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Contents

Preface .................................. VI
List of Contributors and Invited Discussants ................. VIII
Wagner, R. C. (Newark, Del.): Application of High Voltage Electron Microscopy (HVEM) to Visualize the Three-Dimensional Structure of the Vesicular System in Thick Sections ........................................... 1
Casley-Smith, J. R. (Adelaide): Vesicular Form and Fusion - As Revealed by Freeze-Immobilization and Stereoscopy of Semi-thin Sections: Implications for Permeation via these Structures ................................................. 6
Frøyær-Jensen, J. (Copenhagen): The Vesicle Controversy ......................... 21
Discussion of the Presentations: Wagner, Casley-Smith, Frøyær-Jensen .......... 43
Clough, G.; Michel, C. C. (London): Quantitative Transport of Macromolecules by Endothelial Cell Vesicles ........................................... 51
Schneeberger, E. E. (Boston, Mass.): Vesicular Transport across Pulmonary Capillary Endothelium in the Fluorocarbon Exchange Transfused Rat ............ 59
DeFouw, D. O. (Newark, N. J.): Morphometric Studies of Endothelial Vesicles of Alveolar Vessels in Edematous Lungs ............................................. 67
Discussion of the Presentations: Clough, Schneeberger, DeFouw .............. 80
Taylor, A. E.; Korthuis, R. J.; Townsley, M. I. (Mobile, Ala.): Use of Lymphatic Protein Fluxes to Assess Vascular Endothelial Selectivity to Macromolecules .... 100
With the very beginning of the enormous impact of electron microscopy on cell biology, vesicles of ca. 500–700 Å in outer diameter were recognized as a regular component of a variety of endothelial cells. In his famous and frequently, yet in most cases erroneously cited short report on these structures (the correct title of the journal is: J. appl. Physics and not J. appl. Physiol.), Dr. Palade assumed even at that time (1953) that the vesicles may represent a system for transporting fluids across the capillary wall and may account for the high permeability rate of the capillaries; by means of a vesicular shuttle. This suggestion established the ferry boat theory of vesicular transport. At the beginning, most physiologists rejected this new kind of a transport mechanism on the grounds of quantitative considerations, until electron dense tracers with a wide spectrum of molecular weights became increasingly available which definitely established vesicular transport as a biologically significant means for the normal transendothelial movement of plasma proteins. In addition, the vesicles appeared to be the most likely candidate for the so-called large pores introduced by Pappenheimer into the permeability discussion. Although several laboratories published experimental evidence indicating that a vesicular shuttle cannot be the correlate of the large pores; the majority favored vesicular transport as a realistic mechanism to explain the normally occurring transcapillary transport of high molecular substances, particularly of plasma proteins.

This long held assumption became substantially questioned, because the analysis of ultrathin serial sections resulted in a new three-dimensional model of vesicular organization. According to this all vesicles are gathered into small intercommunicating clusters of racemose configuration which either open to the luminal or to the abluminal surface, but never simultaneously to both. So called
"free" vesicles are absent. The immediate opposite of this is a hypothesis named "transcytosis". This designates an active, continuous process of vesicle fusion by which either transendothelial channels or fenestrae are formed. Since the majority of both structures is equipped with size-limiting structures, such as delicate diaphragms and localized strictures, fenestrae and channels are assumed to be the structural correlates of the "small pores", whereas the few truly "open" channels and fenestrae (without diaphragms) represent the "large pores".

To evaluate the present state of the art, we have gathered experts from different laboratories from all over the world who employ different experimental models and techniques to achieve a better understanding of the structure-function interrelationship of capillary endothelial cell vesicles.

Munich/Linköping, September 1985
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