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CELL VOLUME CONFERENCES

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ABSTRACT

This mini-review describes the history of cell volume conferences with the emphasis on the research of cell volume sensitive peptide exocytosis initiated by Prof. Monte A. Greer as well as the recent achievements on the study of the mechanisms of cell volume adjustment and their implications in the regulation of metabolism, gene expression, cell proliferation and death.

KEY WORDS: history of cell volume conferences.

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International Symposium on Cell volume and function, 1997

Local Organizing Committee of the Joint Conference of the Slovak Physiological Society, the Physiological Society and Federation of the European Physiological Societies, Bratislava, 2007

Five International symposia on Hormones in Milk,

President of International Organizing Committee: the First Joint Conference of Physiologists from Central Europe, Piešťany, 2002

Cell swelling-induced peptide exocytosis – how I get engaged

In the years 1977–78 I spent postdoctoral fellowship in Oregon Health Sciences University in Portland in laboratory of Prof. Monte A. Greer. During my later visit in 1990 Monte told me about very interesting effect of hyposmolarity on protein and peptide secretion. In early eighties they studied the dynamics of *in vitro* hormone secretion of adenohypophyseal cells induced by various secretagogues. Accidentally they found unexpected and stricking dose-related stimulation of secretion of LH by dilution of the perfusion medium with distilled water. They had expected that any efflux of hormone induced by dilution of the medium with water would most likely be due to osmotic lysis of the cells. However, repeated hyposmolar stimulation over a 5-hr experimental period produced similar secretory response each time and did not depress the stimulation of thyrotropin (TSH) and prolacti

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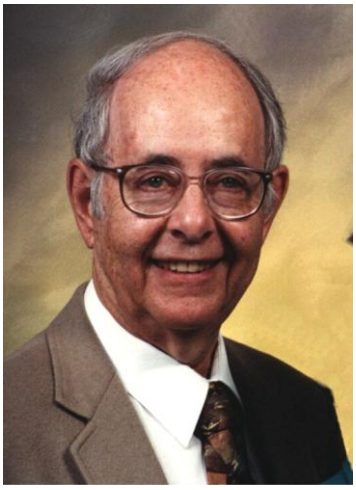
(PRL) secretion induced by the same dose of thyroliberin (TRH) given at the beginning, middle, and end of the experimental period [1, 2]. Moreover, hyposmolarity simultaneously stimulated secretion of all hormones they had measured (growth hormone, PRL, TSH, luteotropin, adrenocorticotropin). They believed that this interesting effect may be clue to understanding exocytotic process [1]. Later they discovered that similar mechanism inducing insulin release *in vitro* had been described by Blackard et al. in 1975 [3].



Prof. Monte A. Greer, Oregon Health Sciences University. Pioneer in the field of neuro-endocrine regulation and cell swelling-induced protein and peptide secretion (exocytosis).

Monte Greer was surprised and disappointed by lack of interest of scientific community in this phenomenon. We started Portland – Bratislava collaboration supported by project of US-Slovak Science and Technology cooperation program. To break isolation we were looking for groups studying various aspects of cell volume regulation and effects. We contacted Florian Lang, one of the organizers of the conference „Interaction of Cell Volume and Cell Function" held in 1990 in Innsbruck and organized with him International symposium „Primary Role of Cell Volume Changes in Controlling Cell Function" in Smolenice Castle, 1997 in Slovakia. Meeting excellent scientists presenting cutting edge results of knowledge has been very important for our further research. Apparently most of participants shared this feelings and a series of special conferences devoted to cell volume in 1–3 years intervals has been held since that time (Table 1). Despite rigorous scientific criticism, atmosphere of all meetings was extremely friendly; full of understanding and mutual support. Cell volume has been appreciated as important field also by Physiological and Pathophysiological world and European societies by organizing cell volume symposia, workshops or sessions as part of program of their congresses (Table 2).

Table 1

Congresses on Cell Volume	
1990	Innsbruck, Austria, "Interaction of Cell Volume and Cell Function". Organizers: F. Lang, D. Häussinger
1997	Smolenice Castle, Slovakia, "Primary Role of Cell Volume Changes in Controlling Cell Function". Organizers: V. Strbak, M.A. Greer, F. Lang
2000	Berlin, Germany, "Cell Volume: Signalling and Regulation". Organizer: F. Wehner
2001	Queenstown, New Zealand, "Molecular Mechanisms in Cell Volume Regulation". Organizers: J. Leader, J. Bedford, P. Donaldson, E.K. Hoffmann, K. Spring
2003	Dayton, USA, "Cell Volume & Signal Transduction". Organizers: P. Lauf, N. Adragna
2005	Copenhagen, Denmark, "Cell Volume Control in Health and Disease". Organizers: E.K. Hoffmann, I.H. Lambert, S.F. Pedersen, D. Klaerke, A. Schousboe
2007	Salzburg, Austria, "Cell Volume Control: Functions – Molecules – Interactions". Organizer: M. Ritter
2009	Okazaki, Japan, Joint Symposium "Physiology of Ion Transport and Cell Volume Regulation". Organizers: Y. Okada, S. Uchida, H. Sakai
2011	Tubingen, Germany, "Hydration & Cell Volume Regulation – Mechanisms and Regulation". Organizers: F. Lang, E. Shumilina, H. Osswald
Coming conference	
2013	Moscow, Russia, August 26–29, "Cell Volume Regulation: Novel Therapeutic Targets & Pharmacological Approaches". Organizer: Sergei Orlov

