
Some Genetics for Some Jews

A Jewish Look at the Human Genome*

Robert Pollack

Chapter 3 of Rambam's *Mishneh Torah*, *Hilkhot Talmud Torah*, begins:

Three crowns were conferred upon Israel: the crown of Torah, the crown of priesthood, and the crown of royalty.

Aharon merited the crown of priesthood, as [Bemidbar 25:13] states: "And it will be an eternal covenant of priesthood for him and his descendants after him."

David merited the crown of royalty, as [Tehillim 89:37] states: "His seed will continue forever, and his throne be as the sun before Me."

The crown of Torah is set aside, waiting, and ready for each Jew, as [implied by Devarim 33:4]: "The Torah which Moses commanded us is the inheritance of the congregation of Jacob." Whoever desires may come and take it.

Lest you say that the other crowns surpass the crown of Torah, [Mishli 8:15–16] states: "By me, kings reign, princes decree justice, and nobles rule." Thus, you have learned that the crown of Torah is greater than the other two.

Rambam goes on to make the point in his own special way, enjoining that when hiring a teacher of Torah for oneself or one's child, one should give a learned *mamzer* precedence over an ignorant man, even if that ignorant man happens to be the *kohen gadol* himself.

Rambam is pushing a point, to make a critical distinction, *Vhavidil*. By distinguishing the availability of the "inheritance" of Torah from the father-to-son inheritance of priestly obligations and privileges, and from the royal pre-

*This essay is based on a talk given to the Center for Jewish-Christian Studies and Relations of the General Theological Seminary, New York City, in March 2001.

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rogative to pass a Jewish Kingdom to one's child, he is telling us that no aspect of Jewish life available to him was biologically inherited. The inherited priesthood needed a context of Temple sacrifice, and the Davidic reign needed a Jewish nation. In his time, all that Jews had left was Torah.

Though many of my best friends are *kohanim* and a few might be descendants of David, royal inheritance is not any more available to us than to the Jews with whom Rambam studied and prayed. And though the *kohanim* may still set themselves apart in some ways—how else could Rabbi Neil Gillman have helped redeem our grandson, our daughter's first-born son?—the Temple is far away, and the kingdom not much closer at hand. While the Jewish nation has its national homeland back, it is unlikely—even in comparison with recent electoral events in the United States—that Israelis will ever have the chance to vote for a handoff of ultimate temporal power from parent to child.

With this as background, let's look again at what we may yet inherit, albeit in a different, non-genetic way: "The crown of Torah is set aside, waiting, and ready for each Jew. . . ." Take these characteristics of the crown of Torah one at a time.

It is "set aside." In the dichotomy of *kodesh v'hol*, the study of Torah is intrinsically *kodesh*. The crown of understanding cannot be taken, any more than it can be inherited. It can only be given, as a reward for study, for understanding, and for the enactment of what it teaches.

It is "waiting." The understanding of Torah does not require that one be born into the correct family, or into the correct moment. Rather, any moment is as good as any other to begin studying, and any Jew is as authentic as any other, in terms of the right and the obligation to begin studying.

It is "ready for each Jew." The depth of understanding of Torah necessary for the gaining of the crown cannot be the same for each Jew. Instead, for each one of us, it is the saturation of our individual capacity to learn, rather than our particular level of innate, inherited capacity, that yields one of us the crown, and not another. No wonder we say in the Sh'ma, *v'she'nantam l'vanekha*—"teach them thoroughly to your children. . . ." We have no other choice; for our children we have no genetic, inherited shortcut to offer.

In summary, Rambam is saying that not only is the crown of Torah not inherited, but neither is any aspect of one's wish to receive the crown of Torah. Both are wholly a matter of choice and the will to follow Torah in each generation; neither is at all a matter of biological inheritance.

Moreover, he has no fourth crown to mention at all; no crown of sensitivity, no crown of spirituality, no crown of religiosity. Now step back and ask what this has to do with our sense of ourselves as Jews: Whatever *pintele yid*, whatever special Jewish soul we may wish to think we have, Rambam is saying that it must have been the product of what we were taught and what we learned, not what came to us through our ancestors' DNA.

