UNIVERSIDAD DE LAS PALMAS DE GRAN CANARIA

Instituto Canario de Investigaciones Agrarias
Gobierno de Canarias

Placental-Udder axis: role on colostrum production and lactation development

Argüello, A., Castro, N., Morales-delaNuez, A., Moreno-Indias, I., Sánchez-Macías, D., Krupij, A., Ruiz-Díaz, M.D., Hernández-Castellano, L.E. and Capote, J.

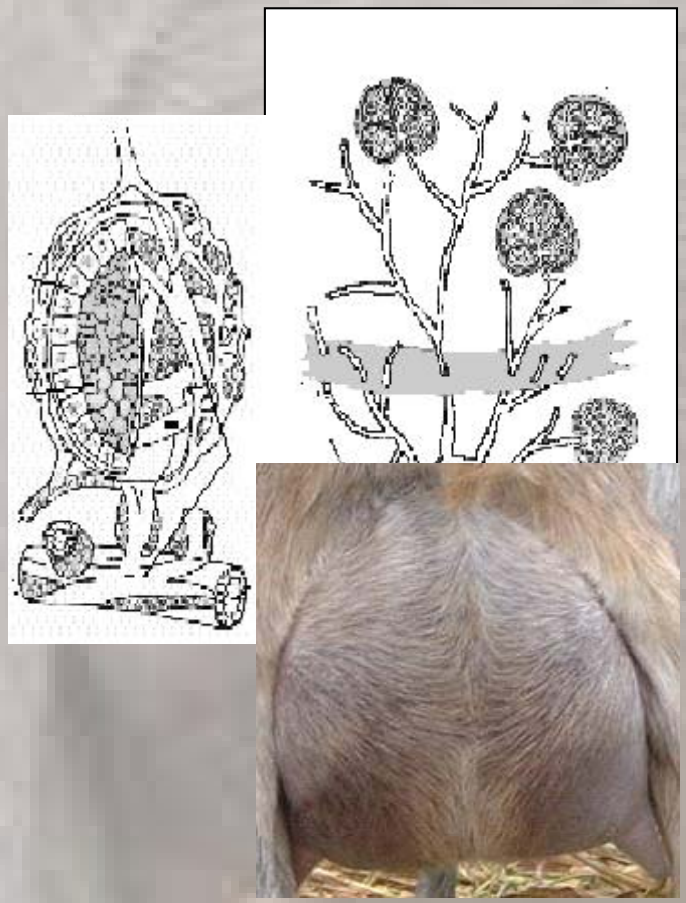
Crete, 2010

Structural differentiation of the mammary gland is regulated by hormonal balances

De Louis *et al.* (1980)

Placental-Udder axis: role on colostrum production and lactation development

- **Formation of lobulo-alveolar structure**



- **Secretory activity**

- **Hypertrophy of epithelial cells**

De Louis *et al.* (1980)

Hormonal control on the mammary gland differentiation

De Louis *et al.* (1980)

Stricker, P., and F. Grueter. 1928. Action du lobe antérieur de l'hypophyse sur la montée laiteuse. C. R. Acad. Sci. Biol. 99:1978.

Cowie, A. T. 1970. Influence of hormones on mammary growth and milk secretion. Page 123 *in* Lactation. I. R. Falconer, ed. Butterworths. London.

Denamur, R. 1971. Reviews of the progress of dairy science. Section A. Physiology. Hormonal control of lactogenesis. J. Dairy Res. 38:237.

http://www.greenpeace.org/mexico/news/ma-z-que-da-a-a-las-ratas-fue

Hormonal activity of the feto-placental unit on the control of the mammary gland function

De Louis *et al.* (1980)

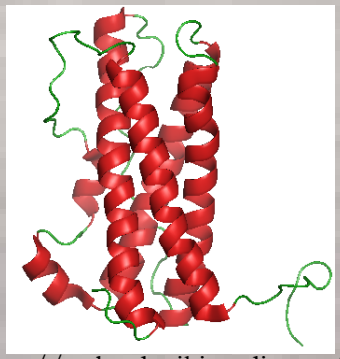
Development of lobuloalveolar
(~ 80 d gestation)

Cellular multiplication increase
(> 120 d gestation)

