MAY | 2023

BIO-BABBLE

Newsletter of the Australasian Biospecimen Network Association

...IT IS COMING!

Granted, the above is an extremely vague statement - but given the number of events on the Australasian biobanking calendar in the next 12 months, vague felt apt!

For those who attended ISBER 2023 in Seattle, USA, we hope you all had a wonderful time and enjoyed both the program and networking opportunities it afforded. Special shoutout to ABNA's Anusha Hettiaratchi, Co-Chair of the meeting program for a comprehensive and thought provoking series of symposia and workshops. Special mention also goes to ABNA's Wayne Ng who officially began in the role of Director at Large IPR - congratulations Wayne! The strong (or perhaps just vocal) Aussie and Kiwi contingent were noted on multiple occasions and was particularly apt given we are delighted to now officially announce that in **2024 ISBER will be held in Australia!!** Hosting a global biobanking event provides a huge opportunity for Australasian Biobankers and we are excited to showcase the scope and depth of talent from Australasian biobankers!

Closer to home, ABNA's 20th Anniversary Conference is well underway with the program now taking shape with **registrations opening on 1 June**. Abstract submissions will open on the same date and we encourage those submitting to embrace the theme and have some fun with titles! The Committee are also excited to announce that they are working with collaborators to lock in a number of publication opportunities for high-quality abstracts - but more on this later!

The second session of ABNA's Seminar Series is also rapidly approaching on 6 June and will focus on diversity in biobanking ecosystems, covering academic, industry and clinical biobanks. For those who are yet to register, please visit the ABNA website for further details or go directly to the Seminar Series website HERE.

We know our members are linked to many other networks including museum, botanical and veterinary organisations if there are events that we're not aware of that are of value to our members - please let us know, we'd love to hear from you!

ABNA Seminar Series
Seminar 2 (virtual)
June 6, 12 noon AEST

ABNA 20th Anniversary Conference
18-20 October
Registration open 1 June

ISBER Annual Meeting
Melbourne, Australia
9-12 April

5 MIN WITH A BIOBANKER

We approach a different professional in the biobanking arena with the same five questions each month.

This month we speak to Dr Alison Parry-Jones, Operations Director, Wales Cancer Biobank and the incoming ISBER President.

THE QUICK QUESTIONS

Red or white wine?

White - Difficult to choose, wouldn't turn anything down!

Mac or PC?

Mac

Batman or Superman?

Hmm, not really my thing but if I had to choose - Superman

Lord of the Rings or Harry Potter?

Harry Potter - My kids grew up with Harry Potter, so fond memories of reading it to them and then going to the films as our Christmas Eve outing.

1. **How long have you been working in biobanking?**
   19 years
2. **Which advance in science/research do you think has had the most impact on you as a biobanker?**
   Genomics and Stratified Medicine. The progress of technological advances that have made tumour characterisation a possibility, opening up targeted therapies, has given challenges along the way for biobanks to support the early research but the positive outcomes for cancer patients are immense.
3. **In retrospect, given the experience you have now, what one piece of advice would you give to yourself at the start of your biobanking career?**
   It's not as simple as it sounds or others think it is. Biobanking is a team effort with many moving parts, within the biobank and with all stakeholders - be prepared to constantly review, engage and educate.
4. **Your career on record: name 3 songs/albums that best tell the story of your biobanking career:**
   Answer Accidents will Happen - Elvis Costello
   I fell into biobanking after working in a research support role and offering to help an academic out with his pet project, the rest is history!
   Don't Stop Believin' - Journey
   It sometime feels as if we're constantly fighting the same battles to stay afloat
   Twenty Years - Placebo

MY ISBER CONFERENCE, SEATTLE 2023

By Associate Professor V Krishnan Ramanujan

The ISBER 2023 annual meeting was built around the theme "Building Biobanking Bridges" and the symposia, workshops and the round table discussions aimed to articulate this theme in the diverse talks spread throughout the four days of the meetings. As I was privileged to be part of the multi-national, multi-disciplinary task force that worked towards the planning of this annual meeting, I had the opportunity to witness first-hand the intellectual cauldron that slowly and steadily shaped the annual meeting agenda over the period of 10 months. It was a gratifying moment to see the final program agenda but I was more grateful to see all my task force friends in three-dimensions in the same time-zone, peeled away from the zoom screens! The Seattle meeting saw twice the number of participants more than that seen in the last year annual meeting and it is sign that we are finally out of the grips of the corona pandemic. The annual meeting had a nice blend of talks that were mostly aligning with the theme. The vendor exhibits could have shown a better variety of tools and technologies, but the displayed ones were engaging nevertheless. The overall successful meeting is an epitome of the hard work that the administration team, the board of directors and the program planning task force have all put in.

