



V Ljubljani, 07. 08. 2017

VABILO

Slovensko fiziološko društvo vljudno vabi na predavanje z naslovom

»Role of phospholipase D-derived phosphatidic acid in neuroendocrine secretion.«

Predaval bo

Dr. Nicolas Vitale

v sredo, 18. 08. 2017 ob 14:00 uri v veliki vajalnici PAFI, Zaloška 4 v Ljubljani.

Predavanje bo v angleškem jeziku.

Summary:

The secretory pathway in neuroendocrine cells involves vesicular trafficking that leads to the release of hormones and neuropeptides in the extracellular medium. The final stage of this pathway, known as regulated exocytosis, consists of the tethering and docking of the mature vesicles or granules to the plasma membrane and ends by the fusion of secretory and plasma membrane. In addition to the important role played by proteins, recent studies have highlighted the involvement of membrane lipids to promote regulated exocytosis. Among them, phosphatidic acid (PA), the simplest glycerophospholipid, is known to generate membrane curvature and recruit key proteins. In a consequence, PA appears as an attractive candidate to regulate different steps of the exocytotic process. Using adrenal chromaffin cells as a model of neurosecretion, our previous studies demonstrated that PA synthesis by the enzyme phospholipase D1 (PLD1) at the plasma membrane plays a positive role during secretory granule exocytosis. More recently, using amperometric recordings and electron microscopy on PLD1-knockout mice, we found that PLD1 regulates the fusion pore dynamics and promotes docking of secretory granules in chromaffin cells. Novel PLD1 inhibitors reproduce the effect on exocytosis observed in PLD1-knockout chromaffin cells, confirming the essential role of PLD1 activity in this process. Using this pharmacological approach, we aim now to further understand the precise role of PLD1-derived PA on the recruitment of secretory granules to the plasma membrane. To follow the dynamics of granules, we performed time-lapse confocal microscopy in chromaffin cells where PLD1 activity is inhibited. Tracking analysis showed a reduced motility of the granules consequently to inhibition of the enzyme. Of interest, the granules that display a directed trajectory have their motility specifically reduced, suggesting that PLD1-mediated PA modulates transport of granules toward the plasma membrane. Furthermore, analysis of plasma membrane sheets by electron microscopy indicated that PLD1 could contribute to the formation of actin bundles, essential cortical cytoskeletal structures that link docked granules to plasma membrane. With the help of a genetically encoded PA probe expressed in chromaffin cells, we evaluated the precise distribution of this lipid near the exocytotic site and cytoskeletal structures, as well as its potential molecular partners during exocytosis.

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EDUCATION-POSITION

- DR2 INSERM: November 2006
- Researcher at INSERM since December 1997.
- 1995-1997: postdoctoral training at the Pulmonary Critical Care Medicine Branch Laboratory (NIH, Bethesda, USA) directed by Dr. Joel MOSS. *Cellular and molecular characterization of the GTPase ARD1.*
- 12/09/1994: Ph.D. directed by Dr. Marie-France BADER *"Trimeric G-proteins and exocytosis: evidence and function in the secretory mechanism of chromaffin cells."*

AWARDS

- 2006: Award from the Fondation pour la Recherche Médicale (Alsace, FRANCE).
2008: Guy Ourisson Prize from the Cercle Gutemberg (Strasbourg, FRANCE).
2009 & 2013 Thesis Prizes from the « Société de Biologie de Strasbourg » for supervised PhD students.

GRANTS as PI

- ANR-Blanc 300,000 €(2005-2008)
Picasso exchange program 6,000 €(2006-2007)
ARC grant 50,000 €(2007-2009)
FRM Alsace grant 6,000 €(2007)
ANR-Blanc 457,000 €(2009-2011)
Ecos-Sud/Mincyt exchange program 15,000 €(2010-2012)
Ligue contre le cancer 120,000 €(2013-2015, 2017)
FRM 400,000 €(2016-2019)

EXPERTISE:

- Editor Scientific Reports (Nature Publishing Group) 2011- to date.
- Editorial board member The journal of Biological Chemistry 2006-2010; 2012-2016
- Editorial board member Current Chemical Chemistry 2007 - to date
- Editorial board member Frontiers in Neuroendocrine Science 2010 - to date
- Editorial board member Alzheimer's & Dementia: the Journal of the Alzheimer's Association 2012-to date.

PUBLICATIONS/BIBLIOMETRY

From 1993: 115 peer reviewed publications: 26 first author and 30 last author.
20 publications IF>9 - 36 publications 5<IF<9 - 46 publications 3<IF<5
Web of Science h-factor: 35; Citation Number: 4319