Tucked away in a molecular biology research lab in the Bronx, the unassuming **ben Torah,** *family man, and* **einekel** *of both the Dombrover and Nadvorner Rebbes furiously works around the clock. His twofold mission: to spare Jewish families from the nightmare of incurable genetic illnesses and to develop new approaches that dramatically improve the lives of those grappling with genetic disorders.* ***Mishpacha*** *speaks with Dr. Berish Rubin, the researcher whose devotion, compassion, and burning sense of mission have transformed the lives of Jewish families around the globe*

The Mentsch Behind the Microscope:

Dr. Berish Rubin and His Mission

by Margie Pensak

Berish Rubin starts his day like many chareidi men. He wakes up before 7 a.m., rushes off to shul to daven Shacharis, followed by a *shiur*, and returns home briefly before commuting to work. His cell phone is set to ring daily at 1:23 p.m., to remind him to get ready for the 1:40 p.m. Minchah. After Minchah he heads back to work. All typicality ends here, mostly due to the fact that Dr. Rubin loves his job and has a driving passion which does not allow him much time to rest. Knowing that Jewish children and families need his assistance, it is his feeling that every day makes a difference. Berish Rubin lives day in and day out with Hillel's perspective, *im lo achshav eimasai* — if not now, when?

Eureka! It was in the summer of 1999 that Berish Rubin, PhD, head of a molecular biology research lab and professor of biological sciences at Fordham University — a Jesuit university located in Bronx, New York — was approached by Dor Yeshorim's founder, Rabbi Yosef Ekstein. Rabbi Ekstein, father of four children who died from Tay-Sachs disease, informed Dr. Rubin that because the mutation for Familial Dysautonomia (FD) — also known as Riley-Day Syndrome or hereditary sensory neuropathy Type III — had not been identified, couples primarily of Ashkenazic heritage were having children with this serious neurological disorder that severely compromised their lives.

Individuals with FD are born with an error in their DNA, or genetic material makeup, and are affected with a variety of symptoms. They include: decreased sensitivity to pain and temperature, cardiovascular instability, recurrent pneumonias, vomiting crises, blood pressure swings, an absence of overflow emotional tears, and gastrointestinal dysfunction.

The search for the gene marker causing the syndrome, which has a history of several hundred years among the Ashkenazic population, actually began in 1993 by a well-known group of scientists at Harvard Medical School. Six years later, they still had not isolated the marker; Rabbi Ekstein hoped that Dr. Rubin could do what the Harvard team had not. After reviewing the scientific literature, Dr. Rubin felt that if this top team of researchers had not been able to identify the mutation in six years, what was the likelihood of his group succeeding?

But Rabbi Ekstein persevered. In the spring of 2000, Dr. Rubin again received a phone call from Rabbi Ekstein, who informed him that Harvard's team had still not identified the mutation that causes FD. There continued to be children born in the Jewish community with the disorder. After reviewing the scientific literature that had been published in the past year, which confirmed Rabbi Ekstein's update, Dr. Rubin discussed the matter with the director of his laboratory, Dr. Sylvia Anderson. Together, they decided to make an attempt at identifying the causative mutation.

Within a labor-intensive three-month period, Dr. Rubin's research team found the FD-causing mutation. Needless to say, there was a great deal of excitement in the laboratory when they were able to notify Rabbi Ekstein of their findings. Within weeks, Dor Yeshorim incorporated a genetic test for FD into its screening program which tests for a variety of genetic disorders occurring in the Jewish population, among them: Tay-Sachs, cystic fibrosis, and

Fanconi Anemia. Baruch Hashem, those who are currently being tested no longer have to be concerned about the risk of having children with these dreaded disorders, which only occur in the children of parents who are both carriers of the disease-causing mutation. Dor Yeshorim testing of singles, prior to marriage, eliminates any guesswork.

"In our community, parents of young men and women are cautious about allowing their children to marry healthy individuals who have a sibling with an unknown disorder," notes Dr. Rubin. "Since the diseases we work on can only occur in children where both parents carry the mutation, if we can figure out the genetic cause of a disorder, we can test the prospective boy or girl and ascertain whether there is a risk with going ahead with the *shidduch*. Because of our discoveries, many young couples have gotten married without any concern about having a child with a particular genetic disorder."

