

## CLL RESEARCH: IS OUR GLASS half empty or half full?



**H**uman nature is to highlight the positive aspects; we all want to be successful and demonstrate progress. This issue of *CLL Research Momentum* continues to emphasize the progress made in diagnosis, management and survival of CLL.

I am extremely proud of what CLL Global has accomplished in the last five years. However, I want to give you an honest account of where we stand in eliminating this disease. All of us need to appreciate that people are still suffering as a result of CLL, and we still have a long way to go before it is no longer a threat to people's well-being and life. This is a straight-forward account of the underbelly of CLL.

My views on progress are realistically optimistic- my glass is half full. We have made great advances in controlling CLL. Nevertheless, as we dig deeper into the biology of CLL, the situation becomes more complicated. We have found successful strategies to treat certain groups of patients. This is allowing us to focus on what needs to be done for those who do not respond as well or at all. We are rigorously investigating how to improve treatment for all CLL patients.

Immune suppression is frequently an issue for patients regardless of their response to treatment. The suppression can even be caused by treatments, as most therapies injure immune cells. Patients in remission are still susceptible to persistent fatigue, sinus infections, risk of shingles and other more severe complications. The major complications which emerge in the long-term consist of secondary cancers including acute leukemia, persistent autoimmune complications causing low blood counts and the development of Richter's Transformation. Richter's is a transformation of the CLL into a large cell lymphoma. We will not be able to prevent Richter's Transformation until we better understand the cause. We are currently investigating the role of viruses in this transformation with the hope of developing preventive strategies.

The best approach to dealing with other long-term complications is to prevent them from occurring. We need to put greater emphasis on vigilance against the development of secondary cancers. Patients cannot underestimate the value of skin protection, routine colonoscopies, mammograms and gynecologic and genitourinary evaluations.

I do not wish to convey a sense of pessimism, nor am I underestimating the progress that CLL Global has made in the last five years. We truly have made great strides. In this issue, we share some of the successful outcomes from projects we have funded. Success comes with a story, and ours is an interesting one. Some of you know it;

some of you are a part of it. All of you can read about the origins of the organization on the next page. Everyone involved in CLL Global has one focus: to advance our knowledge of CLL.

Besides our grant recipients, there are numerous individuals behind the scenes who play an integral role in developing better treatment strategies. We introduce you to two scientists working in the lab to decipher new tools.

One of CLL Global's platforms is to encourage researchers to develop a career focused on CLL. Young minds can provide fresh ideas that senior researchers might overlook. In this issue, Dr. Silvia Deaglio, a former grant recipient, shares how CLL Global funding advanced her scientific career.

This issue gives you an opportunity to become more familiar with the CLL Global Alliance program. The Alliance was created to provide an environment for collaboration. Twice a year, we meet face-to-face to encourage collaboration. Earlier this summer, we convened in Spain to present data and develop new strategies. After each meeting, I am amazed at the enthusiasm of the Alliance members and their drive to make progress.

The situation for CLL patients has improved and will continue to do so. Passionate and energetic commitment to understanding the natural history of CLL is crucial. Researchers are becoming more effective in controlling CLL with the progression of technology and the growth of knowledge about the disease. This could not be done without the financial assistance our donors provide.

I thank you for providing the funds to keep the effort going and hope that you will continue to assist us in making future grants possible as we strive to complete the CLL puzzle. We remain committed to the development of new tools and treatments for CLL. We will continue to report to you our findings and our successes. I have a personal commitment to see a cure for CLL developed and to report that the glass is completely full. ::

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Dr. Michael J. Keating

Dr. Michael Keating, Professor of Medicine at MD Anderson Cancer Center, serves as president and CEO of the CLL Global Research Foundation. He is an internationally renowned CLL clinical scientist dedicated to patient care and to development of potentially curative CLL therapies.