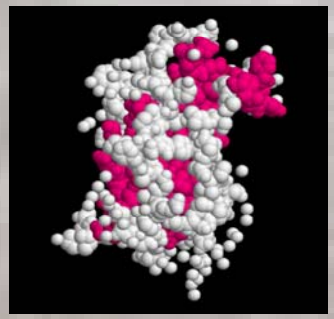
Development of lobuloalveolar
(~ 150 d gestation)

Development nearly complete
(~ end of gestation)

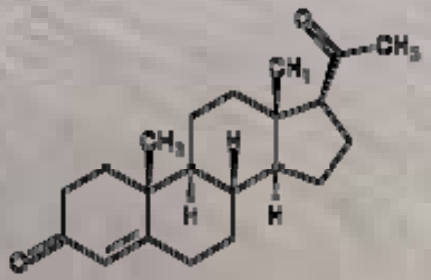
Several hormones play an important role in the mammary gland development



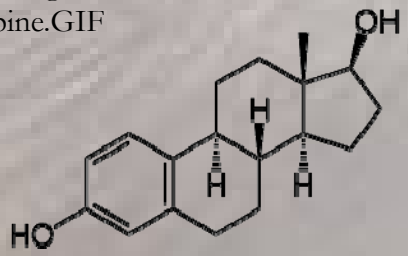
http://upload.wikimedia.org/wikipedia/commons/0/02/PRL_structure.png



http://en.wikipedia.org/wiki/File:Somatotropine.GIF



http://es.wikipedia.org/wiki/Archivo:Progesterone.png



http://en.wikipedia.org/wiki/File:Estradiol2.png

Placental-Udder axis: role on colostrum production and lactation development

Relation Between Hormones and Mammary Gland Function

C. DE LOUIS, J. DJIANE, L. M. HOUDEBINE, and M. TERQUI[1]
I.N.R.A
Laboratoire de Physiologie de la Lactation
78350 Jouy-en-Josas
France

1980 J Dairy Sci 63:1492–1513

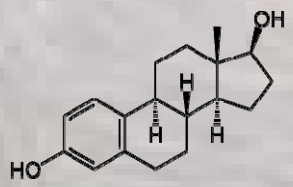
"The feto-placental unit provides the major part of the estrogenic signal from which the epithelial mammary cell is differentiated in presence of hormones (PrL, GH, Progesterone, Placental lactogen and adrenal costicosteroids)..."

Placental growth is crucial for udder development

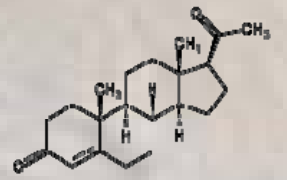
Placental-Udder axis: role on colostrum production and lactation development

http://upload.wikimedia.org/wikipedia/commons/0/02/PRL_structure.png

http://en.wikipedia.org/wiki/File:Somatotropine.GIF



http://en.wikipedia.org/wiki/File:Estradiol2.png

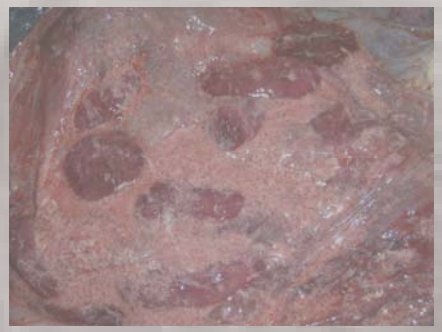


http://es.wikipedia.org/wiki/Archivo:Progesterone.png

ENDOCRINE AXIS

Placental-Udder axis: role on colostrum production and lactation development

"The feto-placental unit provides the major part of the estrogenic signal from which the epithelial mammary cell is differentiated in presence of hormones (PrL, GH, Progesterone, PLACENTAL LACTOGEN and adrenal costicosteroids)..."



Placental lactogen (PL)

- **Mammogenic**
- **Lactogenic**

Denamur and Martinet (1970)

Placental lactogen (PL)

2 Br-α ergocryptine

Second half gestation

DNA content of mammary gland similar

at parturion than untreated animals

(Buttle *et al.*, 1979; Djiane *et al.*, 1975)

Placental lactogen (PL)

Mammary gland development induced

by using of ovarian steroids injections

(De Louis *et al.*, 1980)

Placental-Udder axis: role on colostrum production and lactation development

Ruminant placental lactogens: structure and biology

J. C. Byatt, W. C. Warren, P. J. Eppard, N. R. Staten, G. G. Krivi and R. J. Collier

J Anim Sci 1992. 70:2911-2923.

