Bulletin
of the
American
Academy
of Arts & Sciences

Reimagining the American Economy

THE SEARCH FOR LEONARDO'S GENOME

2022 INDUCTION: OPENING CELEBRATION

2022 INDUCTION CEREMONY

WINTER 2023

The Search for Leonardo's Genome

On June 6, 2022, the Academy's **New York Program Committee** hosted a dinner discussion on *DNA and Art: In Search of the Genome of Leonardo da Vinci*, featuring **Jesse H. Ausubel**, director of the Program for the Human Environment at The Rockefeller University. The evening followed the model of a "Jeffersonian Dinner" in which a group of guests curated for their various perspectives engages in a wide-ranging conversation about a chosen topic over the course of the meal. Eighteen Academy members gathered at the University Club of New York for this dinner conversation. Committee cochair **Kenneth Wallach** (Central National Gottesman Inc.) served as host and provided opening remarks.

During the dinner, Mr. Ausubel described the project he is leading, which is aiming to employ the latest techniques from molecular biology and genetics to make discoveries about da Vinci's attributes and ancestors. Members at the table, who represented various fields, including art history, dance, mathematics, and law, drew on their own expertise to ask salient questions about methodology, application, and the ethical implications of the project. The conversation was lively and continuous, with each member in attendance contributing to the discussion. A lightly revised and extended version of Mr. Ausubel's presentation follows.

Jesse H. Ausubel

Jesse H. Ausubel is Director of the Program for the Human Environment and Senior Research Associate at The Rockefeller University. He was elected to the American Academy in 2011.

I would like to extend my thanks to Carol Gluck, Ken Wallach, and the Academy's New York Program Committee for the opportunity to launch this new round of in-person events; to Laurie McDonough and Patrick Meade on the Academy staff for persevering organizationally through the oscillations of the COVID-19 pandemic; and to all of you for coming to this program.

I propose as our subject the potential benefits of a more frequent marriage of new biology, in particular genomics and microbiology, with art, art history, and the conservation of cultural heritage.

To begin, let's consider a trio of entertaining studies of the scandalous power of human genomics. In a large survey of parenthood conducted in the United Kingdom, in which parenthood was not in dispute, one in twenty-five fathers was not the biological parent. In a similar survey in which parenthood was disputed, 30 percent of the fathers were not the biological parents. In a 2019 study conducted at the U.S.-Mexico border, 30 percent of those tested were unrelated to the children they claimed as their own. Biology can both end and begin mysteries.

Now let's consider the power of art as demonstrated by money. The global art market today is valued at approximately $65 billion annually, and about 40 percent goes through New York City. Hong Kong is the second art market capital, followed by London, Paris, and Geneva. Most of the demand is for postwar, contemporary, and

modern art. Sales of Old Masters, such as Leonardo and others who worked in Europe before 1800, make up less than 5 percent.

Attribution and authentication are crucial matters for buyers, sellers, and intermediaries, including dealers and auction houses. Hundreds of years ago the art market invented blockchain, a fancy word for reliable provenance. Provenance and connoisseurship – intelligence without artificiality – establish identity in art markets.

Identity requires comparison – a reference and hopefully a match. The match can pair fingerprints, retinas, voices, faces, or other images or attributes. Natural history museums and botanical gardens preserve a so-called holotype, a single physical example of a reliably described organism, in a jar or drawer as a reference specimen against which to establish the identity of other specimens. Taxonomists build botany and zoology on such collections of plants and animals.

The art world has been utilizing chemistry and physics for a long time. X-rays and other types of radiation reveal images; carbon-14 and other radioactive isotopes disclose dates; and mass spectrometry and gas chromatography identify materials used in the art.

Mentioning the description of animal species offers me a chance to explain a thread in my own story. I have devoted much of my career to censusing the diversity of marine life. Until recently, to identify most marine animals one had to capture them, which can be harmful, or photograph them extensively, which is often difficult in a vast dark ocean. Over the past twenty-five years, I have been part of a community that has developed affordable, scalable techniques for identification that are much less harmful to the organisms, such as collecting the DNA that the animals shed in sea water and recording the sounds the animals make.