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## CLL GLOBAL'S BEGINNINGS:

# from concept to reality

**C**LL Global Research Foundation began as a concept from patients with chronic lymphocytic leukemia (CLL) and their families. Their generosity enabled the establishment of the Foundation, and the continued kindness of numerous people and organizations allows CLL Global to grow. How did CLL Global go from concept to reality?

The idea originated from Glenn Friedly, a businessman who retired early after being diagnosed with CLL at the age of 50. He was relatively young for having CLL, and his disease progressed rapidly. He took it upon himself to visit a number of oncologists. He went to Dana-Farber Cancer Institute in Boston, MA, Royal Marsden Hospital in London, a cancer center in Miami, FL and another one in Palm Beach, FL. He also went to MD Anderson Cancer Center in Houston, TX where he met Dr. Michael Keating.

At the time of his visit to MD Anderson, a clinical trial for FCR (a therapeutic combination of fludarabine, cyclophosphamide and rituximab) was under way and Glenn ultimately chose this treatment for his CLL. In his mind, FCR showed the most promise for remission even though it was a fairly new therapy. Dr. Keating's enthusiasm was also a big part of Glenn's decision. Dr. Keating was the most encouraging of the oncologists that he had seen for his CLL. With low platelets, no energy and little oxygen in his blood, this was possibly Glenn's only shot at survival.

When he came for follow-up appointments, Glenn and Dr. Keating frequently discussed the inadequate research being conducted for CLL and the need for additional support. Glenn recalls Dr. Keating discussing the difficulties in getting funding for CLL research.



Although CLL is the most common adult leukemia, the population of CLL patients requiring treatment is small compared to other cancers. Also, the average age of CLL patients is 70. Many of these patients may develop and succumb to other complications before their CLL progresses enough to become an issue or require treatment. The bottom line was that CLL did not represent a major market for the pharmaceutical industry. Subsequently, there was not much funding allocated to CLL research.

A number of foundations are established by people trying to focus more attention on an area that is not adequately funded. The recurring theme in each of these organizations is to take care of yourself and your family. Glenn came to the conclusion that the primary people interested in funding

research for CLL would be patients with CLL and their loved ones. Dr. Keating sees patients from near and far, all of whom have a vested interest in life. Glenn's proposition was simple. Establish an organization and have patients, their families and their friends put their own fate in their hands.

Glenn felt that Dr. Keating was capable of embarking on this proposition. "He had optimism and a passion for finding a cure and helping people," Glenn stated. As his leukemia moved into remission in the early 2000's, Glenn and Dr. Keating both became convinced of the power of a patient-driven organization dedicated to CLL research.

While Dr. Keating did not have the expertise to organize and run a non-profit organization, he did have a base of intelligent, experienced patients. As he discussed the concept with some of them, he soon realized that his patients were enthusiastically offering their suggestions and their help. Many of those patients turned to their network of professional colleagues who were also willing to help. Dr. Keating received assistance from attorneys, accountants and experienced non-profit professionals.

In the beginning, there was significant discussion regarding the organizational structure. A variety of meetings were held to discuss the concept and how to turn it into a reality. Multiple patients, relatives, friends, scientists, academics, philanthropists and business executives provided input. Jeff Taylor, the husband of one of Dr. Keating's patients and executive director of a non-profit healthcare research institute, kindly offered his expertise. He provided significant input regarding the formation of the organization.



The expanded network of colleagues and contacts led Dr. Keating to an attorney who graciously provided legal expertise to handle the incorporation of the organization as well as strategic thinking.

Because of his involvement in the CLL research community, Dr. Keating was well aware of investigators throughout the world that were conducting innovative research. Therefore, it was important to have the ability to fund research throughout the globe. Other imperatives were transparency and minimal dollars for fundraising. The consensus of Dr. Keating, Glenn Friedly and other visionaries was to operate with low overhead so that the bulk of funds would be allocated for research. CLL Global's administrative overhead remains extremely low, at five percent.

A rapid turn-around of scientific findings was also important in order to accelerate research. CLL Global has chosen not to fund exploratory basic research, but to focus on translational research that will be meaningful in the clinical setting. Grant recipients are expected to have results applicable in the clinic within two to three years of funding.