Table 2

Symposia and Workshops on Cell Volume as part of program at International Congresses	
2002	Piešťany, Slovakia, February 5–8, 2002, First Joint Conference of Physiologists from Central Europe, Symposium „Cell Volume: Regulation and Function". Organizer: V. Štrbák
2003	3rd Federation of European Physiological Societies Congress, Nice, France, June 28 – July 3, 2003, Symposium „Cell volume: Regulation and Functional Impact". Organizer: V. Štrbák
2006	Beijing, China, June 28 – July 1, 2006, 5th International Congress of Pathophysiology Symposium "Cell Volume, Physiological and Pathophysiological aspects". Organizer: V. Štrbák (chairs V. Štrbák and Y. Okada)
2010	Montreal, Canada, September 22–25, 2010, 6th International Congress of Pathophysiology, Workshop, Cell Volume Regulation. Organizer: V. Štrbák. Chairs: V. Štrbák (Bratislava, Slovakia) and S.N. Orlov (Montréal, Canada)

Various functions of cell volume. To survive, cells have to maintain their volume within certain limits. Protective mechanism(s) should have to develop in early forms of life to assure survival in changing environment. Diverse experimental approach revealed that phylogenetically divergent organisms employ uniquely adapted mechanisms of cell volume regulation [4]. Cell volume

perturbation elicits a wide array of signaling events, leading to protective and adaptive measures [5–8]. In higher organisms cell volume responses to osmotic challenge are

Conference 2007 in Salzburg, Austria, "Cell Volume Control: Functions – Molecules – Interactions". Organizer: M. Ritter (in the middle in blue shirt).

Conference 2009, Okazaki, Japan, August 3–6, 2009, Joint Symposium "Physiology of Ion Transport and Cell Volume Regulation". Organizers: Y. Okada, S. Uchida, H. Sakai. From the left Yasunobu Okada, and Else Hoffmann.

Conference 2009, Okazaki, Japan, August 3–6, 2009, Joint Symposium "Physiology of Ion Transport and Cell Volume Regulation". Organizers: Y. Okada, S. Uchida, H. Sakai. From the left Vladimir Strbak, Sergei Orlov, Ryszard Grygorczyk.

integrated into a signal transduction network regulating various cell functions; it has become evident that cell volume should be considered a second message in the transmission of various functions; alterations of cell volume and volume regulatory mechanisms participate in a wide variety of cellular functions [5]:

Metabolism. Cell volume was shown to be important determinant of proteolysis and protein synthesis in the liver. It has been also demonstrated that cell volume changes exerted by hormones and amino acids play a crucial role in their role in regulation of hepatic protein metabolism [9–11].

Cell volume affects *gene expression* [5, 12].

Cell volume affects *apoptotic death and cell proliferation* [13–15].

Cell migration [16].

Cell volume mediates various *hormone actions* [5, 9–11].

Hydrogel nature of mammalian cytoplasm contributes to osmosensing and extracellular pH sensing [17].

Cell swelling-induced *peptide and protein exocytosis* [18].

More about my favorite issue:

Cell swelling-induced peptide and protein exocytosis. Cell swelling induces peptide exocytosis using unique signa-

ling pathway [19]. Hyposmotic-induced secretion in normal cells is not mediated by specific receptors, is independent from extra and intracellular Ca^{2+}-sodium and potassium channels activity, prostaglandins, leukotriens, does not involve cytoskeleton, cAMP generation, phospholipase A2, G proteins, protein kinase C [19–21]. It is promoted by swelling of the secretory vesicles [19]. Resistance to endogenous inhibitors is frequent attribute of this type of secretion [19–21]. Swelling-induced secretion involves also secretory vesicles not involved in conventional stimulation [19–22]. Hyposmosis-induced insulin secretion is more sensitive to high cellular cholesterol than conventional one suggesting substantial difference between mechanisms [22]. Participation of sequential exocytosis as dominating mechanism in swelling-induced exocytosis is hypothesized [19–22]. Signaling and response in tumor cells often differs from native cells and varies markedly between cell lines [19].

Pathogenetic implications: cell swelling could be involved in alcohol induced hypoglycemia in diabetic patients and release of peptides from pituitary and neurons [19, 23]. Swelling-induced products could be mediators of ischemic preconditioning involved also in protection of diabetic heart. Swelling-induced exocytosis is an ancient mechanism generally present in cells; in cells engaged in water and salt regulation is covered by specific response mediated by specific signaling [24, 25]. Disturbance of specific response leads to swelling-induced – inappropriate secretion of antidiuretic hormone – SIADH [19, 23, 2]. Exocytosis of intravesicular material has been supposed to help a swollen cell to meet the challenge by expanding the plasmalemma through the fusion with vesicular membrane [18]. Surprisingly, in mammalian cells significant end membrane insertion was observed only during extreme swelling [26].

Recently an interesting hypothesis was published by E. Mariman [27]: during weight loss and shrinkage of cells, adipocytes will automatically change their adipokine secretion profile. Model is based on the fact that chronic change of cell volume results in long lasting stimulation or inhibition of secretion (secretion of leptin and other proinflammatory adipokines is positively related to adipocyte volume). Changed secretion profile of adipokines is a strong regulatory factor promoting regain of body weight. This is interesting view on the possible role of chronic change of cell volume in the pathogenesis of obesity [28].

I believe that cell volume field has big potential leading to important discoveries to motivate organization of many further conferences with exciting program.

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