Short "DNA barcodes" of as few as one hundred letters representing the four bases (cytosine [C], guanine [G], adenine [A] or thymine [T]) that make up a DNA strand, a tiny fraction of the genome, usually suffice to identify the species of a fish from the Hudson River or from the middle of the Atlantic Ocean. Of course, a carefully documented specimen that was properly preserved in a jar in a museum provided some tissue whose DNA offers the sequence, deposited in a reliable database, against which we make the match. In addition to DNA, other molecules can accomplish these identifications. So too can the collection or profile of microbial organisms that live on a critter or inside its cheek, what we call a microbiome. These microbiomes are ubiquitous; our world is not sterile. Microbes abound in your carpet, on a piece of wood, and on the surface of a sheet of canvas or paper.

The art world, exemplified by the extraordinary research labs of the Metropolitan Museum of Art in New York, the Smithsonian in Washington, D.C., the Getty in Los Angeles, and their counterparts in England, France, Italy, and other countries, has been utilizing chemistry and physics for a long time. X-rays and other types of radiation reveal images; carbon-14 and other radioactive isotopes disclose dates; and mass spectrometry and gas chromatography identify materials used in the art.

In cultural heritage, biology has tended to be treated like dirt or contamination to be cleaned away. My suggestion, to use a phrase from Silicon Valley, is to treat biology as a feature and not as a bug.

Let me share another personal thread. Why and how did we become interested in Leonardo? Among my most important mentors is an Italian physicist, Cesare Marchetti, who recently turned ninety-five. About twenty-five years ago, during a visit to Marchetti's home in Tuscany, he asked if I had studied Leonardo, to which I answered no. His response was that the English read Shakespeare, the Germans Goethe, and the Russians Tolstoy, and a good education in Italy must include Leonardo. I should not travel through life without some exposure to Leonardo. He gave me a copy of a book from the 1938 Milan exhibition, republished in 1996, about Leonardo's achievements, spanning from astronomy to zoology.

Over the next fifteen years or so, we had endless fun with Leonardo's puzzles and lists. I became interested in hidden images, anamorphoses, which Leonardo played with here and there. We called them cryptos. A magnificent painting in the Metropolitan Museum by Leonardo's master Verrocchio has a hidden image of the head of a kite (nibbio), a bird featured in Leonardo's drawings and earliest memories. Perhaps Leonardo snuck the image into the painting. His tiny or micro images are also intriguing. How could anyone draw

so precisely and accurately at the scales at which Leonardo worked?

Let's jump ahead to the year 2014. Marchetti and I are having lunch with Brunetto Chiarelli, a bone-and-tooth expert who was then the head of the Institute of Physical Anthropology at the University of Florence. Brunetto suggested we establish a project to obtain and sequence Leonardo's genome. Brunetto believed that with the collaboration of his close friend Henry de Lumley, head of the Institute of Human Paleontology in Paris, we might gain access to the tomb of Leonardo in Amboise in the Loire Valley at the Royal Chateau, where Leonardo spent the last three years of his life under the patronage of Francis I, King of France. Henry was keen to join our effort, and so the Leonardo Da Vinci DNA Project began.

Henry cautioned us that the Count of Paris, another Henri, who was the head of the Fondation St-Louis that controls the Chateau, was unlikely to let us disturb the beautiful tomb, except possibly as a capstone to the entire project if much of what we did was successful. We needed strong reference materials, like holotypes, against which to compare the materials that may or may not be in the tomb. By the way, the tomb was moved and opened during the French Revolution and again later in the nineteenth century, and perhaps on other occasions too. In any case, the animating question for the project became, do the relics that lie in the Amboise tomb contain Leonardo's DNA?