CLL Global has succeeded because of the generosity of so many individuals including the Board of Directors and the Scientific Advisory Board (SAB). The Board has always had a strong representation of patients and family members. After all, CLL Global was established for their benefit, and they have a particular interest in the operation and success of the Foundation. In addition, there has always been representation from the academic, scientific and business communities.

The SAB is comprised of noted CLL physicians and scientists. Each SAB member volunteers their time to review submitted grant applications and recommend how CLL Global's research dollars should be spent. The SAB Chair, Dr. Bill Plunkett has played an important role in shaping CLL Global. He is a long-time collaborator of Dr. Keating and has served as chairman of the SAB since the Foundation's inception. Dr. Plunkett has guided the organization in determining research priorities, ensuring that all applications are fairly reviewed and has spearheaded the efforts to ensure research dollars continue to be used effectively.

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**“He had optimism and a passion for finding a cure and helping people.”**

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Initially, all grants were awarded for individual projects. Up-and-coming investigators were invited to submit a letter of intent. This strategy proved successful in identifying promising technologies. The grants generated new insights and additional research questions to be explored. However, each project was independent and not inter-related. Therefore, CLL Global decided to incorporate a novel idea for CLL research. Rather than award only individual grants, CLL Global would promote integrated research.

The U.S./European Alliance for the Therapy of CLL, known as the Alliance, was established at the end of 2007. Successful CLL investigators, some of whom were previously funded through the individual grant program, were invited to take part in a break-through initiative promoting collaboration and openness. The Alliance is based on five themes important to CLL research; the themes, projects and researchers intentionally overlap. The atmosphere is one of great trust and enthusiasm.

An attractive aspect of CLL Global is that it is not locked into a standard format and can respond quickly as opportunities present themselves. Examples of this include two international initiatives, one in Australia and one in Israel, which were provided seed money to start CLL research programs.

CLL Global maintains a “dollars in, dollars out” approach. As funds are raised, the organization attempts to award money to investigators as quickly as possible. Although small in operation, the efficiency and growth of CLL Global makes it an outstanding model of a non-profit organization.

The future of CLL Global will depend on maintaining an active donor pool. More and more patients seem willing to donate as long as there is open communication regarding where their money is being spent and the success of the programs funded. The level of enthusiasm continues to expand. The talent of the researchers, the board, and those dedicated to CLL Global is outstanding. There is a realistic anticipation that curative strategies for CLL will be implemented in the clinic in the next 3-5 years. ::







L-R: Drs. Helen Heslop, John Gribben Chitra Hosing, Elizabeth Shpall, Catherine Bollard, David Maloney

Sometimes scientists are extremely protective of their data and unwilling to share findings. We intentionally invited investigators with a track-record of collegiality.” Dr. Keating has found that the Alliance investigators are extremely open to presenting original ideas without fear of competitive research. “In a world where so much emphasis is placed on confidentiality, it is refreshing to see a group of investigators willing to collaborate.”

Many of the investigators comment that their own research benefits by soliciting ideas from participants with expertise in other fields. Dr. Zeev Estrov (MD Anderson) remarks “research is improved by soliciting input from your colleagues. Oftentimes, we are busy in our labs and clinics and do not have the opportunity to consult and obtain expert constructive criticism. I may have a planned approach, but someone else in the Alliance may expand my exploration or focus on questions that I did not concentrate on.”

While the Alliance relies on teleconferences and web exchanges for smaller working groups, there is tremendous benefit in bringing together all of the participants. Each of the working groups targets a specific aspect of CLL research; however, the overall problem and goal remains the same for all of the researchers. The in-person meetings are a great opportunity to share new research and spark more collaboration.