My first point is simple: Rambam is correct in modern genetic terms. No DNA sequences are common to all Jews and absent from all non-Jews; nothing in the human genome makes or diagnoses a person as a Jew. In this

sense, there are no special genetics for Jews at all, nor can there be anything specifically Jewish about any human genome. But you say, what about the “Jewish inherited diseases”? If Rambam is correct, then what can we possibly mean by the phrase “Jewish inherited diseases”?

These conditions represent fateful sequences of DNA in our chromosomes, versions of one or another gene shared by many Jews and not found in many non-Jews. Can this be some sort of cosmic joke on us, that nothing important about being Jewish can possibly be inherited through DNA? No.

Rambam’s insight remains untouched by these inherited conditions, genetic facts that reflect not Jewish observance, but Jewish history. They are intimately involved with our Jewish past, but they are the product of our enemies’ actions, not our own. Remember we are still in exile. These diseases, you might say, are Har Esav’s judgment on Har Tzion. To see this logic, one must consider the demographics of the Jewish past. Population statistics of Jews at various times in the past are not easy to obtain, and those that we have are not precise. The best estimates I have found show that, in the long view, Jewish populations have enjoyed only a few periods of smooth, uninterrupted growth in any one part of the world.

From the earliest records to the admittedly partial documentation we have of Jewish populations of different countries in the past five hundred years, a repeating pattern emerges of relatively brief periods of rapid population growth followed by instances of severe, almost complete population collapse, with long intervening periods of low but stable numbers.

Each time a group of Jews survived one of these boom-and-bust cycles, it was as the descendants of a very small number; symbolically, as with the Jewish patriarchs and matriarchs, on just one family. Today about 6 billion people inhabit the earth, and about 13 million of them are Jews. This means that about one person in 500, worldwide, is Jewish.

Three thousand years ago, upon David’s establishment of the first Jewish nation-state, the Jewish population worldwide rose from approximately 500,000 to approximately 2 million, and for a while almost one person in 50, worldwide, was Jewish. But once Jerusalem fell to Babylon 2500 years ago, Jewish numbers declined back down to fewer than 300,000, and afterward, under Greek rule, the Jewish fraction of the population was once again reduced to about one in 500.

Numbers rose to four or five million about 2000 years ago. They remained high, and for the first two Roman centuries, Jews were as many as one person in sixty. Then, as the world’s population grew, the Jewish fraction fell once again, to about one person in 200 by the year 600. For the next millennium, until about 1600, the number of Jews remained about 1 to 1.5 million, while the world’s population more than doubled. As a result, the fraction of the world that was Jewish kept shrinking, until, by 1600, it was back to the one in 500 that it was during the Babylonian exile.

Then an unexpected thing happened: a boom occurred in a fertile part of

Europe and it did not go bust for nearly 400 years. The Pale—a part of eastern central Europe now partially contained within the borders of Russia, Belarus, the Ukraine, and Poland—let Jews live. The medieval Hebrew name for the German lands from which Jews were exiled into the Pale was Ashkenaz, and so Jews from that much larger region still refer to themselves by the Hebrew plural Ashkenazim.

Ironically, the place name derives from the name of one of the grandsons of Noah by his son Japheth, which suggests that from the beginning, local inhabitants of this region were understood by their Jewish neighbors to be very distant relations indeed, not even the descendants of Noah's son Shem, the ancestor of Abraham.

For 400 years the Jews of Ashkenaz stayed put and grew in numbers. In that period—1500 to 1900—the total number of Jews worldwide went from about a million to about 11 million, and almost all of that increase took place among the Ashkenazim. By 1900, one person in 150 worldwide was Jewish, and more than 90 percent of this greatest number ever, had descended from the Jews who had been living in central Europe since the 1500s.

The year 1939 was the peak year for Jews in this world, who numbered between 16 and 17 million and were about one person in 120, worldwide. All but about a million of them were descended from the original settlers of Ashkenaz, although the total number of Jews living there actually decreased in the early twentieth century due to the emigration that brought my grandparents, among many others, to these shores.

