Zhang. *Vessel Plus* 2022;6:20
DOI: 10.20517/2574-1209.2021.140

Vessel Plus

Editorial

Open Access

Learn from the past, review the present, and look towards the future

Jun Zhang

Department of Molecular and Translational Medicine, Paul L. Foster School of Medicine, Graduate School of Biomedical Sciences, Texas Tech University Health Sciences Center El Paso, El Paso, TX 79905, USA.

Correspondence to: Dr. Jun Zhang, Department of Molecular and Translational Medicine, Paul L. Foster School of Medicine, Graduate School of Biomedical Sciences, Texas Tech University Health Sciences Center El Paso, 5001 El Paso Drive, El Paso, TX 79905, USA. E-mail: jun.zhang2000@gmail.com

How to cite this article: Zhang J. Learn from the past, review the present, and look towards the future. *Vessel Plus* 2022;6:20. https://dx.doi.org/10.20517/2574-1209.2021.140

Received: 19 Nov 2021 **Accepted:** 9 Dec 2021 **Published:** 3 Apr 2022

Academic Editor: Alexander D. Verin **Copy Editor:** Yue-Yue Zhang **Production Editor:** Yue-Yue Zhang

This special issue, entitled "Advancements in Cerebral Cavernous Malformations", contains a collection of six articles focusing on the theme(s) relevant to the research field of a very common and major neurovascular disorder, cerebral cavernous malformations (CCMs). As a guest editor, I am honored to summarize this special issue starting with the manuscript "A brief history of cerebral cavernous malformations: a personal perspective" authored by Rigamonti and Vivas-Buitrago[1]. In their article, they summarized the dramatic advancements in the research field of CCMs over the past few decades, with the highlighted major breakthrough focusing on the molecular and genetic nature of CCMs along with major technological advancements. This remarkable progress, personally witnessed by the principal investigator, has been categorized into three categories: pre-magnetic resonance imaging (MRI) techniques, post-MRI analysis, and molecular genetics. The history of CCM research reveals profound efforts made in both clinical and basic science, along with technological innovations and advanced approaches. To tell this amazingly successful story, no one is more qualified than the senior author of this article, Dr. Rigamonti, a pioneer for modern CCM research for his revolutionary CCM genetic discoveries published in the New England Journal of Medicine thirty years ago. Another article, "Unique Contribution of One Patient Advocacy Organization in Advancing Cerebral Cavernous Malformation Research" was contributed by Dr. Lee[2], the founding President and CEO of the world largest CCM organization, Angioma Alliance. Under her guidance and leadership, this organization has grown tremendously from its beginnings as a CCM

patient support and advocacy group, to its role as the major driving force for legislation and patient care, and currently is a major advocacy force to promote CCM research. The annual international CCM research conference, created and organized by Angioma Alliance, has become the largest CCM scientific meeting in the world. In her article, Dr. Lee described how her organization has employed creative patient engagement methods like subsidized genetic testing as well as targeting special/minority patient groups, such as patients with CCM3 mutations, patients with the CCM1 Common Hispanic Mutation, and underserved African American patients, to expand research participation and understanding of the pathogenesis[2], which will provide instrumental information for future epidemiological CCM studies.

The article entitled "Molecular genetic analysis of cerebral cavernous malformations: an update" was contributed by Ricci *et al.*[3], in which they provide an overall update on the current progress in the genetics of CCMs, including the overall relationship of these three CCM genes and an updated listing of the CCM mutations currently identified. They also evaluate the current strategies to examine the impact of the CCM mutations on corresponding protein levels, and recapitulate the available data on penetrance, phenotype-genotype correlations, and founder effects. Another review article entitled "Non-autonomous effects of CCM genes loss", authored by Finetti and Trabalzini[4], focuses on very recent advances in CCM genetic studies, such as CCM onset and progression, loss of a CCM gene in a single cell scale in CCM lesions, and clonal expansions. In a research article entitled "Furry is a component of the CCM3-GCKIII signaling pathway", Antwi-adjei *et al.*[5] generated genetic mosaic Drosophila larvae and adults which are heterozygous for the gene of interest (ccm3 or furry), and isolated homozygous mutant daughter cells for their genetic experiments. They found that wing cells with mutant phenotypes for ccm3, or expressing dominant negative GCKIII, produce identical wing hair defects as mutations in tricornered and furry, which leads to their conclusion that CCM3 and GCKIII act upstream of Furry-Tricornered. They further concluded that CCM3 is a novel component of this ancient kinase signaling cascade, based on the fact that neither CCM1 nor CCM2 orthologs have been reported in flies[5]. Finally, our group[6] contributed a review article, "Calm the raging hormone - a new therapeutic strategy involving progesterone-signaling for hemorrhagic CCMs", to summarize our recent discoveries that CCM signaling complex (CSC) modulates progesterone-mediated actions between classic nuclear progesterone receptors (nPRs) and non-classic membrane progesterone receptors (mPRs) in two nPR(+) (T47D, MCF7) and two nPR(-) (MDA-MB-231, MDA-MB-468) breast cancer cells across three cancer research manuscripts[7-9]. Furthermore, we also demonstrated the impact of this signaling network on the maintenance of the Blood-Brain Barrier in another vascular research manuscript[10]. Last week in the 17th annual international CCM Scientific Meeting, I surprisingly learned that there is an *in-press* clinical study that strongly supports our series of experimental findings, and I am eager to read this new clinical outcome. In sum, the overall goal of this special issue, as the title suggests, is to learn the successful lessons from the past, re-examine our current data and research strategies for better research outcomes, and look towards the future glory of conquering CCMs.

DECLARATIONS

Authors' contributions

The author contributed solely to the article.

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

The author declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Rigamonti D, Vivas-Buitrago T. A brief history of cerebral cavernous malformations: a personal perspective. *Vessel Plus* 2021;5:47. DOI
2. Lee C. Unique contribution of one patient advocacy organization in advancing cerebral cavernous malformation research. *Vessel Plus* 2021. In press.
3. Ricci C, Riolo G, Battistini S. Molecular genetic analysis of cerebral cavernous malformations: an update. *Vessel Plus* 2021;5:31. DOI
4. Finetti F, Trabalzini L. Non-autonomous effects of CCM genes loss. *Vessel Plus* 2021;5:29. DOI
5. Antwi-adjei E, Burguete AS, Ghabrial AS. Furry is a component of the CCM3-GCKIII signaling pathway. *Vessel Plus* 2021;5:35. DOI
6. Zhang J, Abou-Fadel JS. Calm the raging hormone - a new therapeutic strategy involving progesterone-signaling for hemorrhagic CCMs. *Vessel Plus* 2021;5:48. DOI
7. Abou-Fadel J, Bhalli M, Grajeda B, Zhang J. Disrupting the CmP signaling network unveils novel biomarkers for triple negative breast cancer in Caucasian American women. *bioRxiv* 2021. DOI
8. Abou-Fadel J, Grajeda B, Jiang X, et al. CmP signaling network unveils novel biomarkers for triple negative breast cancer in African American women. *bioRxiv* 2021. DOI
9. Abou-Fadel J, Jiang X, Grajeda B, Padarti A, Ellis C, Zhang J. CCM signaling complex (CSC) coupling both classic and non-classic progesterone receptor signaling. *bioRxiv* 2020. DOI
10. Abou-Fadel J, Jiang X, Padarti A, et al. CCM signaling complex (CSC) is a master regulator governing homeostasis of progesterone and its mediated signaling cascades. *bioRxiv* 2020. DOI