# SWCRF-FUNDED RESEARCHERS IDENTIFY A WAY TO DRAMATICALLY ENHANCE THE IMPACT OF THE MOST EFFECTIVE NEW TREATMENT FOR MULTIPLE MYELOMA

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**Treatment of multiple myeloma (MM) patients with Velcade is considered a major advance. However, not all patients respond to Velcade and, among those that do, a recurrence of the cancer is all but inevitable. Scientists funded by SWCRF have identified a mechanism that might explain in part how this happens and show that adding another drug dramatically increases the number of MM cells killed by Velcade and almost completely eradicates the cells that survive the initial Velcade treatment, substantially reducing risk of recurrence.**

Multiple myeloma (MM) is a disease of the blood cells that make antibodies. These cells grow uncontrollably in the bone marrow, destroy bones and damage the production and function of all the blood cells. The five year survival rate for MM is 35% but is improving with new drugs like Velcade being available.

Velcade is a drug that was approved as the first line treatment for MM in June 2008, after having been used as a treatment for recurrences since 2003. As noted above, it is an improvement over earlier therapies. However, many patients do not respond and among those that do, virtually all eventually experience a recurrence of the MM. Most cancer fatalities are caused by recurrences rather than the initial diagnosis.

The mechanism by which Velcade fights MM cells can also cause a cell to become dormant rather than die. Dr. Julio Aguirre-Ghiso's lab identified a response that protected the multiple myeloma cells from the Velcade and enabled some of them to become dormant. The scientists speculated that these dormant cells were responsible for the later recurrence. They demonstrated that simultaneous treatment with another drug, salubrinal, which has no effect on the survival of MM cells, still dramatically enhanced the impact of the Velcade, raising the proportion of cells killed from 50% to 90%. This is achieved by preventing the MM cells from reversing the signals changed by Velcade. Further, the use of salubrinal after treatment with Velcade eradicated the dormant cells surviving the initial therapy. Salubrinal is notable for its lack of toxicity in preclinical models.

The scientists will be investigating these very promising results in a wider variety of multiple myeloma samples obtained from patients.

Denis M. Schewe and Julio A. Aguirre-Ghiso **Inhibition of eIFα Dephosphorylation Maximizes Bortezomib Efficiency and Eliminates Quiescent Multiple Myeloma Cells Surviving Proteasome Inhibitor Therapy** *Cancer Research*, Feb. 2009; 69: 1545-1552.

**Link to Article:**
http://cancerres.aacrjournals.org/cgi/content/abstract/69/4/1545

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