Intellect and Heart Since the Fordham University research team's discovery, numerous other very exciting things have taken place in the lab. The information gained from the discovery of the FD-causing mutation has facilitated the development of therapies for those with FD, allowing many of these children to live relatively normal lives. Children who, before these discoveries, spent much of their lives suffering from FD and were often hospitalized for extended periods of time are now attending regular yeshivos and schools; they are moving through life in a much healthier state. That is not to say that these children are now perfect; their health has improved dramatically, yet there is much that needs to be done. Dr. Rubin feels that every day spent in the laboratory brings the next therapeutic modality that much closer.

Chicagoans Ken and Ann Slaw's son Andrew is a living testimony to Dr. Rubin's work. Andrew was diagnosed with FD when he was four years old. At the age of ten, Andrew endured unrelenting autonomic crisis and was hospitalized for six months. He experienced episodes of violent retching, blood pressure as high as 170 over 110, an accelerated heart rate in the 160s, sweating, and abdominal discomfort. Andrew could eat nothing by mouth. The prognosis was grim. His doctors were just about ready to transfer Andrew into hospice when he began benefiting from Dr. Rubin's new discovery of tocotrienols, a form of Vitamin E that increases the protein that FD children lack. It was able to increase his stamina and energy, and provide stability to an unstable body.

"On Day Three without crisis, Andrew got up from his hospital bed and, with such a broad smile on his face, started jumping up and down on the bed with his sister," recalls Mrs. Slaw. "If there was ever a time in my life that I witnessed a miracle, it was then. The nurses came in and were in tears. A couple of days later we brought Andrew home. When Andrew walked into the house he had not been in for half a year, he said, 'Mom, if I could hug every room of this house, I would.' Then he said, 'I think we need to go out to dinner to celebrate.' My husband and I just looked at each other in amazement while Andrew sat in the restaurant eating sushi, after not being able to eat anything by mouth for six months."

To give *chizuk* to the Slaws, when Andrew was so sick, Dr. Rubin told them not to worry. He and his team were working on therapies for FD and Andrew would be fine. In fact, he promised to join them in Chicago for his bar mitzvah. Being a man of his word, Dr. Rubin attended the *simchah*. He told the Slaws that he wants not only to attend the bar mitzvah of all "his kids," but also to dance at their wedding.

"Each day that ticks away is critical," says Mrs. Slaw. "Every day Andrew wakes up we are grateful, since FD kids can die in their sleep from heart, lung, and kidney complications. And Dr. Rubin gets that; he understands that every day is precious, and he is doing everything he can do to preserve and improve our children's lives."

Blimi* understands this all too well. As the mother of a child with FD, she and her family can testify to the miracles which the Slaws have seen, thanks to Dr. Rubin's findings.

"My child is doing unbelievably well since I started to follow Dr. Rubin's guidance with regard to the administration of green tea capsules and tocotrienols," says Blimi. "For years, we used prescription drugs such as Valium, Klonopin, Catapres, Xanax, and Florinef, to control blood pressure and anxiety that is so common in kids with FD. My child was addicted to these medications, and when these drugs no longer controlled the symptoms, the doctors simply increased the dose. Since she starting to take the tocotrienols and green tea, my child's condition greatly improved and there is no longer a need for any for the previously prescribed drugs. In addition, my husband and I have noted improved self-control, maturity, and calmness, as well as an academic performance, in a mainstreamed yeshivah, that is near the top of the class.

"My child needed back surgery and I approached it with great fear, as surgery on a child with FD can result in autonomic crisis, which can be fatal," continues Blimi. "The anesthesiologist who was scheduled to take care of my child during the surgery contacted Dr. Rubin for guidance as to which drugs can be used safely for a child with FD. The anesthesiologist spoke to Dr. Rubin before, during, and after the surgery and, baruch Hashem, my child sailed through the operation without any complications. Things went so well that we were sent home from the hospital ahead of schedule. It's a true miracle!"

Rallying support for Dr. Rubin is the nonprofit, parent-based organization, FD Now, of which Mrs. Slaw is the chair. In the past year it has raised over $300,000 to help fund Dr. Rubin's efforts. "We believe in Dr. Rubin tremendously," says Mrs. Slaw. "He is very efficient with his spending; he has discovered a lot in a little time. We have this goal in mind to increase the quality of our kids' lives and potentially find a cure. Right now there are additional substances in Dr. Rubin's lab that show promise. Our goal is to raise one million dollars.