Meet the Author AND ABNA's 2023 Keynote speaker!!

Associate Professor V Krishnan Ramanujan has a background in institutional microscopy, state of the art imaging technologies, machine learning models and an AI tool box for image analytics. His interest in digital pathology has led him into the biobanking field where he currently the Director of the Cedars-Sinai Biobank, Pathology and Laboratory Medicine, Los Angeles, California.

Clockwise from top left: View from the podium of the Main Ballroom, Westin Seattle at the opening session of ISBER 2023, out-going ISBER president Clare Allocca hands over to Dr Alison Parry-Jones, participants gather for the conference fun run, Symposium 1 speakers and meeting co-chairs

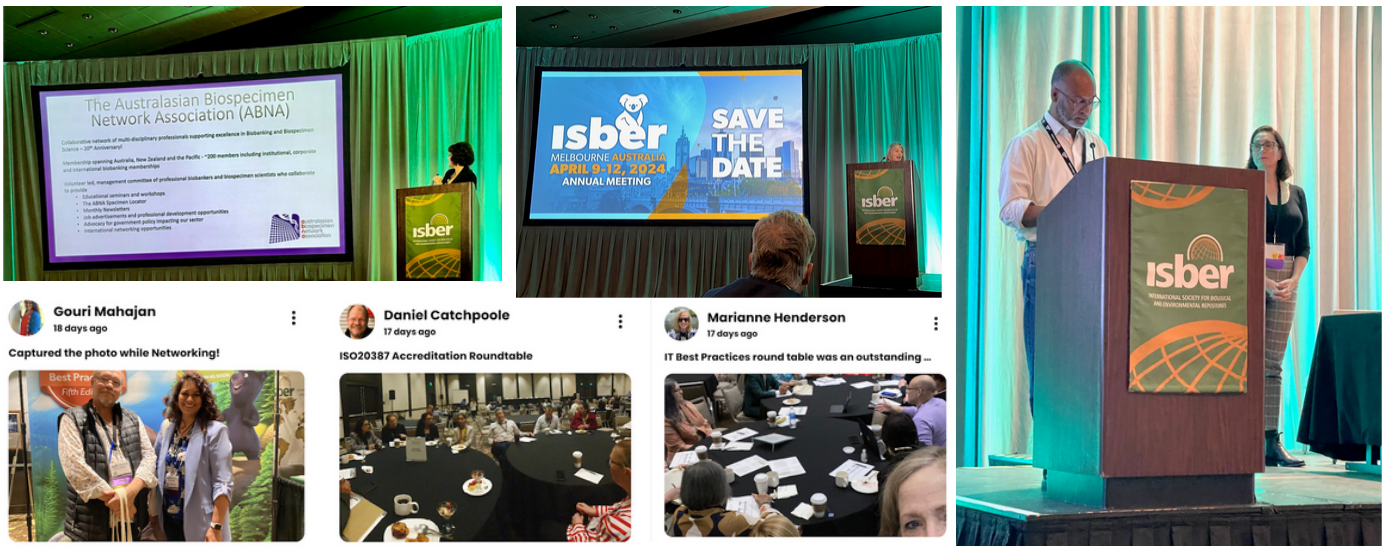
Symposium 1 focused on measuring biobank impact and this session included the Keynote address by Jairam Lingappa from University of Washington, USA. As it is a challenging task to quantify biobanking impact due to geopolitical differences as well as variable organizational vision in the industry, this symposium was a timely effort to address the global economy as well as public health challenges. The speakers in this session from academic and non-academic sectors drove home the point on precision medicine as well as human well-being and demonstrated how a strategic biobanking vision can effectively offer solutions to complex health issues.

Symposium 2A emphasized on how community engagement for biobanking should be part and parcel of every study plan. The need to understand the participant perspective on biobanking while addressing the real-life challenges in community engagement so that one can build an entrustment model was discussed by a set of four speakers. As the practitioners of the biobanking, we need to be prioritizing diversity and equity not because it is a strategy but because it is the right thing to do for the long-term health of the biobanks.

