humanities, namely, the need to comply with two different legislations before accessing the samples (one for genetic resources and one for cultural heritage), along with a high risk of not obtaining DNA. As a result, most studies to date have been done on samples for which the laws regulating genetic resources did not apply, sometimes avoiding the need of reaching Access and Benefit Sharing agreements with the country that originally provided the samples. This phenomenon is likely to worsen in the future, as the archaeological record is a limited resource and competition between laboratories will only widen the gap between developed and developing economies. Because crop archaeogenomics is a new and promising scientific field, it is desirable to begin a dialogue with other basic biological research fields to facilitate the implementation of these agreements so that basic sciences can easily utilize these biological samples while ensuring the rights of all parties involved.

KEYWORDS

access and benefit sharing, crop archaeogenomics, genetic resources, Nagoya protocol, policy

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1 | INTRODUCTION

The field of archaeogenomics has come a long way since the publication of a mitochondrial sequence from a museum-preserved quagga in 1984 (Higuchi et al., 1984) and has recently flourished thanks to the development of genomic sequencing technologies.

Although most archaeogenomic studies have so far been performed in animals (including hominins), plant archaeogenomics has gained increasing attention in the last decade, because few samples are a powerful resource to investigate important events such as plant domestication. Processes like selection, local adaptation and early dispersal of domestic forms have been investigated in major crops, such as barley (Mascher et al., 2016; Palmer et al., 2009), bread wheat (Li et al., 2011), cotton (Palmer et al., 2012), maize (da Fonseca et al., 2015), emmer wheat (Scott et al., 2019) and bean (Trucchi et al., 2021). Plant ancient DNA analyses study both past human–environment interactions and the evolutionary forces that shaped modern crops. Furthermore, knowledge obtained from crop archaeogenomics holds great potential to aid in the development of new conservation strategies, breeding programmes and agricultural practices in response to climate change and human pressure on the environment (Di Donato et al., 2018; Estrada et al., 2018; Hofman et al., 2015; Pont et al., 2019; Przelomska et al., 2020).

With the advent of ancient DNA analysis, legal and ethical issues have arisen. These include the ethical implications of undertaking the genetic analysis of ancient humans, their cultural bonds with present-day communities, competition between research groups, hoarding of material from the Global South, and limits in experiment replication due to the intrinsic value of the sample coupled with their finite availability, both for human (Bardill et al., 2018; Elliott, 2009; Paradise & Andrews, 2007; Wagner et al., 2020) and archaeofaunal remains (Pálsdóttir et al., 2019).

In the case of crop archaeogenomics, many factors (including stochasticity) play a very important role in determining the preservation and the cultural value of the remains (see Box 1 for more details). Usually, the most promising samples consist of seeds or leaves (small amounts of material), and DNA extraction is most often a destructive experimental procedure that effectively impoverishes the archaeobotanical record. Moreover, it is not possible to know what fraction of the archaeobotanical record contains DNA, but so far it seems to be modest, especially for charred remains (Nistelberger et al., 2016). The relative abundance of ancient material has shielded this field from the competition and hoarding that have occurred in human archaeogenomics (Makarewicz & Nimrod Marom, 2017; Morris, 2017). However, the growing interest in the discoveries from crop archaeogenomics, coupled with the constant technical research for improvements (e.g., Brown et al., 2014; Gamba et al., 2016; Lendvay et al., 2018), could rapidly change that.

We discuss here aspects of this research field under the Convention on Biological Diversity (CBD) and Nagoya Protocol (NP) international framework. The field of ancient crop genomics shares many aspects with other basic research disciplines, such as the non-monetary nature of the results, but it has also some peculiarities,

BOX 1 Assessing the value of archaeobotanical samples. Examples from (Zohary et al., 2012)

1. *Uneven geographic distribution of the archaeological record:*

The abundance of archaeological sites is uneven across the globe. Although the archaeological record provides an overall reliable overview of crop domestication in Europe, South-west Asia and the Mediterranean basin, other regions have not been as explored, such as South Asia or in Africa, south of the Sahara.

2. *Type of sample:* Seeds are, together with microscopic pollen, the more resilient parts of the plants and thus represent the most abundant form of crop remains from early farming villages in the old world. On the contrary, horticultural vegetables that furthermore may undergo different food processing techniques are very rare because they have fewer chances to survive as archaeological remains.

3. *Conservation status:* The conservation status will also affect the value of the sample. Samples are usually charred, less commonly desiccated (when located in conditions of extreme dryness such as desertic areas), or waterlogged (e.g., in lakes or wells in anaerobic conditions). They can also be mineralized, in phytolites and coprolites. Desiccated remains have so far proven to be more likely to contain ancient DNA than charred remains do.

