EDITORIAL FOREWORD

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'Caveolae' Review Series

Editorial Foreword – Review Series on Caveolae

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Guest Editor for 'Caveolae Review Series'

In 1953, George Palade described [1], in the continuous endothelium of the heart, discrete features of the plasma membrane defined as spherical membrane invaginations of regular size and shape that occurred either single or in clusters on both front of the endothelial cell; he named them *plasmalemmal vesicles*. Two years later, Enichi Yamada described similar structures on the basolateral side of the gall bladder epithelium, naming them *caveolae intracellulares* [2] due to their resemblance to 'little caves'. Since their discovery, the presence of these membrane invaginations has been documented by electron microscopists in most cell types, with few exceptions. For approximately four decades, the vast data generated by electron microscopy banked on a purely morphological definition of caveolae. In absence of molecular markers, terms such as plasmalemmal vesicles, caveolae, surface vesicles, pinocytic vesicles were used to describe morphological entities that may or may not correspond to what they are believed to mean today. The discovery of caveolin-1 as a molecular marker of these membrane invaginations [3] has enabled biochemical, cell biological and genetic approaches with results that have considerably contributed to our current understanding of these structures.

Based on their lipid composition and biophysical features caveolae are considered a subtype of lipid rafts [4] that form invaginations and are capable of endocytosis [5] and transcytosis [6]. What seems to separate caveolae from other lipid rafts-containing invaginations and endocytotic pathways, is the presence of caveolin 1 as a marker [7–11]. Caveolae have been implicated in many other cellular functions such as endocytosis, transcytosis, cholesterol metabolism, mechanosensing and mechanotranduction, growth factor signaling and other signal transduction events. Several of these caveolar functions have been confirmed by genetic deletion of the *CAV1* locus, which results in loss of caveolin-1 and a dramatic reduction of membrane invaginations resembling caveolae [12,13]. This, however, has also raised doubts as to caveolae participation in many cellular functions such as transcytosis and signal transduction. The *Cav1 null* mice are viable and fertile with quite a mild phenotype, in contrast with the multitude of important cellular functions in which caveolae were implicated. This situation clearly calls

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for the reevaluation of the data obtained so far and points to the fact that operational definition of caveolae as caveolin 1 containing invaginations might need revision.

We have considered it timely to have a debate on how caveolae are defined by different researchers active in the field. This series of reviews in the JCMM, a journal that has shown a long standing interest in the subject, is intended to obviate conceptual differences in caveolar definition strengthening our understanding and possibly lead to the building of a consensus definition of caveolae.

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Guest Editor

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