Occurrence of PL

Primata

Rodentia

http://www.greenpeace.org/mexico/news/ma-z-que-da-a-a-las-ratas-fue

Artiodactyla

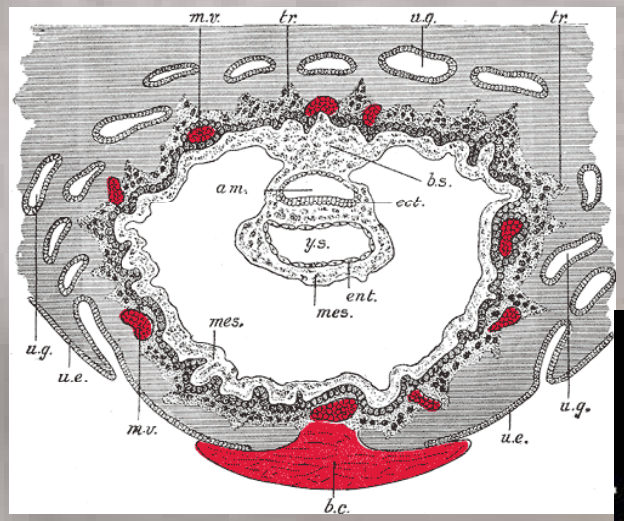
No demonstrated lactogenic activity in placenta of pigs

(Tiedemann, 1979; Dantzer, 1985)

Porcine placenta lacks binucleate cells

Ruminant Placental lactogens

- Somatotropin, prolactin gene family (GH/PRL)
- Trophectodermal binucleate cells

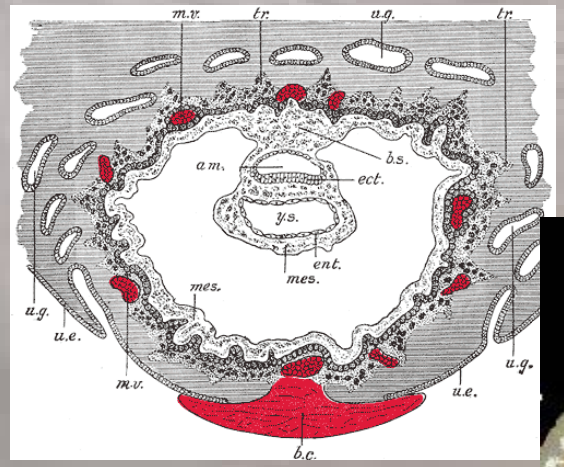


- Secreted into fetal and maternal circulations

Ruminant Placental lactogens

PL concentration

- In fetus decreases with advancing gestation
- In maternal circulation peaks the last third of pregnancy



- Secreted into fetal and maternal circulations

➢ Ovine and caprine PL 23 kDa

Buttle *et al.* (1972)

Forsyth (1974); Kelly *et al.* (1974)

Fetal PL levels are 100 times lower than maternal levels

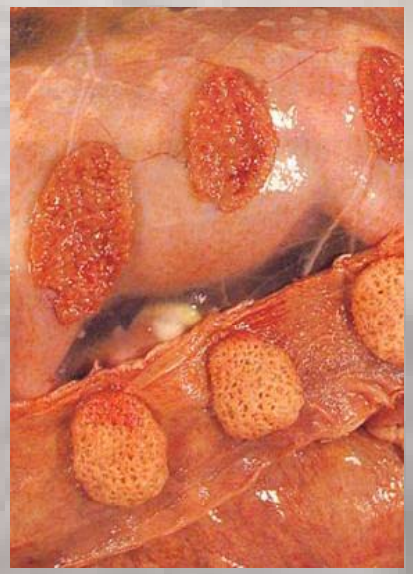
(Butler *et al.*, 1981; Currie *et al.*, 1990)

Higher maternal PL concentration than in cows

(Byatt *et al.*, 1986, 1992)