The demographic losses of 1939–1945 may not be recoverable. In the last thirty years, Jews worldwide have numbered about 13 million, neither growing nor shrinking by much. As the world's population booms, the Jewish portion of it shrinks. That is why today the fraction of the world's people who are Jewish—one in 500 or less—is no higher than it was 2500 years ago, after the first Babylonian exile.

My point in reviewing this set of population figures is not to raise the question of why, since David's kingdom fell, the world has been unable to bear more than one Jew in every 500 people for longer than a century or so. Just the opposite: three times—after the fall of David and Solomon's kingdom 2500 years ago, after the fall of the Hasmonean Kingdom 2000 years ago, and in Ashkenaz after the pogroms and crusades and Black Death of the Middle Ages 500 hundred years ago—the total Jewish population actually grew, and in each case it grew more rapidly than the general population.

Of these three instances, the startling growth of the Jewish population in Ashkenaz is also the source of one of the world's largest founder-effects. In 1500, only a small percent—some tens of thousands—of the world's million or so Jews lived in the Ashkenazic Pale. By 1939, about 95 percent of the world's 17 million Jews either lived in Ashkenaz or were the descendants of people who had lived there until no more than fifty years earlier.

Combining the history of Ashkenaz with data from the genomes of their descendants alive today, we can ascertain a good estimate of how few families

founded today's Ashkenazic Jewish population. When people who carry an inherited condition are also the descendants of a single ancestor, their versions of the affected gene will be identical. If, in addition, they are the descendants of a population that practiced endogamy, then they will share more of their genome than that one gene with others suffering the condition.

Given the great number of versions of each gene available in the human species at large, long runs of identical versions of genes in two unrelated people will never occur by coincidence. But because the surviving population in Ashkenaz was so terribly small in the mid-1600s, and because it grew in an uninterrupted way from such small numbers, a large fraction of Jews today share such long stretches of genes with each other.

This was known in principle, but nevertheless the discovery a few years ago of identical stretches of DNA hundreds of genes long in hundreds of apparently unrelated people from all corners of the world, was a surprise. The people who offered their genomes for this landmark study shared only two things: an inherited tendency to have one's muscles twisting one about—called Idiopathic Torsion Dystonia—and an ancestor who had come from Ashkenaz.

Most people in this study, but not all, called themselves Jews. Sometimes, though, members of an affected family would be shocked to discover that the inherited condition that had brought them into the study very likely meant an unexpected Jewish ancestry. With surprising regularity, when they understood the meaning of the tests done on themselves and their children, they would remember and admit—but not always accept—having Jewish ancestors. The data from this study argued very strongly that the oddities of fate and the murderous intentions of strangers had fixed a history of near extinction 400 years ago in the DNAs of the majority of Jews alive today. According to the scientists who carried out this study, the utter sameness of DNA in persons inheriting ITD worldwide means that every Jew whose ancestors come from Ashkenaz—about nine of every ten Jews alive today—is the descendent of one of no more than about 3000 families who survived the pogroms of the mid-1600s.

Clearly, the shared genes of the Ashkenazim do not define any aspect of their Jewishness. Those descended from Ashkenazic ancestors share a higher-than-average frequency of versions of various genes, only because they are descended from the same survivors of Jewish Ashkenaz. The genomes of other Jews reflect their different histories. Descent from an Ashkenazic family, with or without its attendant inherited conditions, cannot make a person Jewish.

Those who see any aspect of Judaism as inherited must be ignoring the demonstrated fact that Ashkenazim are a founder-effect family genetically quite different from the non-Ashkenazic families who make up most of the Jews of Israel. These Israelis would certainly fail any biological criterion set by Ashkenazic history, and vice-versa.