Our list of questions quickly grew and included a few about Leonardo's ancestry, in particular, about his mother. We know a lot about the family of Leonardo's father, a consequential notary, but distinguished Leonardisti, such as Martin Kemp and Alessandro Vezzosi, hold widely divergent views about his mother, who was probably a local Tuscan peasant or, more dramatically, an enslaved person brought from the Middle East or from Circassia north of the Black Sea. Did Leonardo have an unusual parental combination?

A third set of questions, which makes the project appropriate for The Rockefeller University, a largely biomedical research institution, refers to Leonardo's extraordinary visual acuity both in space and time. Project member David Thaler (University of Basel) has published a remarkable paper exploring the evidence for extraordinary visual acuity in Leonardo's comment on a dragonfly.[1]

Could Leonardo have played major league baseball? Famous art historians and biographers such as Sir Kenneth Clark and Walter Isaacson have written about Leonardo's "quick eye" because of the way he accurately captured fleeting expressions, wings during bird flight, and patterns in swirling water. Until now no one had tried to put a number on this aspect of Leonardo's extraordinary visual acuity. Thaler notes that flicker fusion frequency (FFF) – akin to a motion picture's frames per second – is used to quantify and measure "temporal acuity" in human vision. When frames per second exceed the number of frames the viewer can perceive individually, the brain constructs the illusion of continuous movement. An average person's FFF is between 20 to 40 frames per second; motion pictures today present 48 or 72 frames per second. To accurately see the angle between dragonfly wings

"We know a lot about the family of Leonardo's father, a consequential notary, but distinguished Leonardisti hold widely divergent views about his mother, who was probably a local Tuscan peasant or, more dramatically, an enslaved person brought from the Middle East or from Circassia north of the Black Sea. Did Leonardo have an unusual parental combination?

1. David S. Thaler, "Evidence for Extraordinary Visual Acuity in Leonardo's Comment on a Dragonfly," in Henry de Lumley, ed., *Actes du Colloque International d'Amboise: Leonardo de Vinci, Anatomiste. Pionnier de l'Anatomie comparée, de la Biomécanique, de la Bionique et de la Physiognomonie* (Paris: Centre national de la recherche scientifique, in press), https://phe.rockefeller.edu/wp-content/uploads/2020/06/LeonardoFlickFusionSfumatoPortraitJune182020.pdf.

would require temporal acuity in the range of 50 to 100 frames per second. Further study could compare the genome of individuals like Leonardo and species with unusually high FFF.

A fourth set of questions relates to Leonardo's diet and health. From verified bones, we may be able to learn whether he maintained a vegetarian diet for much of his life, as is widely believed.

One aim of our project is to match the DNA of the descendants against materials found in the tombs of descendants in the Vinci area from say 1600 or 1700. Eventually we might try to open the tomb of Leonardo's father, Ser Piero, and half-brothers in the beautiful Badia Fiorentina near the Palazzo Vecchio in central Florence.

A fifth question, or possibility, is to reconstruct Leonardo's appearance, that is, to go from genotype to phenotype. With enough of the genome, one can now do a reasonable job of reproducing physiognomy. Team members from Craig Venter's Institute have pioneered a technique using genomes to predict what faces look like. Carmen Bambach, curator of drawings and prints at the Met and the author of a monumental four-volume study of Leonardo, neatly summarizes a long-standing debate about representations of Leonardo, including the famous image in Turin that may or may not be a self-portrait.

In the same spirit, team members Francesco Galassi and Elena Varotto of Sicily's Forensic Anthropology, Paleopathology, and Bioarcheology Research Center analyzed shoes that belonged to Michelangelo Buonarroti to estimate his height at 157 centimeters (5 feet 2 inches).