➢ Bovine PL (bPL) 31-33 kDa

(Beckers *et al.*, 1974; Murphy *et al.*, 1982; Arima and Bremel, 1983)



- 200 amino-acid long glycoprotein
- Secreted into fetal and maternal circulation
- 6 isoelectric variants in cotyledonary extracts (pI: 4.85-6.3)
- 3 isoforms in fetal sera (pI: 4.85-5.25)
- Heavily glycosylated

(Byatt *et al.*, 1986, 1992)

bPL levels are higher in fetal than in maternal compartments

(Beckers *et al.*, 1982)

Ruminant Placental lactogens

Table 2. Physiochemical characteristics of ruminant placental lactogens

Species	Molecular wt by SDS-PAGE	Molecular wt estimated from primary sequence	pI[a]	Glycosylated
Bovine	31,00–34,000	22,968	4.8–6.3[b]	Yes
Ovine	22,000–23,000	22,469	6.8[c], 8.8[d], 9.2[e]	No
Caprine	22,500	ND[f]	8.0–8.4[g]	ND

[a]Isoelectric point.
[b]Byatt et al., 1986.
[c]Hurley et al., 1977a.
[d]Chan et al., 1976.
[e]Warren et al., 1990a.
[f]ND = not determined.
[g]Currie et al., 1990.

(Byatt *et al.*, 1992)

Lost or alteration of glycosylation may produce changes of PL

- In its intracellular signaling
- Transformation of agonist to antagonist

(Alvarez-Oxiley *et al.*, 2008)

➢ Bovine PL (bPL)

The specific role of glycosylation of bPL has not yet been deeply investigated

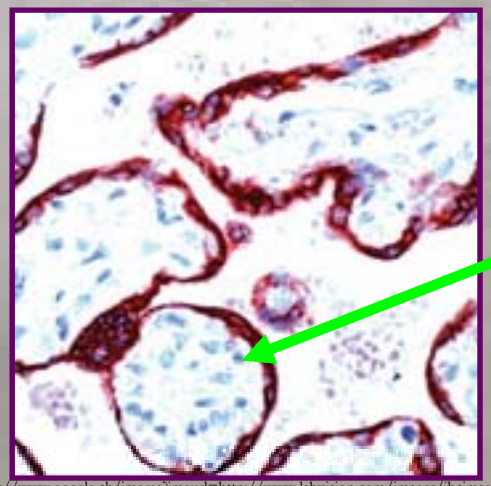
➢ Bovine PL (bPL): synthesis and secretion

- mRNA is transcribed in trophoblastic cells

After 30 days of pregnancy

- 95% binucleate cells express bPL proteins

> 60 days of gestation



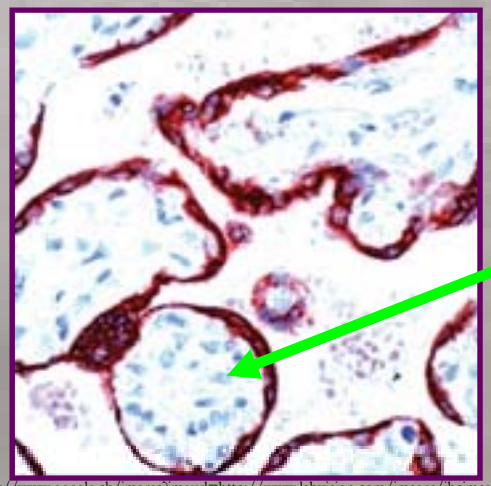
http://www.google.ch/imgres?imgurl=http://www.labvision.com/images/ihcimage/9067.jpg&imgrefurl=http://www.labvision.com/ab.cfm%3Ffirst%3DAntiBody%26second%3D9067&usg=__fD4NjFTH4pwlHMVfYHs8QZ5CjUg=&h=175&w=175&sz=15&hl=de&start=231&itbs=1&tbnid=EWTTVzftQwW32M:&tbnh=100&tbnw=100&prev=/images%3Fq%3Digg%2Bplazenta%26start%3D220%26hl%3Dde%26sa%3DN%26gbv%3D2%26ndsp%3D20%26tbs%3Disch:1