4. *Uneven temporal distribution of the archaeological record:* Within a given archaeological site the abundance of samples can vary between historical periods or sections excavated. This happens for instance at the site of Troy; although it is rich in plant remains in sections dated to the Middle Bronze Age, only a few specimens belonging to the Early Bronze age and Neolithic have been recovered.

5. *Additional value:* some specimens have an added cultural value. The material used to make artefacts (e.g., necklaces made of seeds and baskets made of leaves) is not only informative about the plants themselves but also about the culture that fabricated those artefacts, trade networks, etc. Another example would be for plant remains found in excavations or burials of historical characters notorious to society. Results from these studies would have higher chances to be disseminated by the media because of their capacity to engage society, rather than the strictly scientific findings from those studies.

which include (1) the obligation to abide by both heritage and genetic regulation and the inadequacies of CBD definitions when it comes to archaeobotanical remains; (2) limitations of the current legal framework for Access and Benefit Sharing (ABS) agreements, and (3) possible solutions to improve the current situation.

This opinion piece focuses on archaeobotanical macroremains of crops because of their important role in human development and history. However, we note that plant archaeogenomics includes the analysis of many kinds of remains, among others plant DNA in ancient sediments, coprolites and wood remains. For a more detailed read on plant archaeogenomics, a review covering this topic has been recently published elsewhere (Kistler et al., 2020).

2 | THE LEGAL FRAMEWORK

Geneticists can access archaeobotanical remains either by establishing a collaboration with an archaeobotanist or, when the samples have already been deposited, with a curator of a museum or an herbarium. In the first case, the decision to collaborate will depend on the archaeological project, its director or the archaeobotanist, depending on the institutions involved. In the case of museum or herbarium collections, the decision process varies, but usually involves, an internal or external evaluation of the request as per general disciplinary standards: scientific need, nature of the project and research potential against the need to preserve the collections.

In cases where the collaboration is established between multiple countries, the movement of the samples must be granted following two national laws: that covering archaeological material and, if they exist, that of genetic resources. For the former, export permits have to be requested and accepted by Antiquity Authorities or Heritage Institutions, even though exceptions exist (e.g., Egypt restricts the export of all materials). Agreements usually last for a known time, during which researchers can study the archaeological material. If the analyses entail the destruction of the samples, it is usually harder to obtain the authorization.

Regarding the genetic nature of the material, two international agreements have also been established. The United Nations (UN) CBD entered into force in 1993 with the goals of conserving biological diversity, promoting the sustainable use of its components, and the fair and equitable ABS arising from their utilization. So far, it has been signed by 196 Parties, with the notable absence of the United States, among other countries (Cooper & Noonan-Mooney, 2013). The NP emerged to provide a legal framework to implement the third objective of the CBD, entered into force in 2014 and has 128 Parties. Briefly, the NP sets out core obligations for its contracting parties through mutually agreed terms concerning access to genetic resources, benefit sharing and compliance. It also covers traditional knowledge associated with genetic resources, taking into account the role of indigenous people and local communities (UN CBD, 2011). Each country implements NP with its own national ABS policies and laws, as the CBD recognizes each country's sovereignty over its own genetic resources.

The ultimate intent of these international agreements is to avoid undue appropriation of natural resources and *unfair distribution of benefits arising from their exploitation*. Thus, these agreements were born out of the necessity for international legal and ethical standards that

act upon the increasing globalization and environmental degradation, while promoting the wellness of humanity.

3 | INADEQUACIES OF THE CBD DEFINITIONS AND THE NP FRAMEWORK FOR ARCHAEOBOTANICAL REMAINS

The CBD defines *genetic material* as “any material of plant, animal, microbial or other origin containing functional units of heredity”, and defines *genetic resources* as “genetic material of actual or potential value” (Cooper & Noonan-Mooney, 2013). In addition, under the NP, authorization to use the genetic resources must be obtained *before* accessing them. In the study of crop archaeogenomics, this is particularly daunting because it is not possible to know whether the sample of interest contains DNA without processing it first. Indeed, it is not at all clear if ancient plant remains should be considered genetic resources. Foremost, ancient biological samples include a long list of remains as well as archaeological artefacts, most of which do not contain endogenous DNA at all. Second, if endogenous DNA is still present inside the sample, it is highly fragmented and degraded (e.g., Jónsson et al., 2013; Pääbo et al., 2004), containing numerous nucleotide misincorporations which prevent its functionality (only two notable exceptions have been described so far; Sallon et al., 2008; Shen-Miller et al., 1995).