“Meetings like the one held in Barcelona are extremely fruitful because they expose me to the different culture and the diverse information provided by CLL-oriented scientists and clinicians. We are all tackling the same problems from different angles,” Professor Federico Caligaris-Cappio (Italy) said. “This sharpens my investigation plans and the development of collaborations.” ::

# Victory in Spain:

## ALLIANCE TEAM SCORES

**T**his has been a busy summer for Spain. Before celebrating a World Cup victory, Spain played host to the semi-annual gathering of the U.S./European Alliance for the Therapy of CLL. Organized by CLL Global, the Alliance brings together leading CLL experts. In June, twenty-five clinicians and scientists gathered for two days outside of Barcelona to evaluate the progress made to date.

The presentations at the Barcelona meeting demonstrated that many successful collaborations have been initiated. The Alliance meetings continue to illustrate the willingness of the participants to freely share ideas, data and insights. For those outside of the academic medical research environment, this might not seem like a big accomplishment.

CLL Global President and CEO, Dr. Michael Keating commented, “I have been involved with numerous collaborative projects during my career.

“it is refreshing to see a group of investigators willing to collaborate.”

Almost \$7 million dollars in Alliance grants have been awarded. These grants focus on new drugs, the CLL microenvironment, gene therapy, transplantation and immune therapy. Additional grants focused on genetics will be awarded in the near future. A primary intention of the Alliance is to increase collaboration among CLL experts. At the beginning of the initiative, it was unclear how successful the collaborations would be. Would scientists be willing to move from working in silos to working in teams?



L-R: Drs. Kanti Rai, Carlo Croce, William Plunkett

# Chain Reaction:

## LINKING ALLIANCE IDEAS



L-R: Drs. Nicholas Chiorazzi and Jan Burger

**T**he success of grant projects is often measured by the number of resulting publications and the amount of leveraged grants. CLL Global tracks both of these statistics. Emphasis is also placed on the collaborations that have developed as a result of the Alliance.

The purpose of initiating the Alliance was to bring together leading experts to work on specific areas of CLL research. Two of the intended consequences were to reduce research redundancy and for investigators to find synergies and enhance each other's research. Many recipients are now reporting on their first eighteen months of funding; the chain of collaborations that has resulted is phenomenal.

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**"...CCL3 may become a highly useful prognostic marker in CLL and potentially other B-cell malignancies."**

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A high priority of the Alliance is a better understanding of the CLL microenvironment. This is the area in the body where CLL cells live and grow. Dr. Jan Burger (MD Anderson) previously demonstrated that particular cells in the microenvironment called "nurselike cells" help to keep CLL cells alive for a long period of time. As part of his Alliance project, Dr. Burger is exploring the function of these nurselike cells and how to interrupt the survival signals that CLL cells receive from nurselike cells.

As the leader of the CLL-Stromal Interaction working group of the Alliance, Dr. Burger has formed collaborations with others researching the cells surrounding CLL cells. One example is his collaboration with Dr. Andreas Rosenwald (Würzburg University, Germany) to better understand the genes and proteins of the CLL microenvironment.

Dr. Rosenwald is a leader in the field of gene chip analysis which is used to measure the activity of thousands of genes in CLL and other cells. Using this technology, Drs. Rosenwald and Burger identified genes which become activated in CLL cells by nurselike cells. They also discovered that when the genes are activated, the CLL cells release certain molecules.

One of these molecules is known as "CCL3". Further investigations of CCL3 showed that it can be detected in CLL patients' plasma. Dr. Burger worked collaboratively with Dr. Thomas Kipps (University of California, San Diego) and Drs. Michael Keating and William Wierda (MD Anderson). They measured a large number of plasma samples for CCL3 levels. The results of these investigations extended the gene chip data related to CCL3.

The investigators found that CCL3 levels in CLL patients closely coincide with disease progression and a patient's need for treatment. Because of the simplicity of this analysis and the significance of the prognostic information, CCL3 may become a highly useful prognostic marker in CLL and potentially other B-cell malignancies.