Symposium 2B had a lofty goal of exploring cryobiology technology as well as to cement the practical applications of these technologies the real world. Like any sector in industrial world, academic research in the field of cryobiology has advanced significantly in terms of biopreservation, cryoprotection and the cell membrane property measurements during re-warming and nanoparticle magnetic technology research. The symposium included a few talks from the cryobiology research pioneers as well as some of the conservationists (marine and integrative) who highlighted the success stories of biobanking under challenging wildlife conditions. The need for cost-effective practical utilisation of academic research and the value proposition for building such bridge between science and practice came out seamlessly through the set of presentations in this symposium.

Symposia 3A and 3B aimed to familiarise the academics and public sector biobanks with requirements, opportunities and challenges of the private-public partnership. Another major emphasis was to build a conversation around the data that accompany biospecimens. As there is an increasing awareness of how important it is to build a robust database of metadata and clinically relevant big-data associated with the specimens, there is also a disorganized outlook on the data privacy and the data security models in the biobanking industry. The speakers in these sessions tried to connect the disparate ends such as academic sectors and the industry sectors by laying out a foundation of a common language and a better scheme of expectation management.

Symposium 4 was the highlight of the last day of the meeting with the Seattle-specific Nirvana theme "Biobanking Research – As You are, As you were, As I want you to be". The goal of this symposium was to demonstrate that evidence from biobanking research could promote more sustainable biobanking investments that also deliver better research and other societal benefits. Speakers from three uniquely placed international locations made an excellent pitch for the symposium by articulating on the importance of building in collaboration, not competition, in the biobanking infrastructure as well as to build the patient-centric benefits to leverage the existing infrastructure to go full circle in the biobanking pipeline.



Clockwise from top left: ABNA President Cassandra Griffin presenting as part of the Global Collective Solutions to Challenges in Biobanking, ISBER President Dr Alison Parry-Jones announcing ISBER 2024 in Melbourne, Symposium 4 chair, A/Prof V Krishnan Ramanujan introduces Dr Amanda Rush, screen grabs from the conference app.

Besides the major symposia there were four contributed paper sessions, five educational workshops, two round table discussion sessions and seven corporate workshops. The ISBER 2023 meeting did strike an excellent chord in the attendees' minds what it is to build a better biobanking infrastructure but most importantly, the talks further were able to explain why. As there was a interesting mix of experienced biobankers and the newcomers to the industry, this meeting was indeed an opportunity to build connections with the most updated repertoire of modern-trend topics such as synthetic data, data security and artificial intelligence. I believe that the biobanking ecosystem will keep growing by imbibing the industry standards, quality metrics and by integrating practitioners with diverse intellectual backgrounds. Our quest to bridge the biobanking barriers should always revisit the idea of identifying the new barriers as this biobanking growth happens and in my personal opinion, the ISBER 2023 meeting was a perfect place for that.

BIOBANKING & GENEALOGY: A ROYAL ALLIANCE

By Dr Carmel Quinn

On 6 May 2023, King Charles III and Camilla, the Queen Consort, were crowned in Westminster Abbey, London. While attitudes vary regarding the importance of the monarchy in the present day, the coronation is undoubtedly an historic event, and so the gauntlet was thrown: can we compose an article which links British Royalty with the world of biobanking?

A logical place to begin was to consider the lineage of the British Royal Family, one of the most comprehensive family trees in existence, dating back at least to the Anglo-Saxons in the year 871. An interactive lineage can be viewed on the website of the UK National Portrait Gallery https://www.npg.org.uk/collections/explore/kings-and-queens-a-family-tree which traces the current Royal Family back to Alfred the Great, King of Wessex. Due to issues such as high mortality rates (particularly for children) and the sometime loss of life in battle, there are many instances through history where no (legitimate) heirs survived; this resulted in the breakage of the direct lines of ascent, and the consequent rise of different royal houses asserting their right to the throne.

King Charles III, on the occasion of his coronation

Photo credit: https://www.independent.co.uk/life-style/royal-family/coronation-official-portraits-king-charles-b2335344.html

However, whoever the King or Queen of the day, their coronations at Westminster Abbey date back to that of William the Conqueror in 1066 with King Charles III being the 40th monarch to be crowned at this site (1).

