

Myeloma Research Fund Newsletter

A Donor Advised Fund of the Silicon Valley Community Foundation

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Overview of Fund Activities

Dear Donors, Advisors, and other Friends,

It has been far too long since our last newsletter (a report on our first scientific workshop in April 2004). So long, that we feel we should reintroduce the Myeloma Research Fund (MRF): its history, motivations successes and status. Most importantly we will lay out why we believe that the model we developed for supporting research in Multiple Myeloma is as critical and effective as ever and that it represents best way your support can fight a terrible disease in turn extending the lives and reducing the suffering of patients.

The MRF was founded in December 2000, two months after I was diagnosed with Multiple Myeloma. Discussions with scientists working in the field revealed two encouraging points. First, there was a flood of new results and drug candidates based on better understanding of the molecular pathways of the disease's survival and progression. Better yet, these drug candidates promised a much more focused attack on the disease with much fewer side effects than previous chemotherapy agents. Second, it was clear that the amount of funding in the field was grossly inadequate, even more so when the fraction of that funding which was truly available to new approaches was considered. In fact, there was agreement that funding in the range of \$100K's per year could have a major impact. This was truly a surprise given the billions which go in to cancer research annually.

We chose a strategy of making relatively large grants to a small number of groups, and to commit to funding those groups for multiple years. At the time, other private funding organizations, while raising far more overall, typically made single year grants of less than \$100,000 which might support a single researcher for one year. Our first grants were commitments of \$250k per year for three years.

A Personal Note

My history as a patient as turned out to mirror many of the changes in multiple myeloma treatment. Over the past seven years, I have been on a wide variety of treatments.

Initially I was put on a fairly standard chemotherapy regime known as VAD. Notably, this treatment is essentially obsolete.¹ In early 2001, I underwent an autologous stem cell transplant. In this procedure, your immune system is essentially stored in a freezer while you are administered chemotherapeutic drugs so strong that they destroy your bone marrow. Your stem cells are then returned to you so you can survive the treatment. Like most patients, I enjoyed a partial remission which in my case lasted about 2-1/2 years. After the inevitable relapse I suffered a fracture of my humerus due to the bone eroding effects of the disease. I started a treatment with Thalidomide and steroids. Like many treatments, this worked well, but has its side effects.

Thalidomide belongs to a class of drugs known as immunomodulatory agents (IMiD), which affect particular biochemical pathways which aid the survival and proliferation of the myeloma cell. Some of the first research we funded was on the development of Revlimid an IMiD much more powerful than Thalidomide but with much less neurotoxicity. Another drug our groups worked on was Velcade, a protease inhibitor and the first new anti-myeloma drug introduced in 30 years.

2006 was a difficult year. As one treatment led to another, I suffered more bone disease which led to surgery to put long metal rods in both femurs. I'm presently taking Revlimid and steroids which seems to have slowed these problems and with few side-affects.

When one meets a new MM patient, what one often notes is that doctors now give a much more optimistic picture of survival time and the difficulty of treatment. There are now a large number of promising agents under investigation. The problem has turned to identifying the best ones and in particular the best combinations for trials. Similarly, gene testing is being developed to predict which agents and combinations will be of most benefit to a given patient.

You can be part of supporting this work which may add years to the lives of 10's of thousands of patients and reduce immeasurable pain and suffering. Please join us.

Lew Aronson

1. <http://bloodjournal.hematologylibrary.org/cgi/content/full/106/1/2>

We made these grants to three groups, led by Dr. Kenneth Anderson at the Dana-Farber Cancer Institute (Harvard), Dr. William Dalton at the H. Lee Moffitt Cancer Center (U. South Florida), and Dr. James Berenson at his newly founded Institute for Myeloma and Bone Cancer Research in Los Angeles.

With your help, we were able to meet these commitments and fund a fourth year of \$190k for each group, for a total of \$2.8M. As we had hoped, the size and continuity of our grants has allowed these groups to commit to extended research projects, and the flexibility of our funding has allowed them to look at exciting new areas not supported by conventional funding sources.

In addition to direct grants, we have also sponsored and organized two scientific workshops. As with our funding, we tried to fill a need not met by traditional scientific meetings. While traditional conferences offer opportunities for large numbers of research organizations to share their work in a peer reviewed setting, they are less effective for extended brainstorming among researchers themselves. This is due both to the tight schedules, and the carefully measured nature of comments in such an open setting. Additionally, while a member of a research group might spend a lot of time interacting with other group members, they rarely have the opportunity for the same interactions with peers at other groups. The MRF workshops were designed to overcome these limitations. While limiting the total attendance to about 25, 3 to 5 members of each of the research groups we sponsor were invited. Additional guests were invited from local biotech companies who we felt might offer new points of view and useful collaborations. The companies represented included Hewlett-Packard Labs, Arcturus, Affymetrix, Caliper, Scripps Research Institute, Collaborative Drug Discovery, Proteolix, Scios (a Johnson and Johnson company) and Pharmix. More details on our last workshop can be found on Page 3 and on our website

With your support, we plan to rededicate our efforts. Presently, we have about \$200k available for new grants. Between now and the end of the year, we'd like to increase this to at least \$750k so that we might fund 3 groups at previous levels. We plan on holding a combined proposal review / workshop as soon as possible after the New Year. As we describe on page 3, the field of Myeloma research is ripe for new advances, which we have seen can be translated into real patient benefits in a very short time. It is hard to imagine a more effective use of your philanthropic dollar and we look forward to your help in moving the field forward.

