POLSKY Center for Entrepreneurship and Innovation
THE UNIVERSITY OF CHICAGO

B-cell Depletion Therapy for Treatment of Rare Neurovascular Disease

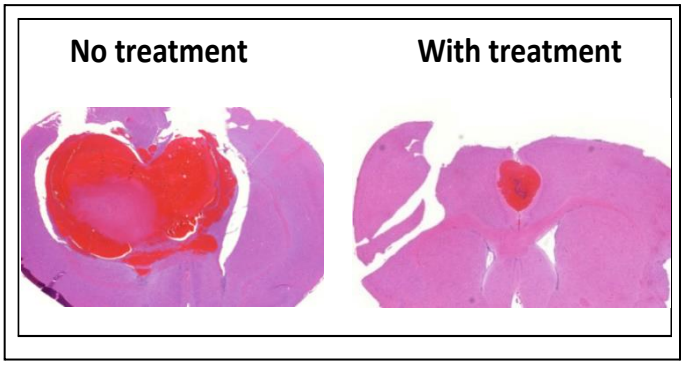
SUMMARY
Researchers at the University of Chicago have discovered an effective treatment for cerebral cavernous malformations (CCM), a disease of the brain blood vessels with rare, highly aggressive genetic forms. The treatment targets a major mechanism of CCM development by depleting immune mediating B-cells, to stop disease progression and new lesion formation in a less invasive manner compared to the current treatment options requiring surgical interventions.

KEY RESULTS
Treatment with antibodies against BR3, a B-cell receptor, significantly reduced the development and maturation of brain lesions compared to the control group using a CCM genetic mouse model that recapitulates the human disease.

ADVANTAGES
- Does not require surgical intervention.
- Reduces development and maturation of brain lesions.
- Prevents CCM hemorrhage.
- Approved drugs developed for other indications are compatible to treat this condition.

APPLICATIONS
- CCM therap

B-cell depletion reduces lesions in murine model of CCM



Cavernous malforamtions, shown in red, and brain hemorrhaging was significantly reduced when treated with anti-BR3 antibody compared with mice that received no treatment.

TECHNICAL DESCRIPTION
Cerebral cavernous malformations (CCM) are enlarged and brittle blood vessels in the human brain, occurring in familial and sporadic forms. Patients may experience headaches, seizures, paralysis, hearing or vision loss, related to bleeding in the brain (cerebral hemorrhage). Rare genetic forms of CCM are highly aggressive, with patients disabled before adulthood. There is no current treatment to prevent lesion formation, maturation or bleeding. Surgical removal of a lesion that has already bled is highly invasive, costly, and can cause serious complications. Such brain surgery does not prevent development of new CCM lesions. Dr. Awad, a leading physician and expert on CCM, discovered that infiltrating clonally expanded B-cells and antigen triggered immune complexes are a typical feature of CCM lesions, and postulated that this autoimmune reaction contributes to CCM lesion development. Using a genetically engineered mouse model, which develops CCM lesions identical to those in human patients, Dr. Awad's group was able to demonstrate that BR3 antibodies effectively eliminated the autoimmune response in the lesions, and B-cell depleted mice exhibited a significantly lower CCM burden, with a reduced number and size of CCM lesions compared to placebo mice, and significantly decreased hemorrhage from the lesions.

REFERENCE
UCHI 2350

DEVELOPMENT STAGE
Pre-Clinical

THERAPEUTIC AREAS
Central Nervous System
Rare disease

PUBLICATION
Shi et al. 2016. J. *Neuroimmune Pharmacol.*

CCM Unmet Need

INTELLECTUAL PROPERTY
PCT/US15/059135

INVENTORS
Issam Awad, MD

Dr. Issam Awad is the John Harper Seeley Professor of Surgery and Neurology at UChicago, and Scientific Advisory Board Chairman of Angioma Alliance. He is skilled in the surgical management of neurovascular conditions affecting the brain and spinal cord, and is a leading physician in treating cerebral aneurysms, and cerebrovascular malformations. He is responsible for major discoveries on CCM disease over more than two decades.

Contact: Sao-Mai Nguyen-Mau, PhD | saomai@uchicago.edu | 773-834-1270