Under the present legal framework, *the intention* to undertake a genetic analysis on an ancient plant specimen turns this sample into a genetic resource. Archaeological plant material is regulated only by Cultural and Heritage laws up until the time a researcher wants to do a genetic analysis on this material. At this point, the sample acquires a *potential value* that turns it into genetic resources according to the CBD terms. Nevertheless, most likely the sample cannot be considered to be *genetic material* because it does not contain DNA, especially if defined as *functional units of heredity*. This high risk of not obtaining DNA from archaeobotanical remains and the additional bureaucratic burden to comply with genetic, cultural and heritage regulations has led to the avoidance of NP-regulated archaeobotanical remains. The main downside of this legal framework is the requirement to enter into agreements *before* accessing the sample and thus be allowed to test the feasibility of the research project (i.e., the presence of analysable DNA in the sample). As a result, at times, the country of origin of the sample, provider country henceforth, is not considered at all in the study. This prevents the involvement of researchers from this country and promotes the *unfair distribution of benefits arising from the use of resources* that the very NP was established to avoid.

4 | THE NEED TO PROMOTE AN ABS AGREEMENT

Although crop archaeogenomics is a basic science field and no monetary profit can be envisioned out of it, it is still necessary to ensure

that research and scientific collaborations follow fundamental ethical principles. All parties involved in a given study should share intellectual and technological benefits, consistent with the intent of the NP to promote developing economies' technical capacities and science building. The field of crop archaeogenomics is usually led by researchers from the Global North even though many plant remains originate from the Global South. There are various reasons embedded in the research area that explain this: First, the generation of the data is a very expensive process. It requires the construction of an exclusively dedicated laboratory facility and continuous expense in laboratory material to minimize the risk of contamination from external sources and cross-contamination between samples (e.g., Krause, 2010; Pääbo et al., 2004). It also requires investment for sequencing and bioinformatic analyses. All these factors, along with the intrinsic uncertainty of obtaining (good amounts of) target DNA, leave developing economies out of the race of leading archaeogenomic studies, even those that have a rich archaeological record.

Second, the data to analyse consist of digital sequence information (DSI) to be processed along with other DSI available in public databases. Currently though, many institutions in developing economies cannot afford the subscription fees for many scientific journals where the information to locate the DSI in repositories is found, hindering their access to new knowledge and the genomic data (Dijkeng, 2012; Helmy et al., 2016). Besides, the lack of basic infrastructures, such as fast and stable internet connection to download the DSI, as well as access to high-performance computers further

hinders the data analysis process. International initiatives such as eILF (*eILF - Open Access Programme*), INASP (*Inasp - Homepage*) and Research4Life (*Research4life Organization*) have incentivized access to science and scientific advancement in the so-called Global South, even if extant inequalities remain difficult to overcome (Powell et al., 2020).

The ultimate consequence of these factors is a movement of ancient biological samples from the Global South to the Global North. Samples are then processed and analysed by researchers in countries that do have the infrastructures to do so (Morris, 2017; Prendergast & Sawchuk, 2018) (Figure 1). Without an ABS agreement, Global South countries that provided the samples risk having a mere testimonial role in the study, if they are represented at all. Considering the studies mentioned in Figure 1 in at least 70% of the cases (8 of 12) where samples were originally excavated in a country of the Global South, no author is affiliated with an institution of a developing economy. When present, authors from institutions in developing economies did not play a major role in the research, as reflected in the affiliation of the first and last authors.

5 | SOLUTIONS WITHIN THE NP

Recently, a new concept has been coined to refer to the colonialist practices that still occur in science, the helicopter research (Minasny et al., 2020). More and more voices are being raised about the need to maintain certain ethical rules when performing research involving