Equally clearly, shared genes bring a shared fate: those Jews who do share a common Ashkenazic ancestry may not have inherited their Jewishness that

way, but many have inherited a shared fate in the form of a genetic problem. One simple fact alone—the baseline of genetic diversity in our species—tells us that many different versions of each gene can be compatible with a healthy life. An unknown number of other variant genes are wholly incompatible with embryonic development; inheritance of any of them leads to the loss of an embryo before birth. In between are the variants of a gene that are compatible with birth, but not with the birthright we have come to expect, a life expectancy of around 80 years or more. Some of these variants are active in early life, causing infantile or childhood inherited diseases such as Tay-Sachs. Other variant genes are not called upon by the body for much of a person's lifetime. Still other variants may lack functionality but have no immediate consequence because a second copy of the gene is able to carry the work for both. When that sole copy of a functional gene is lost—and the older we get the more chance there is of a copy of a gene getting lost in one of our cells—the absence of a second functioning gene may show itself as a late-onset inherited disease.

DNA analysis can be used to find affected individuals in any of these different sorts of families. There are some good clinical reasons for seeking out these genes, and the people who carry them. Once the affected gene is recovered, it can be used to find the functional version from another person, and with that in hand the search for understanding how the normal gene works becomes straightforward science.

On the other hand, members of families with a history of a late-onset inherited condition may find themselves obliged by the same technology to learn about their fate from their genomes at a time when they have no symptoms nor any expectation of treatment once the symptoms appear.

For instance, a 1997 paper in the *New England Journal of Medicine* reports a study in which scientists obtained the cooperation of hundreds of members of Ashkenazic families who did *not* have a family history of breast cancer, and they checked their genomes for mutations in a gene, BRCA1, associated with a high risk of breast and ovarian cancer. The results were a disturbing, unexpected, and unwanted prophetic revelation through science. Two to three percent were carrying one of the two mutations.

This meant that even in the absence of any members with symptoms among members of two or three generations, and certainly in the absence of any symptoms in oneself, everyone in one of these families had a much higher risk of a bad fate than other people—even other Jews—who were not living out a founder-effect laid down by the violence of their ancestors' enemies. Statistically, each woman in a breast-cancer-free Ashkenazic family who is found to carry one of the two mutations in BRCA1 has a greater than 50 percent chance of developing a breast tumor, and a 20 percent chance of developing an ovarian tumor.

What is to be done with these prophecies? They do not come to families prepared by a prior history of disease for news of an inherited condition. Rather, they come to healthy people from unaffected families on the wings of

ancient and recent history, reminders that we are all not only the descendents of our grandparents, but also of their ancestors, people with whom we may think we have nothing in common.

We can be sure that prophetic news of this type—an unclear but high risk of a dread disease at a time when there are no family or personal symptoms—will not be reserved for long solely for Ashkenazic Jewish families. The difficulties lie not only in the discovery of a problem when you had no idea you were at risk; they lie in the wish to do the right thing, when there is no clear idea what that would be.

In the case of a BRCA1 gene, there are only three options once one has found out one carries a mutation, and in the absence of a family history of the disease none alone justify submitting one's DNA to find out. Ovarian surgery means early menopause as well as sterility; prophylactic breast removal is a major operation and while it does lower risk, it does not remove it completely; and surveillance for the appearance of a breast tumor is something every woman should be doing in any event.

In his essay "Catharsis," Rabbi Joseph Soloveitchik describes the paradox in a way familiar to secular scholars of the absurd: the essential element of heroism in Jewish terms is retreat. The paradigm of the hero who retreats is the patriarch Jacob, who wrestles an angel to the ground and then, instead of consummating his victory, lets him go. From such a withholding of final victory Jacob's descendants, the Jews of today, draw their continued existence:

The Torah wants man, who is bold and adventurous in his quest for opportunities, to act heroically, and at the final moment, when it appears to him that victory is within reach, to stop short, turn around, and retreat. At the most exalted moment of triumph and fulfillment man must forego the ecstasy of victory and take defeat at his own hands. . . . By freeing the defeated enemy Jacob defeated himself. He withdrew from a position he had won through courage and fortitude. He engaged in the movement of recoil.¹

To a person guided by Torah as the revelation of an unknowable but caring God, successful medical intervention need not confer any moral grandeur, nor need medical failure imply moral decay. From this Jewish tradition, medicine can perhaps learn to recoil at the moment of victory, to pull back from the opportunity to take on the inappropriate role of judge of another person's fate.

