

Laser Imaging Studies Shed Light On Brain Blood Flow Abnormalities In Myeloproliferative Neoplasms

By Chris Schaffer, Ph.D and Puifai Sakultarm

Myeloproliferative neoplasms are disorders of the blood that present themselves in four main forms: polycythemia vera, essential thrombocythemia, primary myelofibrosis, and chronic myelogenous leukemia. In these diseases, malignancies in the bone marrow lead to abnormal quantities of red blood cells, white blood cells, and platelets. For polycythemia vera and essential thrombocythemia, which share an acquired

require frequent doctor visits to monitor and adjust the blood condition by means of medication as well as phlebotomy. The abnormal circulation can lead to a number of secondary clinical manifestations including neurological problems, which are poorly studied even sixty years after the discovery of myeloproliferative neoplasms.

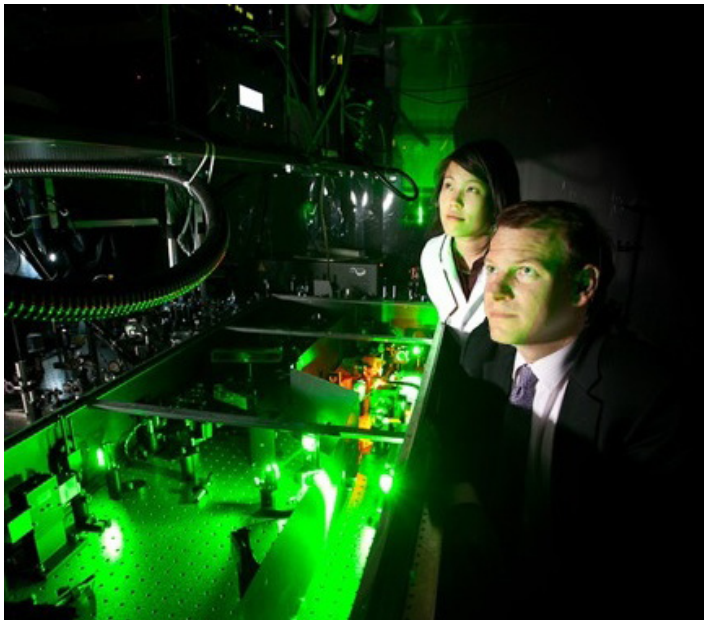
In 2007, Dr. Richard Silver, Weill Cornell Medical College,

This collaborative effort was launched by Ms. Puifai Santisakultarm, then a first-year Ph.D. candidate in Biomedical Engineering, who spent two months working with Dr. Silver in New York to learn the genetic and physiological basis of myeloproliferative neoplasms. She then returned to Cornell University in Ithaca, NY with a background in the clinical side of these diseases and the tools and drive to try to uncover potential mechanisms of microcirculation problems during her Ph.D. research in Prof. Schaffer's lab. With continuous collaboration from Dr. Silver and generous financial support of the Cancer Research and Treatment Fund, Ms. Santisakultarm has made a few very important discoveries in the last four years that may shed new light on how myeloproliferative neoplasms affect brain function.

In her graduate study, Ms. Santisakultarm uncovered a significant amount of brain capillaries with blockages in mouse models of polycythemia vera and essential thrombocythemia. Although there is some clinical evidence which suggests possible cognitive decline in these diseases, no direct observation has pinpointed a potential mechanism for injury to the brain until this detailed study of brain microcirculation using in vivo two-photon excited fluorescent

microscopy. Severe reductions in brain blood flow, such as those Ms. Santisakultarm has shown to occur in mice with myeloproliferative neoplasms, are known to be associated with neurological decline in many disorders such as Alzheimer's and dementia. In addition, the research team found white blood cells and platelets to be the leading reason for these capillary occlusions. The flow disruption is temporary in the case of white blood cells, while permanent in a subpopulation of platelet clots. The results underline alterations in blood composition as an important factor in the health and functions of organs with numerous small blood vessels as well as the roles that various blood cells play in potentially disrupting blood flow.

The knowledge gained from this study has many implications. It demonstrates the significance of physical properties of the blood, which is sensitive to alteration of blood composition, and the attention that physicians must pay to this issue when treating patients. It also generates new ideas for therapeutic strategies for those who suffer from myeloproliferative neoplasms as well as disorders where microcirculation problems play a crucial role. Dr. Silver, Prof. Schaffer, and Ms. Santisakultarm are currently working to test strategies to interfere with white blood cells and platelets aggregation in hope of eliminating the capillary stalls and restoring brain blood flow. This ongoing work has received continued financial support from the Cancer Research and Treatment Fund.



mutation in the JAK2 gene in most patients, quality of life is significantly reduced due to excessive production of red blood cells and platelets. Those affected by the diseases often experience fatigue, chronic headache, and thrombosis as a result of blood flow and coagulation problems. They

and Prof. Chris Schaffer, Department of Biomedical Engineering at Cornell University, set out to explore the impacts of polycythemia vera and essential thrombocythemia on microcirculation of the brain, combining their expertise in hematology and advanced optical imaging.