



RESEARCH AT RAMBAM

- 1,473 ongoing research projects in 2015
- Of these, 442 were new research projects!

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Being Responsible with Knowledge

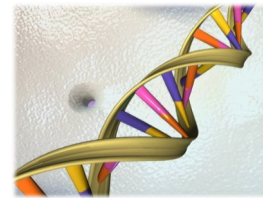
The past 20 years have seen advances in the understanding of our genes and how they contribute to health and well-being. This knowledge has led to the development of new treatments that can reduce our risk for disease, fight the disease itself, and perhaps someday, even cure it!

With this knowledge comes much responsibility. Is genetic research safe? Can it really help?

As we approach the miracle of Passover, sharing about genetic research at Rambam Health Care Campus seemed most appropriate. Just as the observance of that first Passover according to strict instructions led to the saving of many lives—in the same way, genetic research, according to strict protocols and

standards is already bringing new hope to patients worldwide.

We are thankful for the donors who have helped support the research you will learn about in this issue. We also appreciate your prayers that we may humbly and wisely use our knowledge for the betterment of humankind.



Shedding Light on the Heart

Researchers have developed a new experimental approach to treat abnormal heart rhythms using light. First reported in the prestigious journal *Nature Biotechnology*, the study was conducted in the laboratory of Professor Lior Gepstein of the Technion's Ruth & Bruce Rappaport Faculty of Medicine and Research Institute and Director of the Department of Cardiology at Rambam Health Care Campus.

Abnormalities in the function of the native pacemaker cells or in the heart's electrical conduction system, may lead to an abnormally slow heart rate or to uncoordinated contractions of the left ventricle, which could lead to reduced heart function and even heart failure. Traditionally, these disorders are treated by implanting a pacemaker. However,

pacemakers have many limitations including risk of infection, the need for an invasive surgical procedure, limits on how the device is placed, limits on use in children, and even the possibility of side effects that physically affect the heart.

These disadvantages have led to research, looking for biological alternatives to a pacemaker. A new study, conducted by Dr. Udi Nussinovitch (from the Department of Internal Medicine A at Rambam) as part of his PhD work in Professor Gepstein's laboratory at the Technion, is part of this effort.

Optogenetics combines genetics and optics to control well-defined events within certain cells of living tissue. Put simply, optogenetics is the process of understanding and controlling the function of organisms (or in our case, cells)

using light. This field of research has been used primarily in brain research. The Technion-Rambam study is the first to use optogenetics for pacing and resynchronization of the heartbeat.

In the study, conducted in rats, the researchers first directed a beam of blue light at an area in the heart where light-sensitive genes were delivered. This resulted in effective pacing of the heart at different rates, determined by the frequency of the blue light flashes applied. A subsequent study led to improved synchronization of the contractions of the ventricles in rat hearts.

These results are encouraging. However, we must overcome some significant challenges to bring this knowledge into the field of medicine. We must improve the

Biblical Tradition & Modern Science



The Ketef Hinnom
Scrolls in the Israel
Museum.

Credit: Bachrach44
(Own work) [CC BY-
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from Wikimedia
Commons.

The longstanding tradition of the priestly lineage of the Jewish people is well known to biblical scholars. According to this tradition, the first High Priest, Aaron, founded the male dynasty transliterated as the “Kohanim.” Very few of the original commandments and activities of the biblical Kohanim remain in effect today. Best known is the priestly benediction and blessing of peace (Numbers 6:24–26) conveyed to Aaron and his descendants as follows: “May the LORD bless you and guard you; May the LORD make His face shed light upon you and be gracious unto you; May the LORD lift up His face unto you and give you peace.” Remarkably, this blessing was discovered in the Ketef Hinnom archaeological excavations, inscribed on two silver scrolls. Unearthed at an archaeological site southwest of the Old City of Jerusalem, the scrolls represent the oldest authentic original biblical inscription known, dating from 650 BCE.

I too am of the contemporary Kohanim and am frequently

privileged to be called up to the podium. One Sabbath morning, more than 20 years ago, another member of the congregation, also a Kohen, was called up for this first reading. I wondered what he and I shared in common related to our tradition in belonging to the Jewish priesthood. This question was especially intriguing since his family originated from Africa, while mine came from northern Europe. Having been trained in medicine and genetics, I hypothesized that this man of African heritage, and myself of European heritage, along with many men who carry the Kohanim tradition, might share genetic signatures that converge to a common paternal ancestry. Could such a hypothesis be tested? Indeed, the Almighty has endowed humankind with the tools, skills, and knowledge that are necessary.

Ancestry signatures reside in the “chemical alphabet” of our DNA sequences. The signatures for paternal ancestry are located on the Y-chromosome, which is transmitted from father to son. Research investigating Y-

chromosome signatures had already shown that the Y-chromosomes of all human beings converge to a common origin. Therefore, the question I had in mind was this: would self-identified members of the Jewish priesthood (Kohanim) display even more tightly clustered signatures that converged to a more recent founding father?