Another portion of Dr. Burger's Alliance project is to understand how the microenvironment promotes CLL cell resistance to drugs. Dr. Burger is working with Dr. Varsha Gandhi (MD Anderson) of the New Drugs group to look at signaling pathways used between the CLL cells and the microenvironment that allow CLL survival and drug resistance. Dr. Burger has created a laboratory model that mimics the actual microenvironment where CLL cells reside. This model is being used to study the signaling pathways and to develop drug combinations.

Dr. Burger believes the Alliance "provides a unique forum to interact with leaders in CLL research in a trusting, collegial fashion. This is precious in a highly competitive research environment. My lab is working on models that other investigators can then use to test potential compounds." A long-term goal of the Alliance is to establish an accessible model and system of tests in order to rapidly evaluate and advance new potential therapies. ::







## UNSUNG HEROES:

# researchers in the background

Principal investigators, the lead investigators of research projects and clinical trials, are recognized and appreciated for the novel findings of their work. However, the accomplishments of these investigators could not be achieved without the help of “behind the scenes” researchers. They may not always receive the accolades but are essential in advancing CLL research.

These researchers may be visiting interns or fellows spending a short time at a given institution to gain knowledge and experience, technicians whose careers are spent in laboratories or young doctors trying to make a difference in people’s lives. They all are ambitious to leave their footprint in the research world with aspirations of being at the forefront of innovative discoveries.



Dr. Carmen Schweighofer is a “behind the scenes” investigator who is gaining her own notoriety and research funding. She is a postdoctoral fellow in the Hematopathology Department at MD Anderson Cancer Center. She works in the clinical cytogenetics laboratory directed by Dr. Lynne Abruzzo.

Cytogenetics is the study of chromosomes and genes to determine how and why genes and their counterparts affect or control what happens to the body. Clinical cytogenetics cancer research applies this information to patient care.

Dr. Schweighofer came to MD Anderson in 2008 from the University of Cologne in Germany where she was working with Dr. Michael Hallek (CLL Global grant recipient and Alliance member). She traveled to MD Anderson to expand her knowledge of cytogenetic research. Ultimately, she hopes to expand the use of cytogenetic analysis in Germany.

One of Dr. Schweighofer’s current projects at MD Anderson is to conduct genome wide association studies for patients treated with FCR (combination fludarabine, cyclophosphamide and rituximab). Every CLL patient treated with FCR at MD Anderson gives a blood sample prior to, during and after treatment. Dr. Schweighofer analyzes these samples.

Data on thousands of samples is analyzed and recorded so that a correlation can be made between the various genetic flaws CLL patients have and their responses to treatment and survival outcomes. This information has already allowed physicians to make more personalized treatment decisions in recent years. As more data becomes available, patients will have better treatment plans.

Dr. Schweighofer is also working on one of Dr. Abruzzo’s projects funded by CLL Global to study patients with a chromosomal abnormality known as 11q deletion (11q-). This abnormality affects roughly two thirds of CLL patients. It was originally thought that all CLL patients with 11q- were missing a gene called ATM. However,

Dr. Abruzzo recently discovered that not all 11q- patients are missing the ATM gene. This means that there is another gene affecting CLL patients with 11q- that researchers have not investigated. Currently, there is very little data. Dr. Schweighofer is working with Dr. Abruzzo to establish if there will be any clinical significance from this new discovery.

Although Dr. Schweighofer works under Dr. Abruzzo, she says that they work like a team. Everyday they discuss experiments to be performed and work together to determine a game plan. Their relationship is characterized by trust and freedom. Dr. Schweighofer is free to perform her own experiments, meaning she could be credited with a scientific breakthrough.

Dr. Schweighofer has wanted to be involved in cancer research, specifically hematology, as long as she can remember. She stated, “To work with cancer patients is special. There is a serious potential of it being the end of life for patients. The challenge of conquering the disease and the hope of bringing something positive to patients was part of my motivation to go into hematology and oncology.”