How do we set off on this journey that might conclude at Leonardo's tomb in Amboise? An obvious route is via possible living descendants. Leonardo was gay, and no mention has ever been found that he sired children. While he was the only (and illegitimate) offspring of his father and mother, his father sired seventeen other children by several wives. In July 2021, under the leadership of historians Alessandro Vezzosi and Agnese Sabato, the project published "The New Genealogical Tree of the Da Vinci Family for Leonardo's DNA: Ancestors and Descendants in Direct Male Line Down to the Present XXI Generation," an open access ninety-page booklet with a 690-year genealogy that identifies fourteen possible living descendants.[2] Bastards, of course, could intervene, but during April 2022 six of the fourteen possible descendants gave their saliva to David Caramelli's Laboratory of Anthropology, Molecular Anthropology, and Paleogenetics at the University of Florence in order to study their Y chromosomes, which are passed largely unchanged from father to son.

One aim of our project is to match the DNA of the descendants against materials found in the tombs of descendants in the Vinci area from say 1600 or 1700, tombs that for artistic reasons are not very remarkable. Eventually we might try to open the tomb of Leonardo's father, Ser Piero, and half-brothers in the beautiful Badia Fiorentina near the Palazzo Vecchio in central Florence. Renaissance historian Anne Leader has identified the likely spot of the tombs,[3] and we have conducted studies with ground-penetrating radar. But opening an artful historic tomb is a serious matter in Florence as it is in Amboise, and the Florence floods of 1966 may have damaged the contents.

What is most intriguing is the possibility of getting DNA off the pages of notebooks or from the pages of drawings, in particular drawings made by metal or silver point, in which saliva is used to prepare the paper, a possibility introduced and explored by artist Karina Aberg. The laboratory of Tom Sakmar, a colleague at Rockefeller, has been working with great success on techniques to obtain DNA off papers of diverse kinds and ages. The late scholar and dealer Fred Kline provided the Project with fourteen works on paper with reasonably good provenance and/or authentication that are being used in our experiments. Colleagues in Spain, such as Jose Lorente and Christian Galvez, who are interested in Cervantes and other Spanish historical figures are also advancing the techniques, and exploring the possibility to obtain samples from the six hundred pages of Leonardo's

2. Alessandro Vezzosi and Agnese Sabato, "The New Genealogical Tree of the Da Vinci Family for Leonardo's DNA: Ancestors and Descendants in Direct Male Line down to the Present XXI Generation," *Human Evolution* 36 (1–2) (2021): 1–90, https://doi.org/10.14673/HE2021121077.

3. Anne Leader, *The Badia of Florence: Art and Observance in a Renaissance Monastery* (Bloomington: Indiana University Press, 2011), https://iupress.org/9780253355676/the-badia-of-florence.

notebooks held by the Spanish National Library in Madrid, some of which appear to have Leonardo's fingerprints on them.[4]

While writers and artists tend to handle the edges or borders of sheets of paper, leaving DNA there, more historical and artistic value may be found in text and images that are more centrally located. In any case, contamination from many people handling the pages of the notebooks or other sheets as well as other works, such as paintings, is a concern. Our lead contamination expert, Dr. Rhonda Roby, now at California's Alameda County Sheriff's Office, has extensive forensic experience.

Finally, other relics, such as hair or a ring, might merit examination. Unsurprisingly, collectors often contact us about objects they hope to associate with Leonardo, for example, a globe made from an ostrich egg that depicts what Europeans called the New World.

In any case, the key to the game is a match of two or more sources, such as a living descendant's Y-chromosome DNA with a comparable sequence from a notebook page. Once we have that key, we hope to grow the reliable sequence and search systematically, for example, for the genes that influence vision. Our aim and hope are to report some success by the end of 2023.

While Leonardo presents particularly intriguing challenges, the ideas of the project are now "in the air." In 2014, the English were excited to find, with a 99 percent probability, the bones of Richard III in a parking lot in Leicester. Members of our team have been involved in obtaining the DNA of Christopher Columbus. The techniques for locating and piecing together ancient DNA are getting better. Caramelli's lab works on Neanderthals from thirty thousand years ago, as well as Etruscans and even Pompeians smothered by Vesuvius. In another fifteen to twenty years, much of the genomics and microbiology we are doing will become customary parts of history and conservation sciences. It has been great fun assembling the multidisciplinary team to do this work.

