

1 **Version for Submission to AJP-Cell Physiology**

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3 **AJP-Cell Physiology Begins Landmark Reviews in Cell Physiology**

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5 *An Editorial from the senior Editors of AJP-Cell Physiology*

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30 *AJP-Cell Physiology* began in January 1977 upon the conversion of the *American*
31 *Journal of Physiology* into a suite of Journals that embraced different areas of
32 Physiology, either tissue-specific, or, as for *AJP-Cell Physiology*, covering the realm
33 of cells and molecules as the fundamental levels of organisation of physiological
34 processes.

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36 The first issue of *AJP-Cell Physiology* included ten research articles that included a
37 broad range of cell and tissue systems and research areas, several of which
38 continue to this day and will be recognizable to today's readers and authors (Fig. 1,
39 *the first contents list*). Thus, 2017 is the fortieth anniversary of the inception of *AJP-*
40 *Cell Physiology*. It was decided at our senior Editors' meeting during Experimental
41 Biology 2016 to mark this event by beginning an occasional series of authoritative
42 Reviews that would address the progress of central research areas in cell and
43 molecular physiology and pathophysiology during the last forty years. It was also felt
44 that these Reviews, by providing context on the development of major fields along
45 with open questions and remaining controversies, would have an additional value for
46 the next generation of researchers.

47

48 We are delighted to begin this series with a landmark Review contributed by
49 Professor Mordecai P. Blaustein, of the University of Maryland at Baltimore.
50 Professor Blaustein, a discoverer of the Na⁺/Ca²⁺ exchanger, provides a personal
51 perspective on the development of laboratory research into the endogenous
52 ouabain/Na⁺ pump endocrine system and its role in Na⁺-dependent hypertension [1].
53 This article is especially appropriate to mark *AJP-Cell Physiology's* anniversary year,
54 because Dr. Blaustein's hypothesis on the relationships between Na⁺ and Ca²⁺ ions,

55 their pumps, blood pressure regulation and hypertension was published to great
56 attention in *AJP-Cell Physiology* in May 1977 [2].

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58 In the 2017 Review, Dr. Blaustein provides a personal account of discoveries related
59 to how cardiotonic steroids work in treating heart failure, the relationship between
60 endogenous cardiotonic steroids and blood pressure, and the identification of this
61 circulating, endogenous organic compound, known as ouabain. The story began with
62 an experimental finding in arthropods and led to the revelation of pathogenic
63 mechanisms and development of therapeutic interventions for human cardiovascular
64 disease. Dr. Blaustein also summarizes work with mouse models carrying mutations
65 in pump subunits and endogenous ouabain signalling in the brain. The Review
66 touches on other research fields, such as muscle fatigue, neurobehavior and
67 inflammatory response. This fascinating read provides a concise summary of the
68 status of this important field, and also offers numerous historical perspectives and
69 views (biographical and others) that convey true love and excitement for science,
70 even in face of all too familiar setbacks and rejections.

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72 Dr. Blaustein's historical overview of the Na⁺-pump and Na⁺/Ca²⁺ exchanger is very
73 inspiring and reminds all scientists that we need to 'look' backwards to 'see' the
74 future. Younger scientists can gain a wealth of knowledge from prior research to aid
75 them to formulate their own research ideas. At the same time, as discussed in the
76 Review, ongoing controversies remain. In the next forty years, new technologies, "big
77 data" and quantitative models will undoubtedly provide a new integrative framework
78 to understand the physiology and pathophysiology of blood-pressure regulation and
79 to fine-tune clinical treatments.

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81 The publication of this Review in 2017 marks the beginning of an occasional series of
82 outstanding Landmark Reviews. We hope that readers of *AJP-Cell Physiology* will
83 find these articles valuable and stimulating.

84

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86 **References**

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89 *Physiol Cell Physiol.* 2017 Sep 27:ajpcell.00196.2017. doi:
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91 2. Blaustein, M.P. Sodium ions, calcium ions, blood pressure regulation and
92 hypertension: a reassessment and a hypothesis. *American Journal of Physiology -*
93 *Cell Physiology* Published 1 May 1977 Vol. 232 no. 5, C165-C173.

94 (Figure 1 is on the next page).

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102 Figure 1. The Index page of the first issue of AJP-Cell Physiology.

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No. 1 JANUARY 1977

PERSPECTIVE	
<i>A. P. Fishman</i>	C1
EDITORIAL	
<i>P. Horowitz</i>	C3
Reorientation of myofilaments during contraction of a vertebrate smooth muscle <i>B. A. Fisher and R. M. Bagby</i>	C5
Differentiation between endogenous pyrogen and leukocytic endogenous mediator <i>C. A. Mapes and P. Z. Sobocinski</i>	C15
How <i>Gymnodinium breve</i> red tide toxin(s) produces repetitive firing in squid axons <i>M. Westerfield, J. W. Moore, Y. S. Kim, and G. M. Padilla</i>	C23
ATP utilization associated with recovery metabolism in anaerobic frog muscle <i>R. R. DeFuria and M. J. Kushmerick</i>	C30
Stratum corneum of frog skin: inferences for studies of Na entry and transport pool <i>S. I. Helman and R. S. Fisher</i>	C37
Separation of active and passive components of short-range stiffness of muscle <i>D. L. Morgan</i>	C45
Control of intracellular Ca^{2+} activity in rat myometrium <i>R. A. Janis, D. J. Crankshaw, and E. E. Daniel</i>	C50
Sodium in smooth muscle relaxation <i>T. S. Ma and D. Bose</i>	C59
Effect of inhibitors on transepithelial efflux of Na and nonelectrolytes in frog skin <i>T. U. L. Biber and T. L. Mullen</i>	C67
Afferent discharges from venous pressoreceptors in liver <i>A. Nijima</i>	C76
ANNOUNCEMENTS	C82

2 MARCH 1977

Neurotrophic regulation of insulin-sensitive amino acid uptake in rat fast muscle

104

105

106

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C82