Invited review

The biological relevance of a medieval king's DNA

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Abstract

The discovery of the presumably lost grave of the controversial English king Richard III in Leicester (UK) was one of the most important archaeological achievements of the last decennium. The skeleton was identified beyond reasonable doubt, mainly by the match of mitochondrial DNA to that of living maternal relatives, along with the specific archaeological context. Since the genetic genealogical analysis only involved the DNA sequences of a single 15th century individual and a few reference persons, biologists might consider this investigation a mere curiosity. This mini-review shows that the unique context of a historical king's DNA also has relevance for biological research *per se* - in addition to the more obvious historical, societal and educational value. In the first place, the historical identification appeared to be a renewed forensic case realising a conservative statement with statistical power based on genetic as well as non-genetic data, including discordant elements. Secondly, the observation of historical non-paternity events within Richard III's patrilineage has given rise to new research questions about potential factors influencing the extra-pair paternity rate in humans and the importance of biological relatedness for the legal recognition of a child in

the past. Thirdly, the identification of a named and dated skeleton with known historical context serves as a reference for bioarchaeological investigations and studies on the spatio-temporal distribution of particular genetic variance. Finally, the Richard III case revealed privacy issues for living relatives which appear to be inherent to any publication of genetic genealogical data.

Keywords

Ancient DNA, King Richard III, Genetic genealogy, Forensic identification, Celebrity genetics

Main text

The discovery of the presumably lost grave of the English king Richard III (1452-1485) underneath a car park in 2012 caught the attention of a broad international public (1, 2). The fascination was mainly stirred up by Richard III's general fame, the controversy surrounding his popular image as a cruel and powerful person, and the as yet mysterious circumstances in which he became king and died two years later in battle (3, 4). The chronicle narrating the miraculous finding and the oldest cold case to date, only increased public interest (5). The genetic identification analyses to be performed on any interesting skeleton found were already announced before excavations started on the Grey Friars site in Leicester, the birthplace of DNA fingerprinting (1). They were performed on a male skeleton excavated in the choir of the former church, which was later identified as being Richard III.

Although researchers at that time had already successfully performed historical identifications using DNA, e.g. the Romanov family (6, 7), the identification of a 15th century individual was still a huge achievement (8, 9). The first prerequisites needed for this feat were to discover the resting place of the person under study, to receive permission for excavation and to find enough qualitative human remains to perform molecular analyses. This is no easy task, which the many unfruitful attempts to conclusively identify remains of Richard III's sister Margaret in Mechelen (Belgium) illustrate (2, 10). A second necessity was finding appropriate and consenting relatives to adopt the so-called genetic genealogical approach for identification. These relatives are often several generations removed from the individual in question, therefore only non-recombining DNA markers might be informative. Thanks to linear

inheritance, any biological relative in direct maternal or paternal line carries a closely related mitochondrial DNA (mtDNA) or Y-chromosomal haplotype, respectively (11). Nevertheless, only a minority of ancestors has such currently living direct descendants or relatives (12). Finally, ancient DNA handling and analysis requires specific expertise. To date, only a limited amount of DNA data from Richard III's remains is available, including the mitogenome and Y-chromosomal profile used in the genetic genealogical approach. Additional DNA analyses have been performed to predict the eye and hair colour in order to realise a facial reconstruction (Figure 1a) (13). The sequencing of the complete genome of Richard III has been announced, but not yet accomplished (14).

The identification of Richard III was immediately put forward as the most important archaeological discovery of the 21st century (15). The remains did partly reveal the physical appearance of and the real story behind this king, whose famous image was until then mainly formed by controversial Shakespearean literature hailing from the Tudor era (16). Subsequently, many articles focussed on insights relevant for historical and archaeological sciences (2, 17-19). Moreover, the discovery of such cultural heritage has also direct socio-economic relevance: it rapidly boosted the international profile of Leicester and its university, which has been appreciated as an invaluable PR-stunt (20). The funeral of the Richard III was a large event that increased cohesion among citizens (21) and brought inspiring challenges for the city's multicultural atmosphere and image (22). The visitors to the repository of the remains in Leicester cathedral (Figure 1b) leave a substantial and durable economic impact (23). The identification also encouraged a broad and young public to acquire knowledge in history and science. The Richard III case has even been noted as an educative example among scholars since it clearly demonstrated the importance of multidisciplinary research. Forensic geneticists and pathologists, osteologists, archaeologists, weapon experts, engineers, Latinists, historians, and genealogists worked together and successfully united the fields of science and humanities (20). However, this case-study is not a curiosity with merely historical, societal and educational value: here, we particularly focus on the genetic identification of Richard III and its relevance for specific research fields in biology, four of which are discussed below.