"Dr. Rubin is quite a mentsch," continues Mrs. Slaw. "It's rare to find in a human being both intellect and heart — Dr. Rubin has both. He gets worried when Andrew is in crisis. He really takes a personal interest; his patients are not subjects. It's kind of like we are all one big *mishpachah!*"

What is Dr. Rubin's take on his life's work?

"In *parshas Pekudei*, when Bnei Yisrael completed the construction of the Mishkan, the Torah says that Moshe Rabbeinu *bentsch*ed them," notes Dr. Rubin. "Rashi says that Moshe said to them, 'May the Shechinah rest in the work of your hands and may the pleasantness of the Ribono shel Olam be upon us.' The text of this Rashi is taped to my desk. The *zchus* we have had in finding the mutation that causes FD, the therapies for those with FD, and various other discoveries we have made for Klal Yisrael, are a gift from the Ribono shel Olam."

Darker and Lighter Sides of the Lab While the joys of success that Dr. Rubin and his team experienced have been

PERSONALLY SPEAKING

What is the driving force fueling Dr. Rubin to fulfill his mission? No doubt, his deep commitment and perseverance in working day and night for the *klal* can be credited to a combination of his family background and upbringing; his strong roots and natural inclination to help others that he has inherited from his holy ancestors.

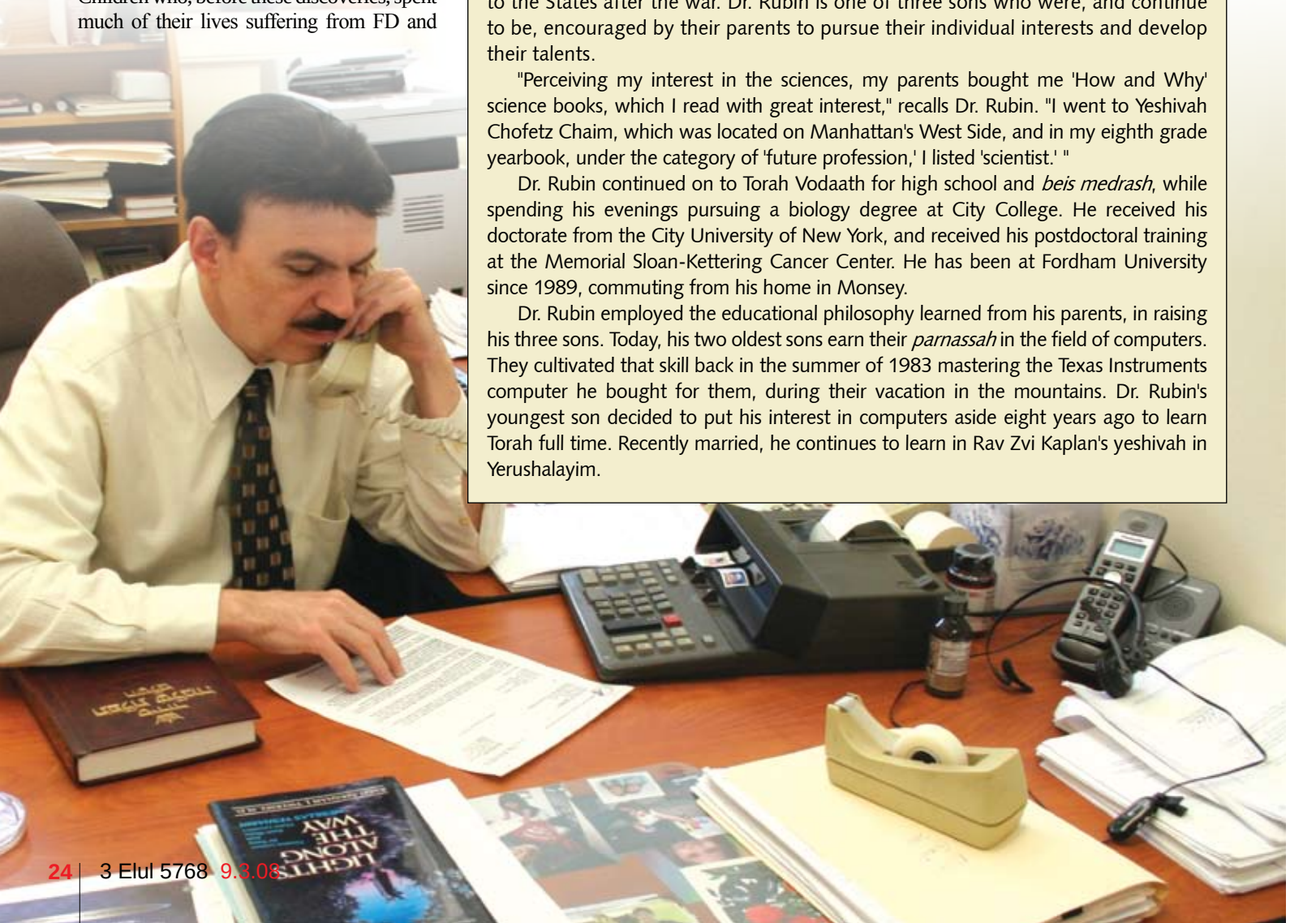
Dr. Rubin was born to parents with distinguished chassidic lineages. On his paternal side, he is the grandson of the Dombrover Rebbe, Grand Rabbi Yissachar Berish Rubin of Dombrova, who lived in Berlin, and later in Washington Heights, New York, and a direct descendant, *ben achar ben,* of the Ropshitzer Rebbe. On his mother's side, he is a great-grandson of Reb Mordechele Nadvorna, and a descendant of the Baal Shem Tov.