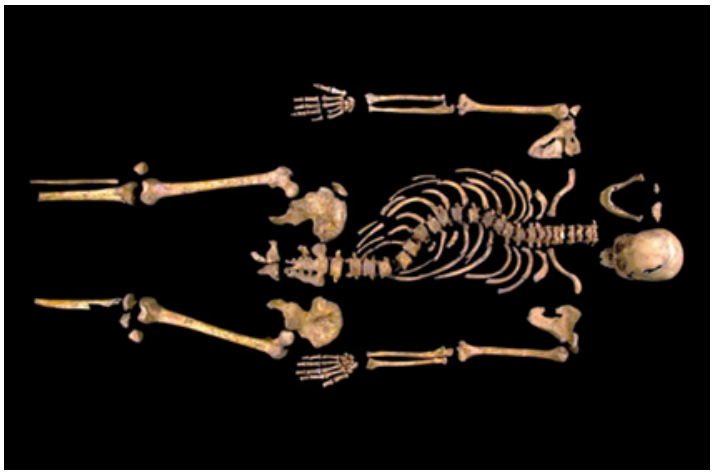
For those interested in the unrivalled pomp and ceremony of this most recent coronation, a comprehensive description has been compiled by the BBC https://www.bbc.com/news/uk-65342840

Finding a lost King

One fascinating royal story with a biobanking angle is that of the discovery of the remains of King Richard III. Richard III was a member of the House of York, the last of the Plantagenets, and was king from 1483 until his untimely death at the Battle of Bosworth Field in 1485. King Richard is infamous as being the hunchback king, accused of imprisoning his nephews in the Tower of London and ordering their murder. This popular persona is immortalised in Shakespeare's play, Richard III wherein the king is portrayed as physically deformed and scheming, although it is thought that this negative image was deliberately exaggerated by the Tudors, to justify their takeover of the monarchy after Richard's death (2).

After more than 500 years, the whereabouts of Richard III's remains was unknown. But in 2012, after extensive research, an archaeological dig was begun in a carpark in the English city of Leicester specifically to search for the grave of the king. Skeletal remains were unearthed, and carbon-dating confirmed these were from the correct period to be those of the king. The skeleton also displayed clear signs of scoliosis of the spine, another tantalising pointer towards the identity. However, identification was announced as being 'beyond reasonable doubt' only after genetic analysis, confirming a mitochondrial DNA (mtDNA) connection between the skeleton and 17th & 19th generation descendants of Richard's sister Anne of York, whom had been independently identified via painstaking genealogical research (3,4).

One of the key figures in the identification of Richard III was the historian, Dr John Ashdown-Hill. Back in 2003, Ashdown-Hill, who specialised in late-medieval English history, had been challenged to find the mtDNA sequence of Richard III and his siblings, in order to confirm the suspected remains of a sister, Margaret of York, who had been buried in Belgium. Initially, Ashdown-Hill sought to access mtDNA from a hair known to have belonged to King Edward IV (elder brother of Richard III) and housed in the Ashmolean Museum in Oxford. Unfortunately, the mtDNA was too degraded to be useful, and extensive genealogical tracing was then necessary to identify a living descendent for mtDNA comparison. Although this took Ashdown-Hill 2 years to complete, this same lineage was then established when mtDNA was required for comparison with that extracted from the bones suspected to be those of Richard III (4).



The skeletal remains of Richard III, clearly displaying curvature of the spine: Richard is thought to have suffered from adolescent idiopathic scoliosis.

Image source: https://www.nytimes.com/2013/02/05/world/europe/richard-the-third-bones.html

Genetic & Molecular Genealogy

Genetic genealogy combines traditional genealogy (family history research) and genealogical DNA tests for information about an individual's ethnicity, as well as links to other living relatives who have also participated in the process and are therefore included in reference databases (9). It is now commonplace for people to submit DNA to well-known companies such as Ancestry.com or 23andMe out of curiosity about their family history. This inevitably results in the accumulation of enormous amounts of genetic information with some controversy around potential uses of this data, e.g., in criminal investigations. Some of these have been discussed in an article discussing forensic genealogy in the August 2022 edition of Biobabble: 'CSI: Biobanking' by Georget Reiche-Miller. An additional option offered by some of these 'direct-to-consumer' genetic testing companies is to provide information about an individual's disease risk; this can also be controversial, e.g., according to whether clinical validation of these disease variants is available, and whether or not recipients are prepared to receive this information (10).