Stored in membrane-bound secretory granules in BNC

➢ Bovine PL (bPL): synthesis and secretion

PL proteins stored in membrane-bound secretory granules in BNC

- **May enter in maternal circulation by exocitosis of granules**
- **Mechanism by which enter in fetal circulation is unclear**



http://www.google.ch/imgres?imgurl=http://www.labvision.com/images/ihcimage/9067.jpg&imgrefurl=http://www.labvision.com/ab.cfm%3Ffirst%3DAntiBody%26second%3D9067&usg=__fD4NjFTH4pwlHMVfYHs8QZ5CjUg=&h=175&w=175&sz=15&hl=de&start=231&itbs=1&tbnid=EWTTVzftQwW32M:&tbnh=100&tbnw=100&prev=/images%3Fq%3Digg%2Bplazenta%26start%3D220%26hl%3Dde%26sa%3DN%26gbv%3D2%26ndsp%3D20%26tbs%3Disch:1

The mechanism controlling the synthesis and secretion must be elucidated

Ruminant Placental lactogens

Synthesis and secretion

Late gestation ↓ BNC expressing oPL

Fetal cortisol regulates the number of BNC

↘

May control oPL production

(Braun *et al.*, 2007; Ward *et al.*, 2002)

Mechanism of control has not yet been elucidated

Pattern of maternal PL concentration

↑ Gestational age

Peak during last trimester

↓ At partum

(Kaplan and Grumbach, 1965)

(Ogren *et al.*, 1989; Robertson *et al.*, 1990)

(Beckers *et al.*, 1982; Currie *et al.*, 1990; Handwerger *et al.*, 1977)

Peripheral bPL concentration

- Gestation stage
- Placental mass
- Fetal weight
- Litter size
- Nutritional status

(Alvarez-Oxiley *et al.*, 2008)

Placental lactogens biological activities

- Studied in rodents

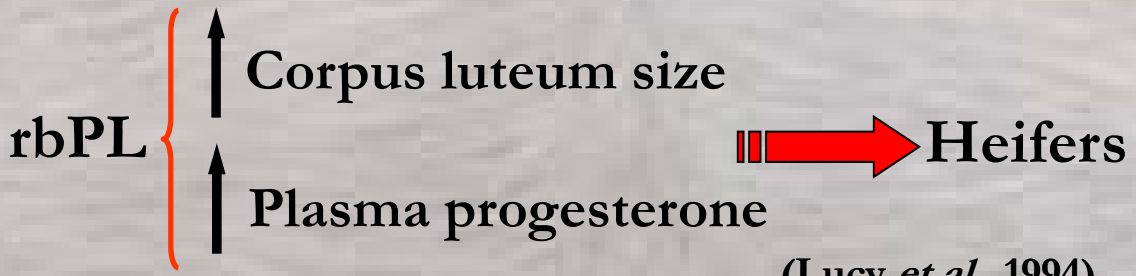
Linzer and Fisher (1999)

* Luteotrophic activity
* Mammogenesis
* Lactogenesis
* Fetal growth

In ruminants biological functions are not fully understood

Placental-Udder axis: role on colostrum production and lactation development

- **Luteal function**



(Lucy *et al.*, 1994)

oPL: No effects on P_4 secretion

(Waters *et al.*, 1985)

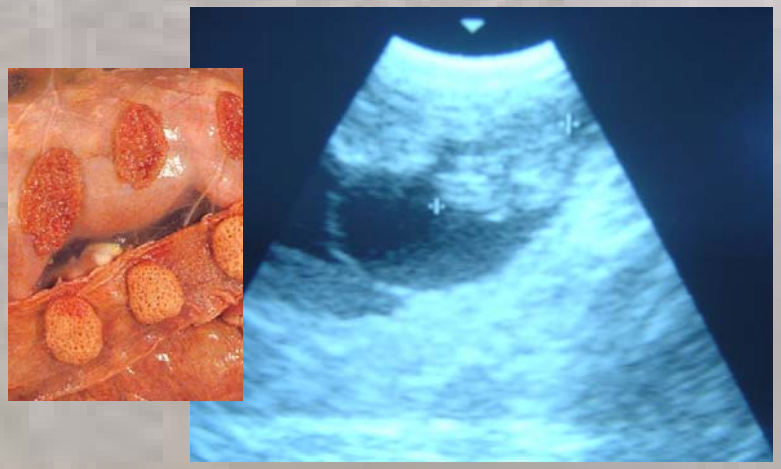
PL-mediated signaling system in Corpus luteum in cows