Dr. Rubin's father, Rabbi Meyer Rubin, arrived in the United States just prior to World War II, and was a Rav in Washington Heights. His mother, Chaya, who was imprisoned in a variety of concentration camps, including Auschwitz, immigrated to the States after the war. Dr. Rubin is one of three sons who were, and continue to be, encouraged by their parents to pursue their individual interests and develop their talents.

"Perceiving my interest in the sciences, my parents bought me 'How and Why' science books, which I read with great interest," recalls Dr. Rubin. "I went to Yeshivah Chofetz Chaim, which was located on Manhattan's West Side, and in my eighth grade yearbook, under the category of 'future profession,' I listed 'scientist.' "

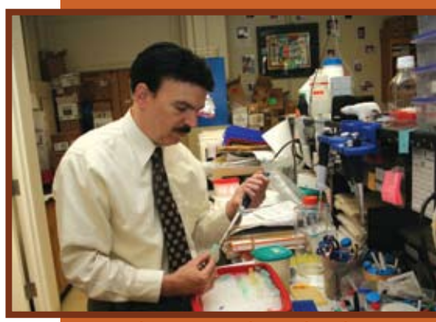
Dr. Rubin continued on to Torah Vodaath for high school and *beis medrash*, while spending his evenings pursuing a biology degree at City College. He received his doctorate from the City University of New York, and received his postdoctoral training at the Memorial Sloan-Kettering Cancer Center. He has been at Fordham University since 1989, commuting from his home in Monsey.

Dr. Rubin employed the educational philosophy learned from his parents, in raising his three sons. Today, his two oldest sons earn their *parnassah* in the field of computers. They cultivated that skill back in the summer of 1983 mastering the Texas Instruments computer he bought for them, during their vacation in the mountains. Dr. Rubin's youngest son decided to put his interest in computers aside eight years ago to learn Torah full time. Recently married, he continues to learn in Rav Zvi Kaplan's yeshivah in Yerushalayim.

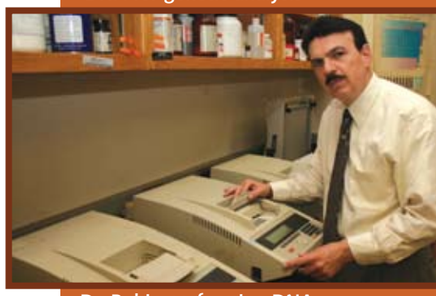


"It's rare to find in a human being both intellect and heart — Dr. Rubin has both. He gets worried when Andrew is in crisis. He really takes a personal interest; his patients are not subjects. It's kind of like we are all one big *mishpachah!*"

