Journal of Cellular Biochemistry 86:420–421 (2002)

LETTER TO THE EDITOR

P-Cadherin Expression in Canine Lactating Mammary Gland

To the Editor: We read with interest the article recently published by Peralta Soler et al. in Journal of Cellular Biochemistry on the expression of the P-cadherin soluble fragment in human milk. In this article, the authors reported that a high concentration (100–400 μg/ml) of a soluble 80-kDa fragment of P-cadherin adhesion protein was present in human milk. They evaluated the pattern of P-cadherin expression in normal lactating mammary tissue, through immunohistochemistry, immunoprecipitation, and Western blotting, using a monoclonal antibody to the extracellular domain of P-cadherin (BD Transduction Laboratories, clone 56) [Peralta Soler et al., 2002]. In lactating tissue, P-cadherin appears as a protein secreted by epithelial cells, rather than a cell–cell adhesion protein, while in the non-lactating mammary gland, P-cadherin is restricted to myoepithelial cells, and is present at sites of cell–cell contact [Peralta Soler et al., 2002]. Recently, we have found a similar distribution of P-cadherin while studying its expression in canine mammary tumors.

P-cadherin expression has been described as a marker of aggressiveness and poor outcome in human breast cancer [Soler et al., 1999; Gamallo et al., 2001; Paredes et al., 2002] and, since there are no studies on P-cadherin expression in canine mammary tissues hitherto described, we sought to evaluate the immunoexpression of this adhesion molecule in this animal model. The study of the biology of spontaneous mammary tumors in the dog, which is one of the most prevalent neoplasms in this domestic animal, may be of interest for the clinical management of human breast cancer [Mottolese et al., 1994]. Most importantly, the study of canine mammary tumors may serve as an ideal model to evaluate P-cadherin expression, owing to the high frequency of tumors showing features of a myoepithelial/basal cell differentiation/histogenesis.

Immunohistochemistry and evaluation of P-cadherin expression in canine mammary gland tissue was performed as described in our recent study [Paredes et al., 2002]. To the best of our knowledge, up to now, there are no specific antibodies against canine P-cadherin; thus we used the anti-human P-cadherin antibody from Transduction Laboratories (clone 56, 1:50 dilution). To optimize the immunohistochemistry technique to canine mammary tissue, heat-induced antigen retrieval was carried out using an EDTA buffer (Lab Vision Corporation, Fremont), pH 8.0, in a boiling bath, during 20 min.

Our findings largely corresponded to the previous observations in human breast tissue, by Peralta Soler et al., 2002, reinforcing their results. In normal non-lactating canine mammary glands, P-cadherin was restricted to the myoepithelial cells (Fig. 1A). In canine lactating, pseudo-lactating mammary tissue, and in areas with pseudolactional hyperplasia of breast lobules and ducts, P-cadherin was found in secretory luminal epithelial cells and milk secretion (Fig. 1B). Its expression in luminal epithelial cells was strong and cytoplasmic, similar to that of a secreted protein, which suggests that P-cadherin is not functioning as an adhesion molecule, and could be involved in canine breast tissue remodelling, since it only appears in luminal epithelial cells during the lactation period.

On the other hand, milk secretion P-cadherin may derive from proteolytic cleavage of the

*Correspondence to: F.C. Schmitt, Institute of Molecular Pathology and Immunology, Porto University, Rua Roberto Frias s/n, 4200, Porto, Portugal.

Received 17 April 2002; Accepted 3 May 2002

DOI 10.1002/jcb.10245

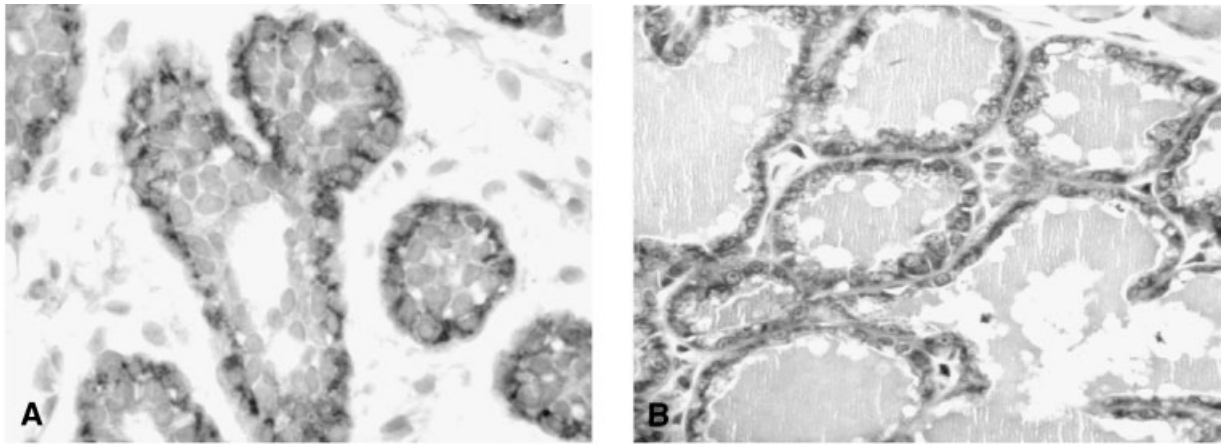

Fig. 1. Immunohistochemical analysis of P-cadherin expression in canine mammary tissue, using a monoclonal antibody specific for the extracellular domain of this protein, and a streptavidin-biotin method on archival paraffin-embedded tissue sections. (**A**) Normal non-lactating canine mammary lobule, with P-cadherin expression restricted to the myoepithelial cells; 200 ×. (**B**) Canine lactating mammary tissue, with strong and cytoplasmic P-cadherin expression in secretory luminal epithelial cells and in milk secretion; 200 ×.

extracellular adhesion domain (cadherins shedding), but it still remains unknown.

REFERENCES

Gamallo C, Moreno-Bueno G, Sarrio D, Calero F, Hardisson D, Palacios J. 2001. The prognostic significance of P-cadherin in infiltrating ductal breast carcinoma. Mod Pathol 14:650–654.

Mottolese M, Morelli L, Agrimi U, Benevolo M, Sciarretta F, Antonucci G, Natali PG. 1994. Spontaneous canine mammary tumors—A model for monoclonal antibody diagnosis and treatment of human breast cancer. Lab Invest 71:182–187.

Paredes J, Milanezi F, Viegas L, Amendoeira I, Schmitt F. 2002. P-cadherin expression is associated with high-grade ductal carcinoma in situ of the breast. Virchows Arch 440:16–21.

Peralta Soler A, Knudsen KA, Salazar H, Han AC, Keshgegian AA. 1999. P-cadherin expression in breast carcinoma indicates poor survival. Cancer 86:1263–1272.

Peralta Soler A, Russo J, Russo IH, Knudsen K. 2002. Soluble fragment of P-cadherin adhesion protein found in human milk. J Cell Biochem 85:180–184.

Adelina Gama
Joana Paredes
Maria F. Milanezi
Jorge S. Reis-Filho
Fatima Gartner
Fernando C. Schmitt*
Institute of Molecular Pathology and Immunology, Porto University
Rua Roberto Frias s/n
4200, Porto, Portugal