In ruminants biological functions are not fully understood

➢ Pregnancy-maternal adaptation

- To mantain nutrients supply for fetal development
- Nutrients partitioning

(Rasby *et al.*, 1990)



In ruminants biological functions are not fully understood

➢ Pregnancy-maternal adaptation

Effect of nutrition

Low BCS

Moderate BCS

Uterine mass lower in low BCS cows

Higher PL in low BCS cows to increase the availability of nutrients in the fetal unit

(Rasby *et al.*, 1990)

➢ Pregnancy-maternal adaptation

Effect of nutrition

Underfed

Wellfed

No plasma PL concentration difference

Underfed group delayed the PL decrease before partum

Underfeeding reduced the colostrum accumulation and production

(Mellor *et al.*, 1987)

➢ Fetal growth

- Stimulates uptake of maternal nutrients to the fetus
- Stimulates the fetus to use the nutrients

ELSEVIER

Animal Reproduction Science 64 (2000) 33–47

ANIMAL REPRODUCTION SCIENCE

www.elsevier.com/locate/anireprosci

Active immunization of ewes against ovine placental lactogen increases birth weight of lambs and milk production with no adverse effect on conception rate

H. Leibovich[a], A. Gertler[a], F.W. Bazer[b], E. Gootwine[c,*]

roPL

- Higher birth weight
- Higher milk yield

> oPL concentration in feto-placental compartment

In ruminants biological functions are not fully understood

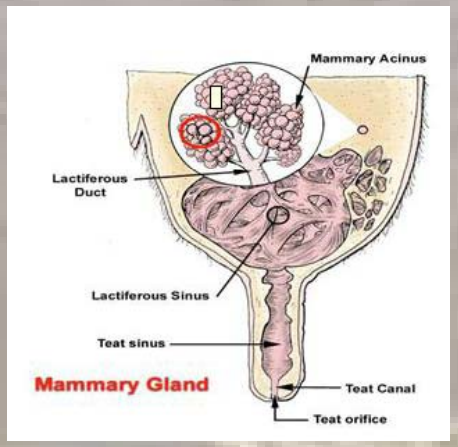
➢ Mammogenesis and lactogenesis

- Lactogenic hormones
- Ovarian steroids

Full lobulo-alveolar growth

Ductal growth

(Connor *et al.*, 2007; Cowie *et al.*, 1966; Kohmoto and Bern, HA; Mulac-Jericevic *et al.*, 2003)



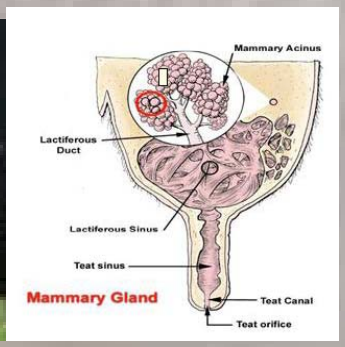
➢ Mammogenesis and lactogenesis

- Bromocriptine treatment during the later half of gestation

→ Mammogenesis not inhibited

bPL: Potential substitute for pituitary PRL !!!!

(Schams *et al.*, 1984)



In ruminants biological functions are not fully understood

➢ Mammogenesis and lactogenesis

- Mammary development is unaffected by deletion of PRL

PL stimulate or support mammogenesis

(Buttle *et al.*, 1978; Forsyth *et al.*, 1985; Martal and Djiane, 1977; Schams *et al.*, 1984)

➢ Mammogenesis and lactogenesis

rbPL > bPRL → Mitogenic activity

bPRL > rbPL → Milk synthesis

(Byatt *et al.*, 1994)