— Mrs. Ann Slaw

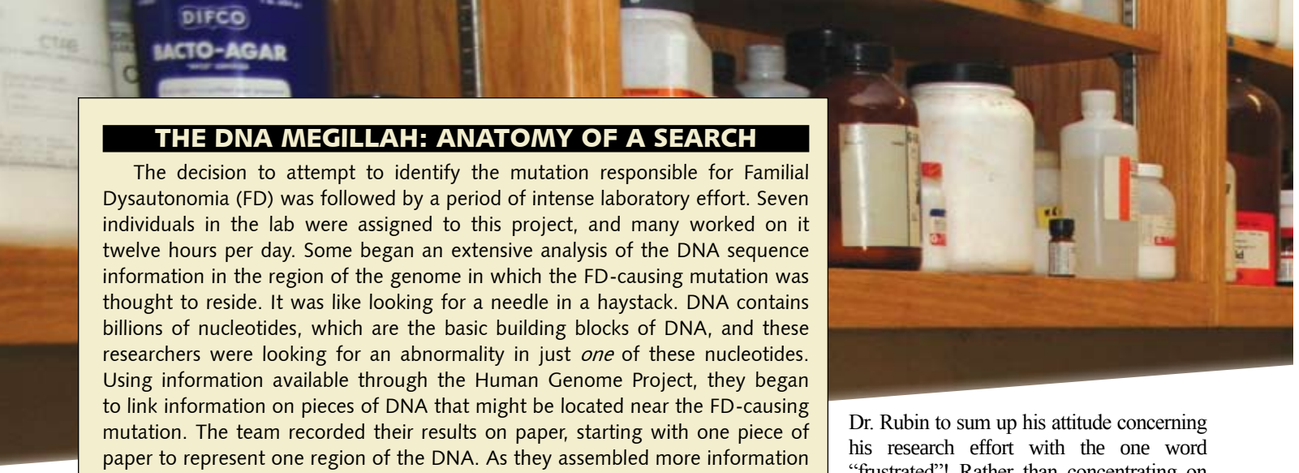


Dr. Rubin using a thermal cycler to produce large amounts of DNA for genetic analysis



Dr. Rubin performing DNA sequence analysis to locate the mutation responsible for another Jewish genetic disease

Removing a frozen tissue sample from a cryogenic tank



THE DNA MEGILLAH: ANATOMY OF A SEARCH

The decision to attempt to identify the mutation responsible for Familial Dysautonomia (FD) was followed by a period of intense laboratory effort. Seven individuals in the lab were assigned to this project, and many worked on it twelve hours per day. Some began an extensive analysis of the DNA sequence information in the region of the genome in which the FD-causing mutation was thought to reside. It was like looking for a needle in a haystack. DNA contains billions of nucleotides, which are the basic building blocks of DNA, and these researchers were looking for an abnormality in just *one* of these nucleotides. Using information available through the Human Genome Project, they began to link information on pieces of DNA that might be located near the FD-causing mutation. The team recorded their results on paper, starting with one piece of paper to represent one region of the DNA. As they assembled more information on the nucleotide sequence adjacent to the region, they taped on a second piece of paper with the new information. As the information grew, so did the number of pieces of paper. At some point it was about 100 pages long. Those working with Dr. Rubin began referring to it as a scroll, but soon after a brief explanation by Dr. Rubin about Purim and the Megillah, everyone referred to it as a *megillah*. "It was interesting to hear the non-Jewish researchers asking each other, 'Where did you put the *megillah*?' " Dr. Rubin recounts.

The number of nucleotides contained in this region was massive, and the task of examining all of the nucleotides was beyond the scope of what Drs. Rubin and Anderson felt they could undertake. While many researchers go through the painstaking task of determining the nucleotide sequence of an entire region of DNA, these investigators decided to forego that task, focusing instead on the characterization of the sequence of the RNA that is encoded by this DNA. It was this critical decision that enabled them to find the FD mutation so quickly. A piece of DNA that is 500,000 nucleotides long might encode an RNA that is only 2,000 nucleotides long; as such, the choice to analyze only the RNA expedites the process by leaps and bounds. Using this approach, Dr. Rubin's team was able to quickly identify the FD-causing mutation.