Lew Aronson

Comments from the grant recipients

“This generous support directly fast forwarded the bench to bedside translation of three new drugs- bortezomib, lenalidomide, and thalidomide, as well combination of bortezomib and pegylated doxorubicin from the laboratory to the clinic and FDA approval to treat myeloma. Several additional targeted therapies have also been validated and under clinical evaluation, and the outcome for myeloma patients today is markedly improved as a direct result of MRF.”

- Dr. Kenneth Anderson, Dana-Farber Cancer Institute

“The Myeloma Research Fund has created a community of collaborating scientists, all focused on the development of new therapeutic strategies to improve the treatment of multiple myeloma. The MRF sponsors national meetings of scientists within the myeloma field as well as leading researchers from basic science disciplines so as to catalyze innovative interactions.”

- Dr. Bradner, Dana-Farber Cancer Institute

Report from the second MRF Workshop

The second annual MRF workshop was held from September 30 to October 2, 2005 in Palo Alto. There were 13 attendees from our sponsored research organizations, and 9 invited guests, as well as the members of the MRF Board of Directors.

Our purpose in holding the workshop in Palo Alto is two-fold: bring the attendees to a site where they don't have the distractions of home, and expose them to research and business activities which may be relevant to their work which occurs in the Bay Area. There are over 300 biotech companies in the Bay Area, and many of them are doing cutting edge work in areas which have relevance to multiple myeloma research. Living in the Bay Area, we are fortunate to have contacts with many of these companies, which can lead to opportune interactions with our sponsored researchers. The invited guests were from Affymetrix, Scripps Research Institute, Scios, Collaborative Drug Discovery, Agilent Labs, Pharmix, Caliper, and Proteolix.

In our first workshop, an invited talk from Tom Baer of Arcturus led to a collaboration with two of our research groups. In the second workshop, an invited talk from Dr. Ben Cravett of Scripps has led to extensive collaboration between his group at Scripps and Dr. Anderson's group at Dana-Farber and Dr. Berenson's Institute for Myeloma and Bone Cancer Research. In addition, the participation in the workshop by Chris Molineaux of Proteolix led to the initiation of a trial of their new proteasome inhibitor by Dr. Anderson's group.

In addition to invited talks, the main activity of the workshop was the presentation of status and preliminary results from our sponsored researchers. Since these presentations are not as formal as papers presented at national conferences, the results are fresher and the conclusions less finished, leading to a lot of discussion and brainstorming. For the lay observer, these sessions were very uplifting. The level of activity in our sponsored labs is high, and there are a lot of promising developments. In particular, Dr. Anderson has made the statement that the increased understanding of the biology of the myeloma cell which has been gained in the past five years has led to much more efficient drug development. Several drug targets have been identified for which drugs can be created, leading to in vitro testing, animal trials, and human trials in rapid order.

Another theme which was continued from the first workshop was the work Dr. Berenson's group has done in creating "mouse models" which can be used for initial drug testing. The IMBCR has succeeded in growing human myeloma tumors in mice in a way that allows the evaluation of drugs on a much shorter (and safer!) time scale than human trials. All of our sponsored groups are benefiting from this work.

In general, the focus of the research into multiple myeloma has shifted away from identifying drugs in isolation to identifying drug combinations which will combat the myeloma cell. As the biology of the cancer cell is becoming understood, it is possible to determine why certain drugs (like Thalidomide, Revlimid, and Velcade) are effective, and what opportunities to kill or control the myeloma cell remain. That has led to trials of a number of new agents, as well as trials of combinations of agents.

John Sanguinetti

About the Fund

The Myeloma Research Fund is a Donor Designated Fund at the Silicon Valley Community Foundation (SVCF)* of San Mateo California. Its goals are:

- To find a cure or method of indefinite control of multiple myeloma in the shortest practical period.
- To find techniques for increasing remission times where the disease is effectively controlled.

As a small private fund, we believe we have the freedom to more effectively direct our resources to the most promising research avenues. We further seek to distinguish our funding from most other private organizations by providing multiple year grants of sufficient size to allow promising ideas to be moved from the research lab to clinical trials. To do so, we seek donors who can commit to five-year pledges of significant size, however, we welcome contributions of any size and duration.

By setting up the Myeloma Research Fund as a donor-designated fund within the SVCF, we are able to ensure that all donations are fully tax deductible. Furthermore, the SVCF manages all donated funds and overseas grants and relations with the recipient institutions, for an overhead rate of 2% (effectively much smaller since most of the funds are quickly allocated and stay at the SVCF for a small fraction of the year, where the overhead is calculated on a quarterly basis). Because of this, and our policy of negotiating grants with no administrative overhead, we have been able to assure that more than 99% of the funds donated will go directly to Myeloma research. We believe this is the most efficient possible use of funds for cancer research.

We would like to extend special thanks to Dr. Robert Kyle, Dr. Ronald Levy, Dr. Bernard Cooper and Dr. Lawrence Leung of Stanford for their help as expert advisors during our annual reviews.

For questions about the Fund, please contact:

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Donations of cash or securities may be made to the Myeloma Research Fund at the Silicon Valley Community Foundation (address below). Instruction may be found on our website located at:

<http://www.myelomaresearchfund.org/MRF/forms.html>

or by contacting:

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(Be sure to include your name and address so that they may send you a tax receipt).

* The MRF was part of the Peninsula Community Foundation which merged with the SVCF in 2006