1. Forensic genetic identification and the public

The Richard III investigation clearly showed the complexity and caveats of the genetic genealogical approach within forensic genetics, a discipline that beyond adding genetic data to a biological trace or remain also needs to communicate results in a transparent and conclusive way (24, 25). The mitogenome sequence of the skeleton matched with those of two living maternal relatives whose most recent common ancestor (MRCA) was Richard III's grand-niece (Figure 2). The lineage was neither found among the 1,823 samples of a British mtDNA database nor in the 26,127 European haplotypes stored in EMPOP (https://empop.online) (13, 26). Among the >250,000 accessible mtDNA profiles of direct-to-customer (DTC) genetic testing companies, only seven independent hits were found (27). Therefore, a coincidental match between the skeleton and the reference persons seemed highly unlikely. However, the skeleton's Y-chromosomal lineage differed from that of five paternal relatives of Richard III (Figure 2). The MRCA of the latter was the 5th Duke of Beaufort (1744-1803), whose MRCA with Richard III was Edward III (1312-1377). One of the five revealed a non-paternity event during the last five generations. The remaining four relatives, however, were also assigned to a different lineage than the one attributed to Richard III, meaning the DNA evidence alone did not suffice to assure the identity (13). Criticism on the statement of identification was even formulated publicly when the different research aspects were considered separately (28). Therefore, the researchers used an innovative Bayesian statistical approach combining probabilities for all genetic and non-genetic elements. They included facts corresponding between known history and the observed archaeological context, such as radiocarbon dating, sex, age estimation, scoliosis and perimortem wounds consistent with medieval battle injuries, as well as the discordant elements, such as a low historical extra-pair paternity rate to deal with the Y-chromosomal mismatch. The evidence for a positive identification was extremely strong after such integrative analysis (13). The researchers systematically tested each alternative, even controversial, hypothesis that might explain the results, including the double hypothesis, according to which a male maternal relative of the king was taken on the battlefield (1). Consequently, the Richard III case is viewed as an example in identification studies *(i)* for the application of a statistical method combining all variables when DNA data only has a limited value or may include inconsistencies,

and *(ii)* for formulating and statistically testing alternative scenarios in contrast to previous studies where only a DNA match with living relatives was declared sufficient evidence (29). Finally, awareness about the complexity of DNA typing and statistical assessment in forensic cases is raised by broad media coverage of such investigations. This may become crucial as results of genetic identification have to be interpreted correctly also by non-experts that have to take decisions at court or in politics (24, 25, 30). Nevertheless, there were also negative reactions by professionals immediately after the press conference on the Richard III case. The researchers in Leicester announced results that were not accessible at that time in order to verify the genetic 'matches' (20). Elsewhere, unjustified but publicly claimed 'matches' using the genetic genealogical approach had to be retracted after statistical analysis was found inadequate (e.g., (29, 31-33)). Therefore, the Richard III case showed that it is important for the credibility of a discipline to provide in-depth results or a peer-reviewed publication when an identification is claimed publicly.

2. Extra-pair paternity behaviour

In an extra-pair paternity (EPP) event, the social father is (unknowingly) not the biological father of his child (34). The frequency and factors that influence the EPP rate are highly investigated in many pair-bound species, as males are investing in paternal care without any direct benefit for their own fitness. Ironically, the knowledge on humans is still limited (35). Genetic genealogical research provides insights by testing potential factors on human EPP behaviour in the past (36-38). The identification of Richard III presented only a single familial line but with the remarkable observation of at least two historical EPP events (13). Beyond wild speculations on when these occurred and historical 'gossip' with likely political motives (39), the observations in this specific patrilineage give rise to biological research questions about human cuckoldry behaviour. One important question is whether the EPP rate was and still is different between socio-economical classes within a population (36). At the time, it was essential for a royal family to have (male) heirs, illustrated by the political disaster of the death of Richard III's only son during his short reign (3, 4). Since EPP was a rarely-raised political issue and the legitimacy of their wives' child could not be opposed legally by others, males in noble families might have accepted EPP to maintain continuity and political stability (39). This specific example reveals the necessity to investigate differences in the (historical) EPP rates

depending on relevant inherited property and political motives (40). Another important question is raised by the fact that the patrilineage between Richard III and his living relatives included two ancestors who were not legally recognised by a father after birth but later when their mothers married (Figure 2) (13, 39). In patrilineages including premarital children, the chance of an observed EPP event is assumed to be much higher, but data are still lacking (41). More research on such patrilineages, like the one of Richard III, will provide insights in evolutionary and historical demography by revealing how often and under which circumstances males invested in non-biological children.