"We did not have the large sums of money and the time that would have been needed to examine the nucleotide sequence of the entire DNA under study," said Dr. Rubin. "We needed to be creative and find a clever way to locate the mutation. The researchers in our lab understood and appreciated the importance of establishing a genetic screening test for FD, and they worked on the project with the attitude that every day made a difference." Their approach clearly worked and Klal Yisrael is benefiting from their creativity, enthusiasm, and success. Employing the same approach, these researchers have also identified the mutations in the Jewish population responsible for Nemaline Myopathy, Leigh Syndrome, and a form of Bloom Syndrome.

very uplifting, aspects of his work have made him aware that there is a darker side to the field of genetics. For example, after Dr. Rubin submitted his findings to a scientific journal for publication, the journal sent the information to the Harvard group and then allowed the Harvard group to submit the same findings. Another disappointment set in, more recently, when he was informed that the Dysautonomia Foundation, which funded the Harvard research group, is trying to control the testing for FD and is planning to collect royalties for each test that is to be performed. With his discovery of the FD-causing mutation, he had expected that testing for this disorder would be made readily available for the Jewish population, without any restrictions.

"Our desire to protect the Jewish community from this type of abuse has required the hiring of attorneys and has cost us tens of thousands of dollars," says Dr. Rubin. "We thought it would be enough to help the Jewish community by finding the FD-causing mutation. Now we find ourselves involved in an intense and expensive legal battle. It was and continues to be a David and Goliath tale. Our small lab, working with a small grant from Dor Yeshorim, found the mutation that the well-funded Harvard laboratory had worked on for years. While we were successful in that race, the one we now face is one that is more difficult to overcome."

Because financial resources are limited to fight this battle, a legal loss may result in FD testing so cost-prohibitive that Jewish couples might again be faced with the risk of having children with FD, Heaven forbid.

This is just one of the factors prompting Dr. Rubin to sum up his attitude concerning his research effort with the one word "frustrated"! Rather than concentrating on how far he has come, he tends to focus on how much more there is yet to accomplish. That sentiment is shared by others in the lab. Dr. Rubin has been fortunate to work with Dr. Sylvia Anderson, who shares his passion for helping those in need. Her long hours reflect this commitment. As intense as their work is, there are times in the lab when things lighten up, due to the fact that Dr. Anderson is not of the Jewish faith and their work deals exclusively with Jews.

"We often are visited in the lab by *frum* people and, as a result, Sylvia has been picking up much about Jewish tradition," explains Dr. Rubin. "She knows not to reach out to shake hands with the men that come to visit and she is learning some Yiddish. It is funny to hear what she comes up with, and to find out that she understood some of what a visitor was saying to me in Yiddish. The questions she asks me sometimes are actually funny. The other day she wanted to know why one of the children we are dealing with is sometimes referred to as Dov and at other times as Ber. I told her it was the same name and didn't bother to elaborate. ["Ber" is the Yiddish version of "Dov" and the two names are often used interchangeably.] She walked out of my office confused!

"Another time we had a funny situation where we were working with the DNA of two children from two different families who had different genetic diseases but shared a last name. One was named Sholom and the other was Shulem. As you can imagine, this led to some interesting conversations as we were discussing the results we got with the two DNA samples!"

Although Dr. Rubin enjoys interests outside of his lab, he often feels that they are consuming too much of his time. Puttering in the yard and working on the landscaping of his property, for example, are reserved for Sunday mornings only. And, rather than relaxing at home after work hours, Dr. Rubin's evenings are often spent in the lab, or around his dining room table giving late night gratis consultations to individuals and families carrying genetic disorders! In fact, he is so personally involved in his work, he has no qualms about giving out his cell phone number to those who may need him, at any hour. It seems that one of the only personal breaks he allows himself to take are for the long distance telephone *daf Yomi shiur* he has Sunday through Friday with his son who lives in Eretz Yisrael.

"The beauty of living in Monsey is that one can catch a minyan at all hours of the night in Vizhnitz," says Dr. Rubin. "I have yet to come there and not find a minyan at 1:00 a.m.!"

No End to the Work "The amount of scientific work I have to do is unlimited," says Dr. Rubin. "There are currently five people working in the lab and they are all extremely busy. I could use another five, or perhaps even ten additional talented people to keep the work moving along at a pace I would be happy with. While we have found the genetic causes for some of the genetic diseases impacting the Jewish population, like Familial Dysautonomia, Nemaline Myopathy, Leigh Syndrome, and a form of Bloom Syndrome, there are so many other genetic diseases affecting our community for which the genetic cause is still not known. People who have close relatives who have these disorders face some incredible challenges.