Dr. Schweighofer will be returning to Germany next year where she will continue to focus on CLL research. Her ultimate goal is to run her own lab and to make a discovery that impacts long-term outcome and response that can be used in patient care. She looks forward to continuing collaborations with MD Anderson as she feels the combined knowledge will ultimately benefit the patients.



Another scientist working hard behind the scenes every day is Dr. William Decker. He is a senior research scientist working in an MD Anderson laboratory headed by Dr. Elizabeth Shpall, a member of the Transplantation/Immune Reconstitution group of the CLL Global Alliance.

**D**r. Decker's expertise is in dendritic cell biology and vaccinations. Dendritic cells are immune cells that recognize and present foreign materials (antigens) to the immune system. He originally came to MD Anderson to work with Dr. Shpall on a vaccine for acute myelogenous leukemia. Six years later, he continues to explore novel treatment approaches with her.

Dr. Decker's primary responsibility is to conduct research for Dr. Shpall and her collaborators to develop potential new remedies by way of cellular therapy. Cellular therapy utilizes the body's cells as a treatment option by teaching the cells to target disease. Dr. Decker also spends time writing grant applications to obtain research funds, and he writes and reviews publications for research journals.

With direction and motivation from Dr. Shpall, Dr. Decker is currently looking at the combination of cellular therapy with a new cancer drug which has shown a positive effect in killing cancer cells in the body. This combination provides a double knock-out against the cancer. Drs. Shpall and Decker are now in the final stages of research and are preparing to write a protocol so that this new combination can be given to patients.

Dr. Decker is also working with Dr. William Wierda, a member of the Gene and Vaccine program of the CLL Global Alliance. Drs. Wierda and Shpall are collaborating through the Alliance, and Dr. Decker is working with Dr. Wierda to turn CLL cells into a vaccine. This is accomplished by modifying the CLL cells with a virus outside the body. After the CLL cell is infected with the virus, it becomes a new cell type. This new cell type allows the immune system to see CLL cells as "foreign", causing the immune cells to kill the CLL cells.

While this therapy works very well in the laboratory, there is a possibility it will not be as efficient when given to patients. This is an issue with almost all potential therapies and only a small percentage of what is successful in the laboratory is reproducible in humans. Dr. Decker may have to make modifications before Dr. Wierda's vaccine can be applied in the clinic. After working on this project for two years, Dr. Decker remains excited about the potential for success.

Dr. Decker is also responsible for a unique mouse colony at MD Anderson. These mice are 100%

immunosuppressed, meaning they have absolutely no immune system. Without an immune system, these mice do not immediately kill the CLL cells. This provides an opportunity for the disease to advance in the mice but more importantly serves as a model for better understanding the disease in humans.

Dr. Decker's fascination with discovery led to his career as a scientist. He wanted to be a scientist since he was 4 years old. He said, "I love what I do and that is priceless." Wherever life takes him, he knows that he will always be involved in implementing basic research with a goal towards translational research.

In regard to his accomplishments, Dr. Decker stated that he has four beautiful kids and a great marriage, so in those terms, he is a success. From a professional aspect, success for him will be to get something to the clinic that actually makes an impact and is a standard of care for at least one subgroup of patients. As he works toward that goal, he is very satisfied playing an important role at MD Anderson and with Drs. Shpall and Wierda. ::



# SIGNS OF SUCCESS: projects reach the clinic

**C**LL Global preferentially funds research with potential for rapid clinical application. This (often) means moving research from the laboratory to the clinic, where patients can directly benefit. Since awarding the first round of grants five years ago, multiple research developments have been brought to the clinic in the form of clinical trials.

## CD3/CD28 MICROBEADS

This technology is applied to patients' T-cells (a type of immune cell) to help the immune system fight infection after treatment. The Phase I multi-center trial, funded by CLL Global, has been open for one year and has completed enrollment.

Following treatment, patients enrolled in the trial receive expanded T-cells, cells that have been modified with the new microbead technology, to overcome immune defects. As of now, ten patients have received the expanded T-cells. The infusions have been well tolerated and there have not been any treatment-related adverse events.

