

**Examination of pituitary adenylate cyclase activating polypeptide (PACAP) in the sheep  
mammary gland and milk, and in the lamb plasma after suckling**

Krisztina Pohoczky <sup>1,2,3</sup>, Andrea Tamas <sup>4</sup>, Dora Reglodi <sup>4</sup>, Agnes Kemeny <sup>2,5</sup>, Terez Bagoly <sup>2</sup>,  
Zsuzsanna Helyes <sup>2,3\*</sup> and Levente Czeglédi <sup>7\*</sup>

Short title: **PACAP in sheep milk and plasma during suckling**

<sup>1</sup> Department of Pharmacology, University of Pecs Faculty of Pharmacy. Szigeti street 12, H-7624  
Pecs, Hungary

<sup>2</sup> *Department of Pharmacology and Pharmacotherapy, University of Pecs Medical School, Szigeti  
street 12, H-7624 Pecs, Hungary*

<sup>3</sup> *Janos Szentagothai Research Centre, Centre for Neuroscience, University of Pecs, Ifjútság street  
20, H-7624 Pecs, Hungary*

<sup>4</sup> *Department of Anatomy, Centre for Neuroscience, University of Pecs Medical School, Szigeti  
street 12, H-7624 Pecs, Hungary*

<sup>5</sup> *Department of Medical Biology, University of Pecs Medical School, Szigeti street 12, H-7624  
Pecs, Hungary*

<sup>7</sup> *Institute of Animal Science, Faculty of the Agricultural and Food Sciences and Environmental  
Management, University of Debrecen, Böszörményi Street 138, H-4032 Debrecen, Hungary*

\*Correspondence:

Zsuzsanna Helyes.

Department of Pharmacology and Pharmacotherapy

Medical School

University of Pecs

Szigeti street 12.

H-7624 Pecs, Hungary

Phone: +36-72 536 001

*E-mail:* [zsuzsanna.helyes@aok.pte.hu](mailto:zsuzsanna.helyes@aok.pte.hu)

and

Levente Czeglédi

Institute of Animal Science,

Faculty of the Agricultural and Food Sciences and Environmental Management,

University of Debrecen,

Böszörményi street 138,

H-4032 Debrecen, Hungary

Phone: +36-52 508 444

E-mail: [czegledi@agr.unideb.hu](mailto:czegledi@agr.unideb.hu)

\* The authors consider that the last two authors should be regarded as joint Corresponding Authors.

## **Summary**

The aims of this research paper were to determine PACAP and vasoactive intestinal polypeptide (VIP) levels in suckling lambs compared to ewe plasma and mammary gland levels, as well as their age-dependent alterations. PACAP, VIP, PAC1 receptor and brain-derived neurotrophic factor (BDNF) gene expressions were quantified by PCR in the mammary gland. Plasma, milk whey and mammary gland PACAP38-like immunoreactivity (PACAP38-LI) was measured by radioimmunoassay, VIP-LI by enzyme-linked immunoassay in 3 age groups. PACAP38-LI was 5-6 times higher in the milk whey than in the plasma of lactating sheep. It significantly increased in the lamb plasma 1 hour, but returned to basal level 2 hours after suckling. PACAP was detected in the mammary gland both at mRNA and peptide levels. However, VIP mRNA was not present in this tissue. PAC1 receptor mRNA did not show age- or lactation-dependent alterations. BDNF mRNA significantly decreased with age being approximately 60% and 25% in the 3- and 10-year-old sheep respectively, compared to the 3-month-old lambs. Although VIP concentration was almost 2 times higher in milk whey, it did not change after suckling. No differences were found between mammary and jugular vein plasma PACAP and VIP levels of ewes, sheep at different ages or during the daily cycle. We propose a rapid absorption of PACAP38 from the milk and/or its release in suckling lambs. PACAP accumulated in the milk might be synthesized in the mammary gland or secreted from the mother's plasma. PACAP is suggested to have differentiation/proliferation promoting and immunomodulatory effects in the newborns and/or a local function in the mammary gland.