"I recently spoke to a young woman who just found out that her husband has a genetic disorder that took the lives of his father and uncle when they were in their early fifties," says Dr. Rubin. "Her husband is showing early signs of the disorder and if a therapeutic approach is not developed, he could, *chas v'shalom*, face the same challenge as his father and uncle. It is likely that there are approaches that can help address the deficit that this young man has. To investigate the possibility takes the efforts of a talented team of researchers."

Yet others continue to be challenged by these disorders, and seek Dr. Rubin's counsel and friendship, even after their relatives have passed into the Olam HaEmes. Three years ago, Mr. and Mrs. N.*, whose children were victims of a neuromuscular disease, were advised to contact Dr. Rubin by a couple who faced a similar challenge. Ultimately, Dr. Rubin discovered the gene that was responsible for the death of their children; Mr. and Mrs. N. consider Dr. Rubin their savior and their close friend.

"Thanks to Dr. Rubin, we now know why our children died," says Mrs. N. "It's an enormous relief to finally know what went wrong. Because of his discovery, we were able to have healthy children."

Mr. and Mrs. N. marvel over the fact that doctors at universities throughout the country could not figure out what Dr. Rubin so quickly discovered. "He probably knows more today than anyone about genetic diseases, and not only Jewish ones. He has made this his mission," says Mrs. N.

Mr. and Mrs. N. are equally impressed with his humility. "I think Dr. Rubin is a saint," says Mrs. N. "He is so humble that he just truly believes that he found it because he was the correct *shaliach*, not because he is better than anyone else. That has always amazed me. He said we must have had the *zchus* because of the brachos we got."

Dr. Rubin has been a resource for Mr. and Mrs. N. every step of the way, not only from a Torah and medical perspective, but from a human perspective. He was there for them from their initial meeting, and he continues to be there for them today. "He is an incredibly patient and compassionate person," says Mrs. N. "Your pain is his pain. He does this day in and day out, and every person's sorrow is new for him."

*Anonymity preferred. ■

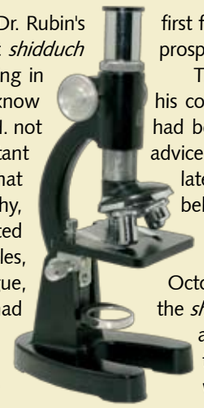
An incubator containing experimental equipment

Dr. Rubin, using a scintillation counter, is determining the amount of radioactivity present in a sample

The cryogenic tanks contain liquid nitrogen, which stores critical samples at less than -320° F

THE SCIENTIST BEHIND THE *SHIDDUCH*

A moving story demonstrates just how precious Dr. Rubin's discoveries can be, and how dramatically they affect *shidduch* prospects. After Rabbi H.* completed his stint learning in a British yeshivah, about eight years ago, he got to know Dr. Rubin. As *Hashgachah* would have it, had Rabbi H. not learned in England, he would not have met his distant cousin who lived there and would not have known that the cousin had two daughters with Nemaline Myopathy, a neuromuscular disorder. These children exhibited moderate weakness in their leg, arm, and trunk muscles, along with some mild weakness of their face, tongue, and throat muscles. Unlike normal children, they had decreased or absent reflexes and weak respiratory muscles. They live challenged lives; indeed, death often occurs in Nemaline Myopathy victims within the first few years of life due to respiratory failure. The *shidduch* prospects for these girls' siblings seemed dismal at best.



Then Rabbi H. referred his cousin to Dr. Rubin. Although his cousin was skeptical, since no one throughout the world had been able to help him as of yet, he followed Rabbi H.'s advice and contacted Dr. Rubin in May of 2003. Four months later, Drs. Rubin and Anderson discovered the mutation behind the girls' syndrome.

Timing was everything, in this case. The girls' healthy brother became engaged just one month later, in October. Had Dr. Rubin not made his discovery when he did, the *shidduch* would likely not have been made. The discovery allowed for Dor Yeshorim to test for the mutation, with the resulting conclusion that a Nemaline Myopathy birth was impossible for this new couple.