3. Bioarchaeology

Bioarchaeology describes the contextual analysis of biological remains from past societies to realise comparative studies on e.g. violence, colonialism, and health (42). Remains of a single individual, like that of Richard III, may contribute to these broad studies because the known point of time and life story associated with the remains make it possible to validate specific results of bioarchaeological – including genetic – investigations. This improves the interpretation of (many) other anonymous skeletons of individuals which possibly lived or died under similar circumstances in the same period. Most attempts to discover such "identifiable graves" to use as reference were not successful (43). The single case of Richard III did already have wide implications for non-genetic methodologies, like isotope-based palaeodietary and migration reconstructions. The isotopic data of the skeleton would suggest that Richard III had migrated to a different area in the last few years of his life (44). As this was not the case according to known history, the results were explained by dietary differentiation since he became king. A similar validation exercise was realised within tool mark analysis: traumata on the named skeleton could be interpreted using data known from battles, weapons and armour of that time (19, 45, 46). Research also provided insights on food patterns (44), medical care (47-49) and hygienic conditions of the highest social class in the Late Middle Age (50), something that was not possible with anonymous graves. Genetic investigations on the micro-level of a known individual will enable spatio-temporal analyses to locate the occurrence of genetic variants within a well-known historical and familial context (51, 52). This might become relevant when the whole genome of Richard III will be available, e.g. to investigate if genetic factors might explain his scoliosis (48).

It is generally accepted by scholars that our characteristics are co-constructed by genetic and environmental factors. Still, deterministic accounts remain popular (53, 54), also because of the widely advertised idea that DNA informs our sense of identity and best lifestyle (55, 56). Therefore, the study of Richard III's full genome might become a challenging exercise for bioarchaeologists and geneticists in interpreting and communicating genetic variants for a single individual. Due to the biographical details and controversial character, this interpretation will be especially thought-provoking in the Richard III case if variants are associated with personality or psychological makeup. Such discussions already appeared when a link between the king's distorted physique and character was suggested immediately after identification of his skeleton (16).

4. Genetic privacy

Since the 'next-generation sequencing revolution', many initiatives are taken to maintain the privacy of DNA donors when genetic data are publicly available (57). Anonymous publication is, however, hardly feasible for genetic identifications in which the combination of name and genetic data is essential *per se*. Nevertheless, any debate about the privacy of an individual that died several centuries ago, is almost of a philosophical nature, especially because there seems to be no one that would be harmed by publishing data (58, 59). Still, the Richard III case revealed the difficulty of guaranteeing genetic privacy in the context of the publication of DNA results together with patri- and matrilineages of living relatives, even in a carefully performed historical study (13). All DNA donors gave a detailed informed consent to analyse and publish their results (Turi King, pers. comm.) but a privacy issue is still existing for all other family members assumably carrying the same Y-chromosomal or mtDNA lineage. Any person may test their relatedness via a commercial DTC genetic test, with consequences for genetic anonymity (60) and kinship inference (11). The lack of counselling in those cases is substantial and an unexpected result is a radical event for every party involved (61), not only when a pedigree is the reason for societal privileges (62). The consequences for families of publishing genetic genealogical information are often only realised afterwards (29, 63). Sequence data might additionally impact privacy when variants are related to medical conditions (64), as already illustrated for Richard III's mitogenome (13).

Excluding genetic genealogical data from publication in an identification case is not an option either. Since the Richard III study, several approaches were proposed to circumvent the privacy issue. An ethical analysis described the (theoretical) possibility of a familial or generational consent in which DNA donors have to inform close family members and all third parties (65). Another solution was realised in the forensic identification of a blood stain attributed to the Belgian king Albert I, where independent external review of (the quality of) the data and statistical interpretation guaranteed scientific accuracy. The complete methodology, statistical analysis and the names of the DNA donors were published, however, no DNA information was given to guarantee the genetic privacy of living relatives (66).

