

University of Massachusetts Medical School

eScholarship@UMMS

---

UMass Center for Clinical and Translational  
Science Research Retreat

2012 UMass Center for Clinical and  
Translational Science Research Retreat

---

May 22nd, 4:30 PM - 6:00 PM


## Genetic determinants of cerebral edema in severe traumatic brain injury: A pilot study of the role of CACNA1 and AQP4 gene mutations

Raphael A. Carandang  
*University of Massachusetts Medical School*

*Et al.*

### Let us know how access to this document benefits you.

Follow this and additional works at: [https://escholarship.umassmed.edu/cts\\_retreat](https://escholarship.umassmed.edu/cts_retreat)

 Part of the [Genetics and Genomics Commons](#), [Nervous System Diseases Commons](#), [Neurology Commons](#), [Surgery Commons](#), and the [Trauma Commons](#)

---

Carandang RA, Muehlschlegel S, Hall WR, Ouillette C, Brown RH. (2012). Genetic determinants of cerebral edema in severe traumatic brain injury: A pilot study of the role of CACNA1 and AQP4 gene mutations. UMass Center for Clinical and Translational Science Research Retreat. Retrieved from [https://escholarship.umassmed.edu/cts\\_retreat/2012/posters/7](https://escholarship.umassmed.edu/cts_retreat/2012/posters/7)

Creative Commons License



This work is licensed under a [Creative Commons Attribution-Noncommercial-Share Alike 3.0 License](#). This material is brought to you by eScholarship@UMMS. It has been accepted for inclusion in UMass Center for Clinical and Translational Science Research Retreat by an authorized administrator of eScholarship@UMMS. For more information, please contact [Lisa.Palmer@umassmed.edu](mailto:Lisa.Palmer@umassmed.edu).

## GENETIC DETERMINANTS OF CEREBRAL EDEMA IN SEVERE TRAUMATIC BRAIN INJURY: A PILOT STUDY OF THE ROLE OF *CACNA1* AND *AQP4* GENE MUTATIONS

Raphael A. Carandang MD, Susanne Muehlschlegel MD MPH, Wiley R. Hall MD, Cynthia Ouillette RN, Robert H. Brown Jr. MD D Phil,

University of Massachusetts Medical School, Department of Neurology

### Contact:

Raphael A. Carandang M.D., Assistant Professor, Departments of Neurology and Surgery, UMMS; Vascular and Critical Care Neurology, UMMMC, T 508-334-2527, [raphael.carandang@umassmemorial.org](mailto:raphael.carandang@umassmemorial.org)

### ABSTRACT

Cerebral edema is the one of the most significant predictors of poor outcome after traumatic brain injury. It is still unclear what the pathophysiological and cellular mechanisms and predictors of post-traumatic edema are. The exponential growth in genetic information has opened an avenue for investigation in traumatic brain injury and implicated specific genes in the pathophysiology of post-traumatic injury edema. Two examples are the Aquaporin-4 and *CACNA1* genes, which respectively encode water and calcium channels. The *Aquaporin-4* gene on chromosome 18q11.2-12.1 encodes the Aquaporin-4 protein (AQP4) water channel. AQP4 is one of the bidirectional high capacity water channels that is primarily expressed in astrocytic foot processes in the central nervous system at the blood-brain barrier and is thought to be critical for brain water homeostasis. Experimental studies showed that AQP4 deficient mice had significantly reduced cerebral edema and better survival in a water intoxication model. The *CACNA1* gene on chromosome 19p13 encodes the  $\alpha$ 1A subunit of a neuronal calcium channel. Patients with Familial Hemiplegic Migraine and delayed fatal cerebral edema and seizures from minor trauma have been found to have mutations in *CACNA1*, which are hypothesized to enhance development of cytotoxic edema. A missense mutation is reported to enhance risk of delayed fatal cerebral edema. **Hypothesis: The *CACNA1* gene missense mutation S218L and *AQP4* polymorphisms will be over-represented in patients with post-traumatic cerebral edema. Our Specific Aim is to perform full exon sequence analysis of these two genes in 20 well-defined cases of excessive cerebral edema. Our long term goal is to systematically investigate genetic variants as determinants of risk of excessive cerebral edema. It is hoped that this will further elucidate secondary mechanisms of injury specifically in the formation of post-traumatic edema and lead to targeted therapies in the future.**