It will be difficult to change the habits of the day, because for anyone—Jewish or not—who doubts that there is an unknowable deity concerned for the moral content of their individual actions, medicine does have a way of filling the gap, sapping a patient's freedom to choose how to live his or her life. The enormous capacity of science to create tools for the manipulation of

¹ J.B. Soloveitchik, "Catharsis," *Tradition: A Journal of Orthodox Thought*, Vol. 17 (1978), pp. 39–54.

the natural world has helped confer moral authority on medicine by default. The lesson to be drawn from the Jewish tradition is that doctors and scientists have a moral obligation not to fill this gap with their own certainty, if for no other reason than to avoid losing their own God-given free will in turn.

How might this lesson from Judaism play out in more general, operational terms in today's medicine? In the most general terms, Judaism instructs us to redefine medical practice in the following ways. The profession, from basic researcher to primary-care physician, would accept the full autonomy of the patient at all times; the profession would view this autonomy of the patient as a critical aspect of the patient's identity as a unique and complete human being regardless of physical or mental condition; and these obligations would not be less compelling in the last moments before a patient's inevitable death.

For example, while criteria for screening for BRCA1 mutations are in flux, already we can see the outlines of a religiously informed, sensitive policy, one informed by the experiences of the Askenazic community, but not limited to that community. Here, for instance, are the guidelines used by Dr. Freya Schnabel, a Columbia colleague whose practice includes many Ashkenazic families. First, the screen is not to be made available to everyone: in the general population the grounds for a BRCA1 test are either three cases of breast cancer in the family, two in women under age sixty. In Ashkenazic families the criteria are slightly less restrictive, but still stringent: at least two cases of breast cancer, at least one in a woman younger than age sixty.

Second—not a criterion but a boundary—prenatal screening for this adult-onset disease is not to be performed even in affected families. As there is no way to predict the age of onset nor whether the child will indeed develop a tumor at all, there are no grounds to put forward the choice of abortion, as there might be with inherited diseases that occur with complete certainty at birth or at a very early age.

The third, fourth, and fifth criteria speak to the essential inseparability of mind and body and the central importance of psychosomatic and emotional events. Third, anyone entering the process of DNA diagnosis for BRCA1 status must first be counseled and a judgment made of their ability to understand and to accept either a positive or a negative result; fourth, only people who are able to accept the lack of clarity of either result, and are willing to make decisions for themselves about the consequences nevertheless, should be assayed; and fifth, counseling, both psychological and genetic, should continue for at least as long after the result is in as before the decision to be tested.

We may not all be members of high-risk families, but we are all at risk. It remains uncertain whether guidelines like these—which go far toward helping people to choose how to approach the future, while not unnecessarily shadowing anyone's free will with useless genomic determinism—will be applied widely, or whether genomic data stripped of any medical meaning will continue to be imposed on us all.

The last implication of genome-based diagnosis is for everyone to ponder: people—our species—are one family in precisely the same way that Jews are not.

The story of Ashkenazic inherited diseases should make us all sensitive to the larger issues of inherited disease, and of genetic difference. Beyond the obligation this story tells us all to undertake—to accept the evidence and give up vain hopes of any religious birthright in their genes—is an even larger moral duty.

The moral context that gives meaning to science through medicine requires the attention of both science and medicine to a person in all of his or her complexity and variability. The linkage of scientific medicine to religious history rather than to religious values may be more interesting in scientific terms, but it is fatally dangerous in medical terms.

Perhaps the best way to see the difference is to understand that though in social terms people tend to aggregate into groups of majority and minority populations—often separated by religion—by the data of our genomes we are all members of genetic minorities that range in size from the millions of a founder population, to the dozens of an immediate family, to the irreducible minority of one which is at the heart and soul of medicine. It would do us well to acknowledge that nothing in the legacy of human DNA blocks the choice to value the differences among us above the resemblance any of us might have to our idea of an ideal person.