I and my group performed research that has subsequently been reproduced and refined by many different groups over the past 20 years. Two striking findings stand out. Firstly, members of the Jewish priesthood do indeed cluster to a surprisingly small number of paternal lineages in the overall tree of humanity. The largest such lineage, accounting for approximately 50% of contemporary Kohanim (incidentally including myself) have a rather “diagnostic” signature absent in most other men. In other words, the biblical tradition of the Jewish priesthood has been faithfully carried forward within a number of ancient families. These signatures have also enabled us to discover “lost tribes” in communities

Continued on Page 3

Shedding Light (continued from page 1)

ability of light to penetrate through the tissues, ensure the continuous presence of the light-sensitive protein in the heart for many years, and develop a unique pacing device to provide the necessary illumination inside the heart. Nevertheless, this

study has demonstrated the unique potential of optogenetics for both cardiac pacing (as an alternative to electronic pacemakers) and resynchronization (for the treatment of heart failure with ventricular dys-synchrony) therapies.

To learn more about this amazing discovery, watch [Beating Heart Cells Made from Patient’s Skin](#) on YouTube.

Professor Lior Gepstein
Director of Cardiology
Rambam Health Care Campus

Biblical Tradition (continued from page 2)

around the world. Secondly, and perhaps most striking, is the finding that the distribution of these contemporary Kohanim lineages is very similar among Kohanim from geographically dispersed Diaspora communities, ranging from Africa to Europe, to the Middle East to the Far East, and all the way to the Americas. From this latter observation, my colleagues and I concluded that members of these Jewish Diaspora communities were once together in an ancient homeland, from which they dispersed to many parts of the globe. This is consistent with the history of the exiles and migrations of the Jewish people.

if they have some ancestral relationship to this tapestry. In fact, many thousands of people have sought such testing, and have been surprised to discover that they may have some thread of connection to the tapestry of the Jewish people. This is not surprising, given the millennia of Jewish dispersal throughout most regions of the world. However, the finding of such a “thread” of shared ancestry, while uplifting and inspiring, does not necessarily point to nor define the Jewish identity of any given individual. Rather, such an identity is a highly personal matter that integrates cultural, spiritual, historical, family, and many other factors.

disparity. The prophetic teachings and influence of the Reverend Martin Luther King Jr, of blessed memory, had a great impact on me. Dr. King had pointed out that disparities in health represent a severe form of inequality that should be the highest priority for physicians.

Three decades would pass, during which I moved from North America to Israel, before I finally had the tools to address this challenge in collaboration with my research colleagues and several other groups around the world. It turned out that the same tools we used to study the genetic history of the Jewish people, “population genetics” signature approaches, could be used to face this medical disparity in kidney disease.

One of the most powerful clues came from a study that looked at the genetic signatures among Ethiopians and other continental African populations suffering from kidney disease. We identified the specific gene responsible for up to 70% of the excess burden of kidney disease in populations with a Sub-Saharan African heritage. In parallel, independently, and using somewhat different approaches, another collaborative group based in Boston identified the very same gene. The discovery of this gene and the “kidney disease risk” signatures is bringing us closer to developing effective treatment strategies to overcome the health disparity in kidney disease between different populations.

We are all one family—and it is incumbent upon all of us to strive for the day when health and peace are universal.

**Karl Skorecki, M.D., F.R.C.P.(C),
F.A.S.N.**
Director, Medical & Research
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Professor Skorecki’s search for shared genetic signatures was published in Newsweek in 2006.

Our research led to numerous subsequent studies in which DNA sequences traced maternal ancestry as well. These studies have been published in leading scientific journals; they reveal a tapestry of the demographic history of the Jewish people. This tapestry shows common traits of origin in the Near East, with threads from the more than 20 post-Diaspora communities. These DNA signatures also enable people to find out

challenge. Kidney disease specialists have long known that the black community, including African Americans, experiences a more than four-fold increased rate of progressive kidney disease with all of its complications. Most noticeably, and in much higher numbers than other communities, they require dialysis and transplantation. As a young physician in Boston training in Nephrology (kidney disease) I was greatly troubled by this

For more detailed information you may enjoy reading [A Genomic History of the Jewish People](#) (Shemot 2013;21(1):10–15).

Being a medical doctor, with an interest and specialty in kidney health and disease, I felt compelled to try and address a quite different medical

Genetics in the Middle Ages

Genetic studies only began in the mid-1800s with the studies of a Catholic priest, Gregor Johann Mendel. Hence, what could the Rambam and the Jewish sages possibly have to say of relevance regarding genetic research and counseling in the year 2016? You will be surprised to learn that there is a lot to be said, when you read between the lines!