Although still preliminary, the data available suggests that this process can lead to T-cell recovery soon after standard therapy when immunosuppression is at its highest. The remaining patients enrolled on the study need to receive treatment. Comprehensive immune analysis will need to be conducted to determine whether this new combination of therapies translates into a clinical benefit with reduced infections and longer durations of remission.

## 8-CHLORO-ADENOSINE

8-chloro-adenosine (8-cl-ado) is a therapeutic agent which depletes CLL cells of the energy they need to survive. CLL Global helped fund toxicology studies required by the U.S. Food and Drug Administration so that 8-cl-ado could be used in humans.

Dr. Varsha Gandhi (MD Anderson) is responsible for the laboratory data on the compound. A Phase I clinical trial is currently enrolling patients at MD Anderson and is headed by Dr. William Wierda. To date, six patients have been treated with 8-cl-ado.

One of the goals of CLL Global is that recipients will be able to utilize initial support from the Foundation to find other grants to continue the research. Drs. Gandhi and Wierda have subsequently been awarded over \$1 million from federal agencies and private organizations to support the clinical study of the 8-cl-ado trial. CLL Global will share more data from this study as it becomes available.

## COMPOUNDS FROM NATURE

PEITC, which is being studied by Dr. Peng Huang at MD Anderson, is a compound found in vegetables like watercress and broccoli. In the laboratory, strong anti-cancer activity is demonstrated when PEITC is given in high concentrations. Presently, the compound is being formulated into capsules. A future *Momentum* will contain a report on the initiation of the first clinical studies.

CLL Global has also supported research being conducted by Dr. Neil Kay at Mayo Clinic using an oral green tea extract. In the initial study, asymptomatic patients were given varying doses of epigallocatechin gallate (EGCG), a major component of green tea. The majority of patients had a reduction in lymphocyte count and decline in lymph node size. A second study showed similar findings. Both PEITC and green tea represent opportunities to use relatively non-toxic treatments to delay and fight cancer growth.

As CLL Global continues to grow and progress, more exciting results will become available. The Foundation will continue to focus on rapidly advancing therapeutic strategies to the clinic. ::



## REFLECTIONS from a Grant Recipient

*Dr. Silvia Deaglio received a grant from CLL Global in 2006. She is now becoming internationally recognized for her research on CD38. Below, Dr. Deaglio describes how her CLL Global grant has impacted her career:*

“I had the occasion to know the CLL Global Research Foundation initiative through the energetic and enthusiastic advertisement of Dr. Keating. He encouraged young scientists wishing to take their own first steps in the field to apply for a grant from CLL Global. I submitted a letter of intent and my project was selected for funding.

My project focused on whether CLL patients who positively express the enzyme CD38 experience a worse prognosis than CD38 negative patients. Enzymes are proteins needed by cells to perform necessary functions. CD38 is an enzyme found on the surface of leukemia cells in some patients, but not others. The inference is that this enzyme is likely to be important in disease progression.

During the project, we found that CD38 positive CLL cells can respond better to signals from surrounding, non-cancerous cells. Also, CD38 activates a chain of events that induce proliferation and migration of the CLL cells. These preliminary results were eye-opening. Clinical trials using monoclonal antibodies to target CD38 (currently ongoing in Europe) should verify the clinical benefit of our research to patients.

CLL Global was my first grant as a principal investigator. It provided the necessary financial support for those initial studies, and it was the trigger for more funding from other national and international agencies. Not less importantly, it provided an entry ticket for the CLL world and the chance to meet, interact and collaborate with other scientists working in the field. For all of these reasons, I would like to express my gratitude to CLL Global for its policy of providing research support to young scientists.”

*Silvia Deaglio, MD, Ph.D.*  
University of Torino ::

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FIND OUT MORE ABOUT THE PROJECTS WE ARE  
ACCELERATING AT [WWW.CLLGLOBAL.ORG](http://WWW.CLLGLOBAL.ORG)