Whether or not we succeed with Leonardo's genome, a movement to integrate scholarship in biology and art is growing, led by Julie Arslanoglu at the Met and Peggy Ellis of NYU's Institute of Fine Arts. They have hosted two conferences on "Art Bio Matters" and have started a community website.[5]

Let me end with a few general comments to stir some discussion.

One dimension that we did not anticipate and that elicits great interest concerns fraud and forgery. Artists such as Dali, Rothko, and Basquiat are bedeviled by these problems. Building a database of forgers' DNA and including the DNA of artists could help. Living artists might want to deposit their sequences to lessen the chance of future fraud. Project lawyer Eric Rayman has helped us raise the issue of DNA and art law.[6]

"The techniques for locating and piecing together ancient DNA are getting better. In another fifteen to twenty years, much of the genomics and microbiology we are doing will become customary parts of history and conservation sciences.

I mentioned previously degradation and microbiomes. Team members Manolito Torralba and Karen Nelson (formerly at the J. Craig Venter Institute in La Jolla, California) and other colleagues used small, dry polyester swabs to gently collect microbes from centuries-old, Renaissance-style art in a private collector's home in Tuscany. Their findings are published open access in the journal *Microbial Ecology*.[7] Much remains to be learned about how to slow or reduce degradation and also about how to preserve works in conditions of changing air chemistry and climate, not only in museums but elsewhere.

4. During the seminar, Carmen Bambach made the excellent suggestion to consider also as a source of DNA the books kept by Leonardo's father, Ser Piero.

5. Art Bio Matters, https://www.artbiomatters.org.

6. Jesse H. Ausubel, "Some DNA Issues for Art Law," MLRC MediaLawLetter, August 2021, https://phe.rockefeller.edu/wp-content/uploads/2021/09/Ausubel-Some-DNA-Issues-for-Art-Law.pdf.

7. M. G. Torralba, C. Kuelbs, K. J. Moncera, et al., "Characterizing Microbial Signatures on Sculptures and Paintings of Similar Provenance," *Microbial Ecology* 81 (2021): 1098–1105, https://doi.org/10.1007/s00248-020-01504-x.

I also mentioned that biology is a feature and not a bug. We need to ask whether we have been cleaning too aggressively, or without proper preservation of what is removed. New York City's Morgan Library is not only a library but a biological repository that may have the DNA of Mozart, Thoreau, Gertrude Stein, and Sylvia Plath. Appreciating genetics and microbiology might increase the value of many collections.