Moving well beyond the use of genetic genealogy for looking at the ancestry of individuals, 'molecular genealogy' can provide information for population geneticists; this may include data about how inheritance patterns have led to the development of regional populations, of migration, and can even extend to informing how humans have evolved from their earliest ancestors. An Ancestral Recombination Graph (ARG) provides a means of describing how molecular genealogy varies across the entirety of the human genome (11). ARGs are extremely complex, and the sheer volume of data and the number of potential outcomes involved in producing meaningful ARGs has limited progress. In fact, early methods used to produce ARGs could only deal with 10-20 individuals, and although subsequent methods enabled use of larger datasets, accuracy was compromised (11,12). However, advances in computing power along with the tremendous resources available through the UK Biobank, has allowed for development of a new method called 'ARG-Needle' (11,12). Using both genotype and phenotype data from 337,464 individual participants, this method has identified clusters of distant cousins on the basis of shared loci, with some associated physical traits (e.g. they may be taller than average). Apart from satisfying the inherent curiosity of discovering shared ancestry and common inherited traits, this technology can potentially provide valuable information about rare genotype-phenotype associations with relevance for health and disease.

Why mitochondrial DNA?

The absence of recombination in mtDNA, and its restriction to maternal line inheritance (thus avoiding erroneous conclusions though non-paternity), make it particularly useful for genealogical studies. With very little non-coding sequence, almost the entire 16,569-bp human mitochondrial genome (mtDNA) is responsible for producing 13 proteins, 22 transfer RNAs and 2 ribosomal RNAs that are all vital for the oxidative phosphorylation (OXPHOS) process and the production of ATP-1 dependent cellular energy. Single-nucleotide variants were acquired in the mtDNA (mtSNVs) during the migration of humans from Africa as they spread around the world; different mtSNV patterns are used to distinguish geographical region-specific macro-haplogroups (related haplotypes); it is these haplogroups and associated sub-groups that are used for genealogical tracing (5).

As well as being invaluable in the unraveling of ancestral information such as in the case of King Richard, several of these mtSNVs have been shown to affect mitochondrial function, or influence mitochondrial metabolism, (either directly or indirectly) and have been associated with common complex diseases including type 2 diabetes (6), and some neurodegenerative conditions (7). The UK Biobank, with genetic and health information from 500,000 participants, constitutes a tremendous resource for the study of health and disease. The Affymetrix genotyping arrays used by the UK Biobank included 265 mtDNA variants, enabling mtDNA genome-wide association studies (GWAS), further developing the number of known associations of mtSNVs with complex diseases (8).

More than 500 years after his death, after an initial, perfunctory, church burial, the remains of King Richard III were reinterred in a tomb within Leicester Cathedral on 26 March 2015. As technologies improve and costs reduce, genetic genealogy is being increasingly employed to solve historic mysteries. In addition, with the development of progressively sophisticated methods for identifying genotype-phenotype associations, advances in identifying causal variants for rare and complex disease markers will continue to improve. Biobanking plays a central role in this, providing access to quality specimens of known provenance as well as acting as repositories for the enormous amounts of genetic and other data that is needed to carry out these studies. We can only wonder what King Richard would make of it all.

Kings Henri IV & Louis XVI of France

Another genetic genealogy story with royal relevance is that of the attempts to verify biological remains of King Henri IV & King Louis XVI of France. Famously, both King Louis and his wife Marie-Antoinette were beheaded by guillotine as a result of the French Revolution in 1789. Anecdotally, several spectators of this event dipped handkerchiefs into the King's blood and studies have been performed to verify the blood on one of these, by comparisons with DNA from the presumed head of King Henri IV of France, a direct male ancestor of Louis XVI; the mummified head was thought to be removed from a ransacked grave at the time of the French Revolution. Both paternally-inherited DNA (Y chromosome short tandem repeats, Y-STRs) and maternally-inherited DNA (mtDNA) were used across different studies using these specimens. Initial analyses appeared to support the assertion that the mummified head and the blood on the handkerchief belonged to male relatives (13). However, a subsequent study which compared Y- chromosome single nucleotide polymorphisms (Y-SNPs) and mtDNA from known living descendants of the French kings, confirmed that the head and the blood were unlikely to belong to their putative sources; the possibility that these results can be explained by non-paternity or non-maternity events in the royal lineage was not thought likely based on the records of the times (14).