According to the Rambam’s Mishneh Torah (translated as Repetition of the Torah), in the Book “Ahavah” (love), so named because the commands must be observed at all times in order to express the love of God continually, we read the following in the section relating to circumcision:

If the first son of a woman dies because the circumcision weakened him [from excessive bleeding], and her second son dies as well, also due to the circumcision, and both sons are

from the same or even a different father, then her third son should not be circumcised.

Chapter 1, vs 18

At the time of this writing (1170–1180), the Rambam and our other sages knew nothing of genetics, nor of the X- and Y-chromosomes. Only in the early 1800s did modern scientists begin to understand that there are certain inherited diseases that only affect men, but were passed on by the mother. Therefore, they could not have possibly known that Hemophilia A, which occurs in 1 in 5,000-10,000 males, is due to a problem with the X-chromosome that the male infant receives from his mother!

However, our Jewish sages were quite observant, deeply inquisitive, and very bright; they knew how to make scholarly deductions from the facts. They and the Rambam understood that while the death of the first son by circumcision, in and of itself quite rare, might be

accidental, it would be highly unlikely for the death of the second son in same manner to be a coincidence. He and the sages observed that since it did not matter who the father was, the problem had to be transmitted by the mother in some way.

Hence, the Rambam’s work inspires our clinician-scientists. Many important genes were identified here at Rambam Health Care Campus. We also have a strong genetic research program to help our physicians identify and treat genetic disorders—for the benefit of those affected by hereditary disorders.



Moses Maimonides, also known as Rabbi Moshe Ben Maimon (the Rambam)

Shraga Blazer, MD
Director

Department of Neonatology and
the Neonatal Intensive Care Unit
Rambam Health Care Campus

*Language,
Culture,
and
Rambam*

“He Shall Bless You” — *יְבָרַכְךָ (Yvarechcha)*

Sometimes it takes several words in English to express a single word in Hebrew. This is the case with the Hebrew word, *yvarechcha* (יְבָרַכְךָ).

Yvarechcha means “He shall bless you” and is the first word of the Priestly blessing spoken over the nation, as commanded by the Almighty to Aaron the High Priest.

And the Lord spoke to Moses, saying: “Speak to Aaron and his sons, saying, ‘This is the way you shall bless the children of Israel. Say to them:

“The LORD bless you (יְבָרַכְךָ) and keep you; the LORD make

His face shine upon you, and be gracious to you; the LORD lift up His countenance upon you, and give you peace.”

“So they shall put My name on the children of Israel, and I will bless them.”

Number 6:22–27 (NKJV)

This blessing called upon the power of the Lord (using his Holy name), who alone could pour out blessing on the people.

According to Jewish tradition, the priest had to prepare himself to give the blessing, he had to give it with love and the end result was

the imparting of peace on the recipients.

This blessing reminds us as well that “those who bless you shall themselves be blessed” (Genesis 12:3).

From a medical perspective, clinical research at Rambam seeks to be a blessing. We place people at the heart of every research endeavor. The excitement of discovery (our blessing) is truly a blessing to patients worldwide through the resulting medical treatments, therapies, and sometimes, even cures.



RAMBAM Health Care Campus

Creating the future of medicine.

Rambam Health Care Campus

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You Can Help

The generosity of others is helping us replace old equipment, build new facilities, perform research, and care for our patients. Every gift counts. Click on the links below for more information on how you can help support the people of Israel via Rambam Health Care Campus.

Pray for Us and Tell Others About Us:

Visit our [Christian Friends of Rambam Facebook page](#) often for prayer requests and regular updates about what is happening at Rambam.

Friends Organizations: Tax-deductible donations can be made via a Friends organization near you (listed above).

Giving: Please [visit our webpage](#) for more information about how you can make a difference in the lives of the people served by Rambam Health Care Campus.

More about Rambam Research

There are many aspects to research. Many times, the quest for a medical answer begins with an unsolved clinical problem, as was Professor Skorecki's experience (see pages 2-3). In other cases, medical knowledge and curiosity lead to a research discovery with the potential of helping people, as happened with Professor Gepstein (page 1).

Two fields of research urgently in need of your support relate to cancer and cardiovascular disease. Facilities in the new Joseph Fishman Oncology Center, and in Rambam's Cardiovascular Hospital (under construction) will be dedicated to the work of physician-scientists seeking crucial answers to their patient's medical condition.

The ground will soon be broken for construction of Rambam's new Biomedical Discovery Tower, which will meet our long-term needs for clinical research in collaboration with our colleagues at the Technion and from hi-tech industry.

Please consider how you can be part of our vision to place people at the heart of all we do—whether it is direct patient care or research. Your gift, now, in this Passover Season, will be particularly meaningful as we focus on the miracle that saved our people and our nation.

Thank you in advance for supporting the medical endeavors at Rambam Health Care Campus.

"I will bless those who bless you..."

Genesis 12:3 (NKJV)