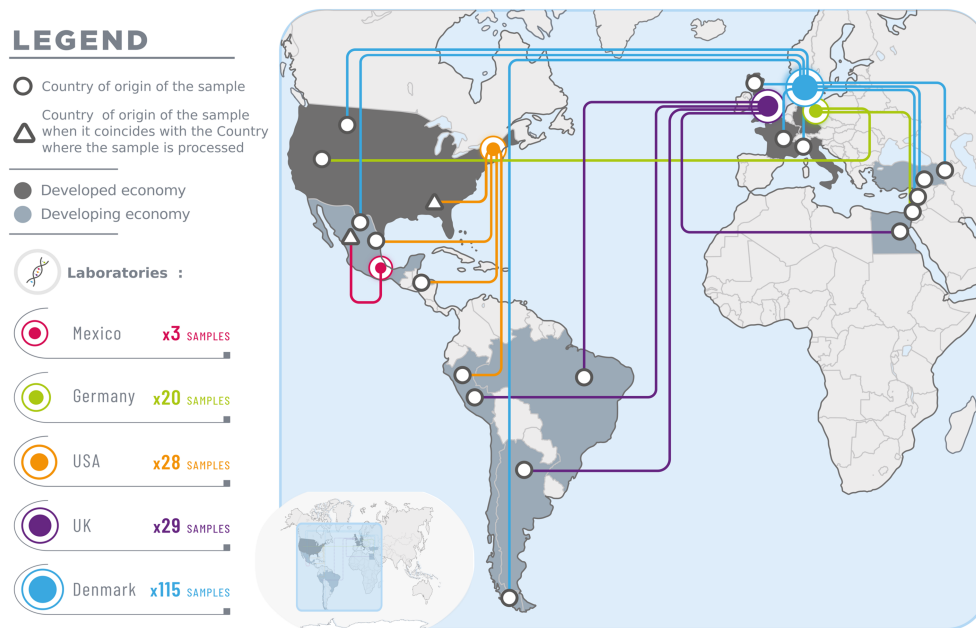


FIGURE 1 Movement of crop macroremains from country of origin to ancient DNA facilities up to 2019. The movement of samples from country of origin to the country where they were processed. The dimension of the dots depends on the number of the resulting scientific publications. This map has a per country resolution, the location of dots/triangles is not related to exact archaeological sites/labs coordinates inside the country. The number of samples analysed is reported on the left panel, next to the country where the analysis took place. The genomic studies considered in this figure are those included in (Kistler et al., 2020), hence reflecting studies published up to December 2019, not a complete survey of ancient DNA studies on plants. Studies about wood have been excluded, not being about crops

countries in the Global South. The NP, through the implementation of the ABS agreement, is the perfect venue to ensure that these non-monetary benefits are included when planning a research project. However, in the specific case of archaeogenomics, there are a large number of samples that were collected before the NP entered into force and therefore escape this regulation. In addition, the need to draft an agreement before accessing samples combined with the high risk of not obtaining DNA from them has a deterrent effect that results in avoiding the selection of NP-regulated specimens.

As other authors pointed out, one solution would be to have specific regulations for ancient (and historical) plant material within the NP. However, this is hard to accomplish, at least in the near future (Sherman & Henry, 2020). A more interdisciplinary strategy is more likely to succeed. There is an ongoing debate around the bureaucratic burden that basic plant research faces to comply with ABS (e.g., Kursar, 2011; Schindel, 2010; Watanabe, 2015). Certain solutions have been proposed, such as mechanisms that would allow differentiating between monetary and non-monetary benefits (Rourke, 2018). We also advocate a solution that goes beyond the specific case of non-modern plant specimens and unites all basic biological research.

We propose two actions that would have a positive impact in the present circumstances. First, add a clause in the NP for all basic science disciplines that do not entail monetary benefits, allowing exploratory analyses on the samples for a short time frame to determine the feasibility of the proposed project. This is similar to the regulations applied in social sciences, where samples are allowed to be studied for a restricted period. Second, a standardized ABS agreement, designed to avoid helicopter research detailing the participation and recognition of all the members involved in the project. The standardization will facilitate the process of sample acquisition for researchers while ensuring intellectual contribution, recognition and transfer of technical and scientific expertise to researchers in the provider country of the samples. An example of access standardization is provided by the multilateral ABS system and standard material transfer agreements of the International Treaty on Plant Genetic Resources for Food and Agriculture (2001) (Rourke, 2018).

6 | CONCLUSIONS

An appropriate legal framework for crop archaeogenomic studies is of particular importance because the current situation promotes the use of plant remains that are not subject to the NP or a national law regulating genetic resources. This is even more true because the distribution of archaeological remains is unbalanced between the Global North and the Global South, the former counting on extensive collections of foreign specimens that predate international agreements. In some instances, this implies the total exclusion of the provider country in the research study, and therefore the impossibility of sharing the benefits of the ongoing research.

Care must be taken, however, to avoid mere testimonial participation by the provider country, and agreements made between the

parties should ensure the active participation of researchers from that country in the study. Indeed, we think that standardization of an ABS agreement for non-monetary benefits focused on avoiding helicopter research practices would have a very positive impact on that regard. This standard ABS form could even exist beyond the framework of the NP and be used more broadly by researchers from the Global North and South before undertaking international collaborations.

Given that crop archaeogenomics is a novel field, which can and likely will grow in the future, we think this is the right time to open a dialogue about possible options to aid easy access to resources for scientists while preserving the archaeological record and granting benefit sharing and inclusion of research institutions in developing economies. Standards in accessing the samples coupled with active sharing of the benefits deriving from the research could help to take away disparities between scientific communities in different countries and support the development of this field worldwide. Even if CBD and NP were drafted to recognize the sovereignty of each country over its genetic resources, we strongly believe that in the end all of us should gain benefit from the reconstruction of past phenomena such as plant domestication, which can be seen as a form of collective heritage of humankind.

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AUTHOR CONTRIBUTIONS

L.B. planned and designed the research. A.I. and L.B. revised the scientific literature and conducted the research of the current international agreements. A.I. and L.B. wrote the manuscript.

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DATA AVAILABILITY STATEMENT

Data sharing not applicable - no new data generated, or the article describes entirely theoretical research

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