By each of us exerting our free will to decide whether it is wise for us to know more or to know less about our own DNA at any given moment, the scientific data of DNA-based medicine may be returned to a proper medical context. In light of the DNA evidence we already have, this means stretching the definition of normal variation to include the greatest possible diversity of inherited appearances and behaviors. Our obligation here is as clear in its own way, as the countervailing trend is in current medical science.

The straightforward agenda of scientists and the short-term acquiescence of physicians fifty years ago lead to the creation of the National Institutes of Health, each institute named for a disease of the middle-aged white men in Congress who distributed Federal money in those days and still do today. These institutes have provided the country and the world with much knowledge of great value, both medical and monetary. But with the creation of cheap, easy scans for mutations in genes like *BRCA1*, knowledge contributed by NIH-supported science has begun to change medicine in ways that deny the meaning medicine provides to science.

In “The Missing Moment,” I drew the following quote from my mentor and teacher, James D. Watson, discoverer of the structure of DNA and founding Director of the Human Genome Project. Writing in the annual report of his laboratory, he said:

If we could use genetic analysis to help work out the biochemical pathways underlying memory and clear thinking, for example, we might be able to find pharmaceutical compounds to improve these most needed human attributes. Thus, those who want to protect the mentally ill or the slow learner may not get what they strive for if they portray them exclusively as victims of their environment. We might like to think otherwise, but only by reducing the differences in human

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beings will we ever have a society in which we can effectively view all individuals as truly equal.

I admire Jim Watson for his unmatched taste in picking the right question to ask of nature as much today as I did when I first met him in the late 1960s, but I know that here he was deeply wrong. We know from a century and a half of research in ecology and evolution that our future as a species lies not in minimizing our differences, but in cherishing them. We know as well from millennia of religious insight that there is no possible way to justify any ranking of one person over another on grounds of any aspect of their physical being. From those two insights we have the chance to work toward a properly informed medicine, capable of using any and all insights from science in a context derived from the insights of many religions, and thereby capable of reducing all data to one purpose: to help people in need, one person at a time.

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RESPONSE BY ELLIOT N. DORFF

Professor Pollack has done us all a great service in informing us about the genetic and demographic facts of our heritage and their implications for how we should treat “Jewish genetic diseases” in our day. I agree fully with the implications he draws—that we need to see each individual “in all his or her complexity and variability.” Rabbis will, of course, immediately think of rabbinic sources that value each person, regardless of anyone’s skills or traits. Perhaps the ultimate expression of that is the Rabbis’ insistence that, when seeing a disabled person, we not recoil or thank God for not making us so; we must rather bless God “for making people different.”

The hard issue that Professor Pollack does not address, however, is how to make the hard choices that we already face and will encounter all the more in the future in using new genetic technologies of testing and, ultimately, of engineering. Specifically, while Professor Pollack rightly, in my view, rejects Professor Watson’s call for finding pharmaceutical compounds to improve memory and clear thinking and, presumably, other uses of medicine to “improve” human beings to some ideal type (i.e., eugenics), that leaves open the difficult issue of where to draw the line between therapy and enhancement. Even if we are not going to try to make every C student into an A student, what about curing retardation? Similarly, in physical matters, should we seek to cure dwarfism? If we seek to cure dwarfism (or blindness, deafness, etc.), does that diminish the self-image of dwarfs (blind or deaf people) or, perhaps even worse, their status in society? For these and countless other examples, where and how should we draw the line between therapy and enhancement? Or, to put it theologically, when do we cease to be God’s partners in the ongoing act of healing, and when do we instead play God? We definitely should heed Professor Pollack’s call for respect for each person, but when is it consistent with that respect to seek to change the person, and when is it not? That is the “Brave New World” that we are now entering.

ROBERT POLLACK RESPONDS:

I am pleased that so learned a scholar of bioethics and Jewish law as Rabbi Elliot Dorff finds himself in agreement with my large premise, that Jews and others should not hurry to join the Genetic Revolution. Rather, I think we agree, we should approach it the way the driver of a school bus should approach a railroad crossing: stopping first, looking both ways, then proceeding with caution, slowly. After all, in both cases, children’s lives are at stake.

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