Conclusion

Genetic information attributed to a single historical individual might seem of highly restricted biological relevance at first glance. Here, we illustrated that biologists and geneticists might benefit from taking "celebrity genetics" seriously. Historical identification cases trigger new research questions and are an opportunity to validate and communicate results in several biological disciplines.

Figures

Figure 1 The genetic identification of Richard III's remains resulted in a representative image of this individual and in an official cenotaph for one of England's most famous and controversial kings; a) While no portrait made during his life is known, DNA-based predictions appeared to match this post-mortem portrait of Richard III from the 1510s (13) (Society of

Antiquaries of London; source: Wikimedia, copyright: public domain); b) The inauguration of this permanent repository of Richard III's remains in Leicester's cathedral marked the closing of a complex and much-discussed genetic identification process (2) (Source: author, May 2015).

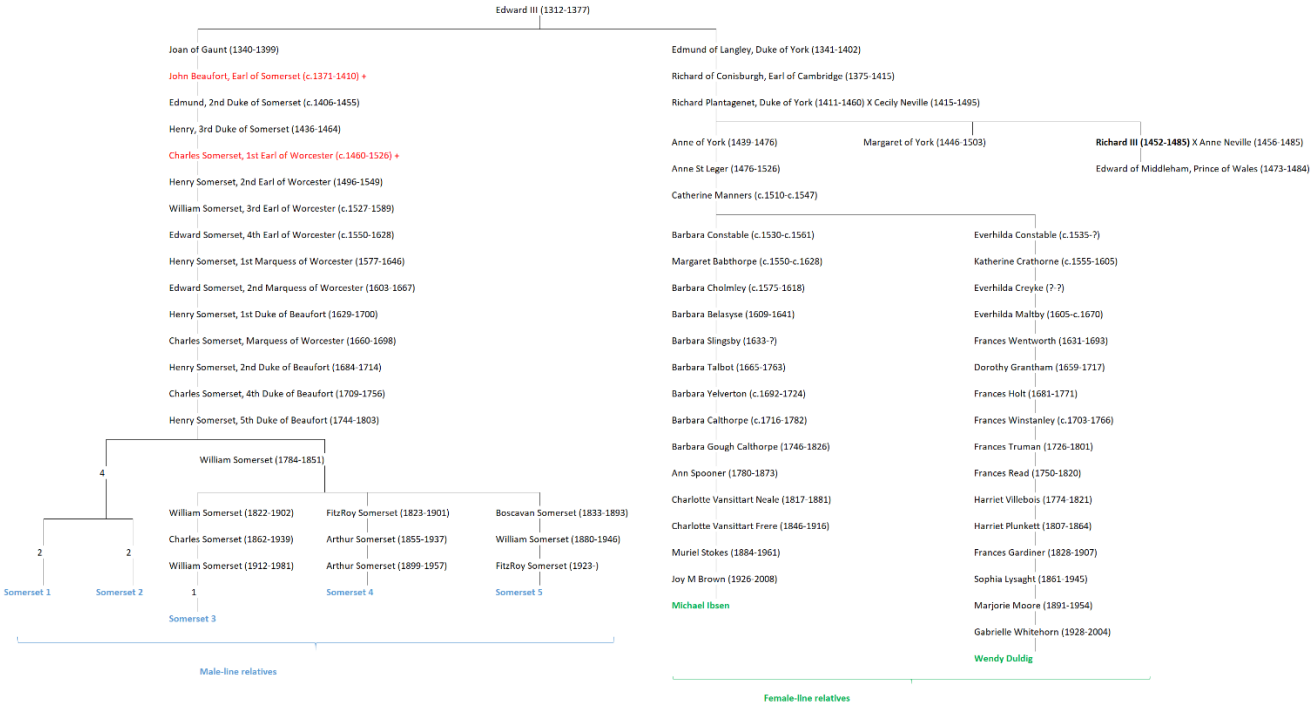

Figure 2 Pedigree showing the genealogical links between king Richard III and the living male-line (given in blue) and female-line (given in green) relatives who participated in the genetic identification study of King *et al.* (13). Numbers indicate the amount of anonymous individuals in the genealogy between named individuals. The individuals given in red were born illegitimate and were later legitimised. Figure adapted from (13, 39).

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