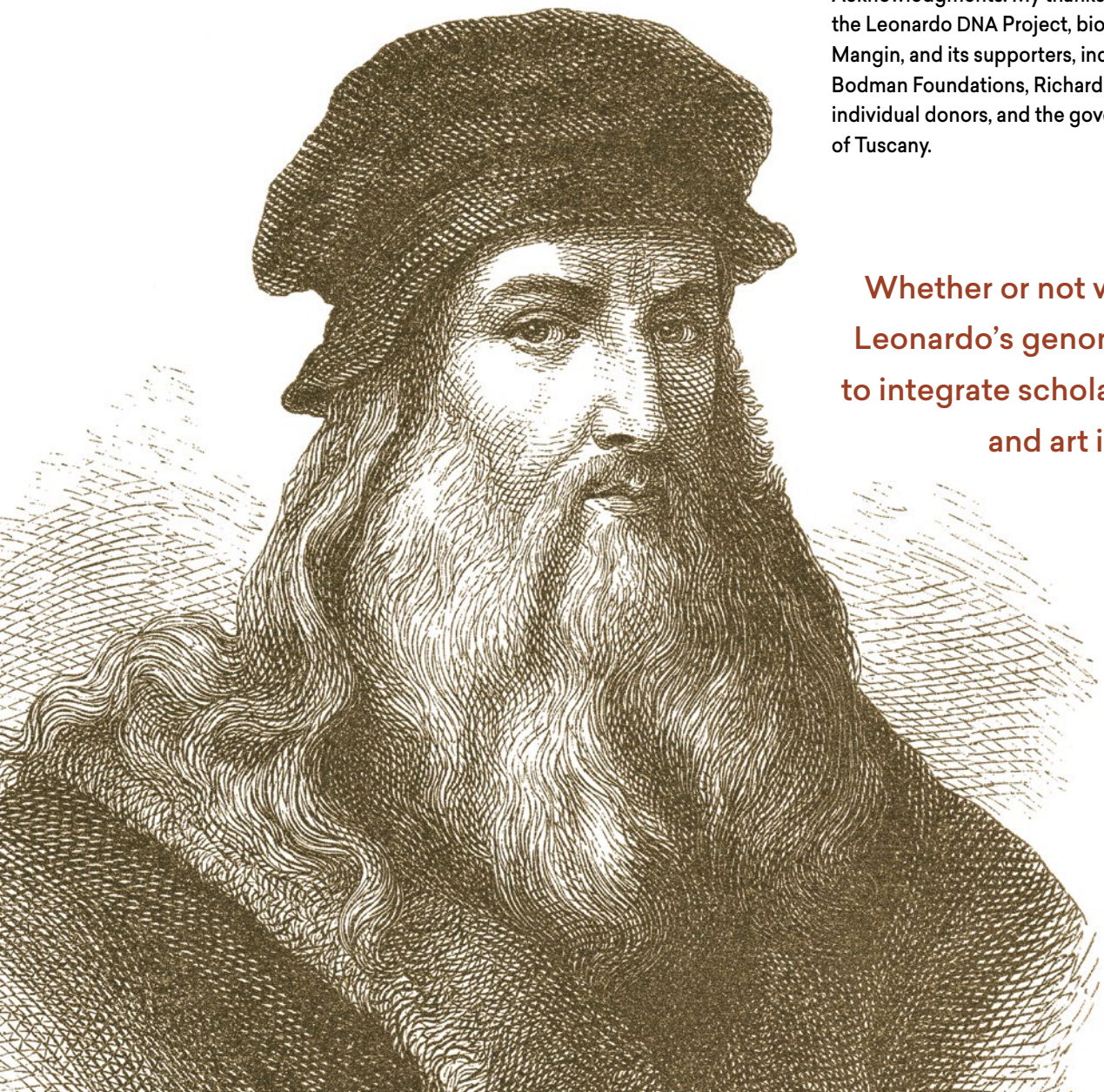
In this vein, we may learn a lot by studying extraordinary human performance, perhaps outliers, of several kinds. The New York Public Library for the Performing Arts has begun a project with Yale University to try to obtain the DNA of Franz Liszt from materials that belonged to him. Liszt experienced synesthesia; he saw musical notes and chords as colors. DNA might also give us wonderful clues to the anonymous artists who worked in ancient Egypt or medieval Ireland or the Kingdom of Benin.

Finally, while our project is decidedly nonprofit, a lucrative entrepreneurial opportunity exists to provide services to auction houses, galleries, and collectors, most powerfully by an enterprise that encompasses genomics, artificial intelligence, and expertise. For example, scanning more than seven hundred van Gogh works might allow a machine to learn a lot about van Gogh, and his DNA could be obtained from his clothing and other personal items in the collections held by the Van Gogh Museum in Amsterdam.

I hope I have persuaded you that such marriages, exemplified by the search for Leonardo's genome, could overcome formerly daunting limits to knowledge and explore not only the unknown but what seemed unknowable.

&

Acknowledgments: My thanks to the coordinator of the Leonardo DNA Project, biochemist Dr. Marguerite Mangin, and its supporters, including the Achelis and Bodman Foundations, Richard Lounsbery Foundation, individual donors, and the government of the region of Tuscany.



> Whether or not we succeed with Leonardo's genome, a movement to integrate scholarship in biology and art is growing.