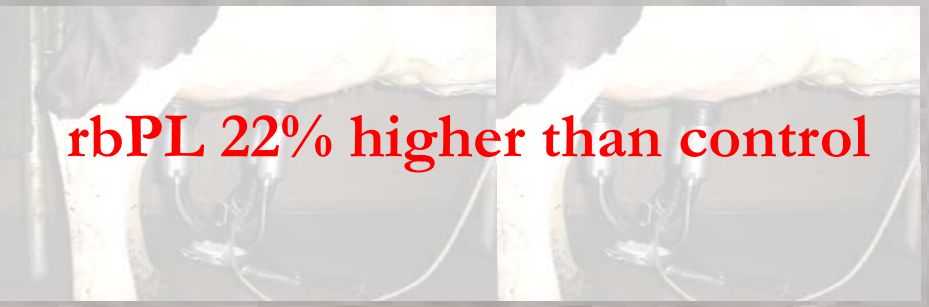
Exogenous rbPL may or may not increase the milk yield

➢ Mammogenesis and lactogenesis

Heifers treated with steroids to induce lactation

rbPL

Milk yield



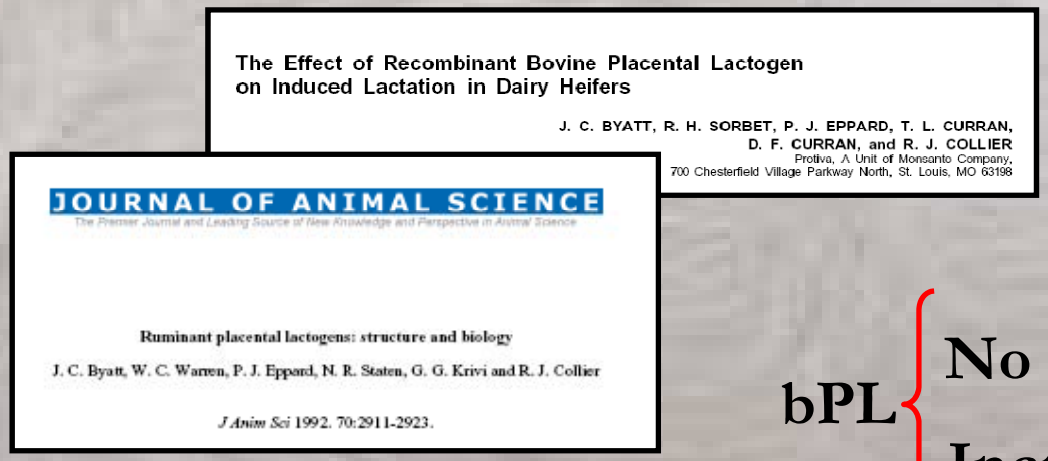
rbPL 22% higher than control

bPL is less potent than bGH inceasing the milk yield

(Byatt *et al.*, 1992, 1997)

Placental-Udder axis: role on colostrum production and lactation development

➢ Mammogenesis and lactogenesis



The Effect of Recombinant Bovine Placental Lactogen on Induced Lactation in Dairy Heifers

J. C. BYATT, R. H. SORBET, P. J. EPPARD, T. L. CURRAN, D. F. CURRAN, and R. J. COLLIER

Protiva, A Unit of Monsanto Company, 700 Chesterfield Village Parkway North, St. Louis, MO 63198

JOURNAL OF ANIMAL SCIENCE

The Premier Journal and Leading Source of New Knowledge and Perspective in Animal Science

Ruminant placental lactogens: structure and biology

J. C. Byatt, W. C. Warren, P. J. Eppard, N. R. Staten, G. G. Krivi and R. J. Collier

J Anim Sci 1992. 70:2911-2923.

bPL
- No effect on lipolysis
- Increase DM intake

bGH
- Increase plasma NEFA
- Increase plasma glucose
- No effect on DM intake

Galatopoietic effect of bPL may be by increase of DM intake

SUMMARY

- Ruminant PL have lactogenic and somatogenic properties mediated through prolactin and somatotropin receptors

- Ruminant PL have biological activities mediated through specific binding sites

- PL levels are different in maternal and fetal compartments

SUMMARY

• In small ruminants maternal PL concentration

is higher than in cows

and it is proportional to placenta mass and

it depends on the number of fetuses.

Although PL concentration in the maternal circulation

is influenced by other factors, such as nutritional status

FUTURE

PL is involved in several biological activities

- To characterized the binding sites

- To clarify the relationship between PL and colostrum production


THANKS FOR YOUR ATTENTION