King Louis XVI of France, reign 1774-1792

Image source: https://www.britannica.com/biography/Louis-XVI

King Henri IV of France, reign 1589-1610

Image source: https://www.britannica.com/biography/Henry-IV-King-of-France

References:
1.https://www.westminster-abbey.org/about-the-abbey/history/coronations-at-the-abbey Accessed 8 May 2023
2.https://www.britannica.com/biography/Richard-III-king-of-England/Reign-and-fall Accessed 8 May 2023
3.https://www.bbc.com/news/uk-england-leicestershire-21063882 Accessed 8 May 2023
4.https://le.ac.uk/richard-iii/identification/genetics/living-relatives Accessed 8 May 2023
5.Elson JL, Majamaa K, Howell N, Chinnery PF. Associating mitochondrial DNA variation with complex traits. Am J Hum Genet. 2007 Feb;80(2):378-82; author reply 382-3. https://doi.org/10.1086/511652. PMID: 17304709; PMCID: PMC1785337.
6.Wang PW, Lin TK, Weng SW, Liou CW. Mitochondrial DNA variants in the pathogenesis of type 2 diabetes - relevance of asian population studies. Rev Diabet Stud. 2009 Winter;6(4):237-46. https://doi.org/10.1900/RDS.2009.6.237. Epub 2009 Dec 30. PMID: 20043036; PMCID: PMC2836195.
7.Cruz ACP, Ferrasa A, Muotri AR, Herai RH. Frequency and association of mitochondrial genetic variants with neurological disorders. Mitochondrion. 2019 May;46:345-360. https://doi.org/10.1016/j.mito.2018.09.005. Epub 2018 Sep 13. PMID: 30218715.
8.Yonova-Doing E, Calabrese C, Gomez-Duran A, Schon K, Wei W, Karthikeyan S, Chinnery PF, Howson JMM. An atlas of mitochondrial DNA genotype-phenotype associations in the UK Biobank. Nat Genet. 2021 Jul;53(7):982-993. https://doi.org/10.1038/s41588-021-00868-1. Epub 2021 May 17. PMID: 34002094; PMCID: PMC7611844.
9.https://sequencing.com/education-center/genetic-genealogy#fn-2 Accessed 10 May 2023
10.https://www.thermofisher.com/blog/biobanking/exploring-ethical-issues-in-commercialized-biobanking/ Accessed 21 May 2023
11.Harris, K. Using enormous genealogies to map causal variants in space and time. Nat Genet 55, 730-731 (2023). https://doi.org/10.1038/s41588-023-01389-9
12.Zhang, B.C., Biddanda, A., Gunnarsson, Á.F. et al. Biobank-scale inference of ancestral recombination graphs enables genealogical analysis of complex traits. Nat Genet 55, 768-776 (2023). https://doi.org/10.1038/s41588-023-01379-x
13. Charlier P, Olalde I, Solé N, et al. Genetic comparison of the head of Henri IV and the presumptive blood from Louis XVI (both Kings of France) Forensic Sci Int Genet. 2013;226:38-40 https://doi.org/10.1016/j.forsciint.2012.11.018
14.Larmuseau MH, Delorme P, Germain P, Vanderheyden N, Gilissen A, Van Geystelen A, Cassiman JJ, Decorte R. Genetic genealogy reveals true Y haplogroup of House of Bourbon contradicting recent identification of the presumed remains of two French Kings. Eur J Hum Genet. 2014 May;22(5):681-7. doi: https://doi.org/10.1038/ejhg.2013.211. Epub 2013 Oct 9. PMID: 24105374; PMCID: PMC3992573.

One for the Bridgerton Fans...

Caution, spoilers for those who have not yet finished 'Queen Charlotte'!

Stories of 'the Mad King' have permeated popular culture and have been recently revived by the portrayal of George III in the increasingly popular Bridgerton franchise. George III was plagued by persistent mental illness, characterised by fits of mania, progressive blindness, loss of hearing and dementia that have been attributed to such causes as Biopolar disorder or Porphyria. As a King who demonstrated a fierce interest in science and research, it seems fitting that investigations into the cause of his illnesss are ongoing using biobanked samples stored in the Welcome Collection, UK. In 2005 a chemical analysis found concentrations of arsenic in the Monarch's hair which may have lead to the exacerbation of his Porphyria. It is thought that tinctures and remedies containing antimony, which contains high levels of arsenic, may have exacerbated his condition later in life.