Rafts and caveolae: which way now?

Edited by Christopher J. Fielding

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Lipid Rafts and Caveolae

From Membrane Biophysics to Cell Biology

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Lipid Rafts and Caveolae, edited by C.J. Fielding, falls into a familiar genre within academic publishing — a selection of researchers within a particular field are invited to write a chapter. Set free from the constraints of peer review, and sometimes with minimal editorial input, they go about their task with varying degrees of diligence and may lapse into selective citation of their own research and personal views. *Lipid Rafts and Caveolae* contains some well-written and useful chapters, but it does not completely avoid the pitfalls inherent in this type of book.

Lipid rafts and caveolae can be viewed as regions within the plasma membrane that differ from the rest of the membrane both in composition and in the way in which lipid-acyl chains are packed next to each other. The potential for such domains to act as organising platforms has lead to much interest from those working on different aspects of signal transduction and membrane trafficking, and this area of research has grown hugely over the past ten years. Caveolae and lipid rafts differ in many respects, and the main reason why they are frequently lumped together is that components of both are resistant to extraction from membranes with non-ionic detergents. Caveolae can be readily defined by the presence of caveolin proteins, but lipid rafts are more elusive — their nature, function and even existence has been keenly debated. Many researchers seem to be backing away from the idea that detergent resistance reflects incorporation into stable microdomains and the field is in a state of flux where a clear definition of what lipid rafts are, and what they are for, is difficult. In the case of caveolae, the surprisingly mild phenotypes of *caveolin* null mice constitute something of 'an elephant in the living room' and challenge models for caveolar function.

Lipid Rafts and Caveolae is therefore published at an interesting time. Four of the twelve chapters focus extensively on non-caveolar lipid rafts, including a well written argument for the existence of rafts by Meder and Simons, the latter being one of the original proponents of the raft hypothesis. This chapter presents the case for modification or refinement of the original idea of rafts as stable entities in the membrane containing multiple proteins, advocating instead the idea of smaller, more transient microdomains that are stabilized or even generated by

protein cross-linking. A chapter by Mayor and colleagues presents the closest thing in the book to a sceptical view of the raft literature, explicitly rejecting the idea that detergent resistance can be related to a specific type of organisation of proteins and lipids within the membrane. This is a very important development, as much of the literature on rafts depends on interpretation of detergent resistance in just this manner. Indeed, the papers describing a putative role for rafts in Alzheimer's and prion diseases discussed by Zurzolo and colleagues later in the book, to some extent, rely on detergent resistance data. The final raft chapter by Damjanovich and colleagues is less cautious than the others. By starting from the assertion that phase separation of lipids has already been proven to occur in the membranes of living cells, these authors run the

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risk of confusing readers that are new to the field as to what is established fact. This (and additional examples in this chapter and others) illustrates one of the problems with books of this type — it is unlikely that the combination of strong editorial input and peer review, to which a review article in a good journal should be subjected to, would allow such overstatements.

The chapters focussing on caveolae are on less contentious ground and succeed to varying degrees in summarising research in particular areas, including endocytosis of caveolae, the role of caveolae in signal transduction and the properties of caveolin proteins themselves. I found the chapter on nitric oxide signalling by Feron particularly illuminating. There are, however, some lapses that might have been corrected by more editorial input. Turner and Sens present a biophysical description of models for the generation of membrane curvature and discuss at length a theoretical view as to whether or not caveolin functions in this process. It is only at the end of the chapter that they emphasize to the reader only that the key experiment has already been performed — *caveolin* null mice have almost no caveolae, defined as highly curved invaginations. In fact, the discussion of caveolae may have been improved in the book as a whole by including a chapter that set out in detail exactly what the phenotypes of *caveolin* null mice are, as currently one is left to glean details from here and there within individual chapters. Although there are issues of redundancy and compensatory mechanisms to consider, models for the function of caveolae ought ultimately to be able to account for these phenotypes (or their absence).

In summary, *Lipid Rafts and Caveolae* contains several good chapters and is generally pitched at the right level to interest those within the field without being impenetrable to those with less specialist knowledge. One can not help feeling that, as with most books of this type, the variability in the quality of the chapters, lack of reviewer input and constant progress within the field under discussion, undermines the whole enterprise, and that review articles may serve as a better source of information.

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