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**Ovine placental lactogen and insulin-like growth  
factor-I: a study of their biological actions  
and potential to enhance animal production**

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for the degree of Doctor of Philosophy  
in Animal Science at Massey University,  
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## ABSTRACT

Ovine placental lactogen (oPL) has been considered to be important in the regulation of fetal lamb growth. Recent sequence studies have also shown that oPL has considerable structural similarity to ovine prolactin (oPRL) and ovine growth hormone (oGH), raising the possibility that oPL may have potential as a stimulator of milk yield and postnatal growth. Evidence from laboratory animals indicates that the biological actions of GH and perhaps PL are mediated largely by IGF-I, acting in both a paracrine/autocrine and an endocrine manner. However, the potential of IGF-I therapy has not been fully explored in domestic animals. Therefore, the overall aim of this study was to examine the biological actions of recombinant oPL and IGF-I and to evaluate their potential use to stimulate performance of farm animals.

In the first three experiments, the biological actions of recombinant oPL were examined in pregnant and lactating ewes, and in young growing lambs, and compared with those of bovine growth hormone (bGH). bGH treatment for 7 days from day 101 of pregnancy increased total uterus weights, but administration of an identical dose of oPL had no effect. Similarly, exogenous bGH over 5 days increased milk yields in lactating ewes, whereas such an effect was not apparent with oPL treatment. However, the reverse situation occurred in young growing lambs in which oPL, not bGH, treatment for 21 days from day 3 of life stimulated growth rate and voluntary feed intake. Different biological actions of bGH and oPL in pregnant and lactating ewes were associated with a situation in which bGH, but not oPL, treatment increased circulating concentrations of IGF-I. Conversely, in young growing lambs, the growth-promoting effect of oPL appeared to be mediated primarily via a change in voluntary feed intake since both oPL and bGH treatment had only small effects on plasma IGF-I concentrations.

The inability of bGH to stimulate plasma IGF-I concentrations in young lambs, accompanied by the lack of a growth-promoting effect of bGH, suggested that hepatic GH receptors (GHR) may not be fully functional at this stage. This hypothesis was examined in an experiment in which the ontogeny of hepatic GHR was assessed by measuring IGF-I responsiveness to a GH stimulus, as well as hepatic GH binding, in lambs of different ages (days 6/7, 20/21, 34/35, and 62/63 of life, and yearlings). Results

showed that the plasma IGF-I response to exogenous bGH in young lambs was much lower than that in yearling sheep. Consistent with this, measurement of hepatic GHR at day 7 and 63 of life, and in yearling sheep, showed that bGH treatment failed to alter GHR number in young lambs, while up-regulating it in yearling sheep. In contrast, non-stimulated GHR numbers were similar across ages. These data suggest that hepatic GHR in young lambs are not fully functional, which may explain the lack of a growth-promoting effect of bGH in newborn animals.

The importance of the GH-IGF-I axis in the regulation of post-natal growth was further demonstrated in an experiment, in which anabolic effects of recombinant IGF-I over a prolonged period (8 or 12 weeks) were measured in energy-restricted sheep. IGF-I treatment elevated circulating concentrations of IGF-I, but depressed plasma GH concentrations. The reduction in circulating GH levels was accompanied by a down-regulation of hepatic GHR. As a result, recombinant IGF-I had little growth-promoting effect although it improved other parameters such as nitrogen digestibility and components of the immune system.

In conclusion, the present study suggests that recombinant oPL, like GH, has potential in improving farm animal production. However, the biological actions of oPL seem to be mediated in a different manner from those of GH. This could have practical implications in situations where GH has no biological actions. For example, in very young lambs in which hepatic GHR are not fully functional, oPL could provide an alternative means to stimulate growth. This could be also true for IGF-I because, in young animals, the negative-feedback regulation of both plasma GH and hepatic GHR concentrations by IGF-I treatment may be less likely to limit a growth response than is the case in older animals.

## EMENDATIONS

<u>Page/Line</u>	<u>Thesis Reads</u>	<u>Should Read</u>
47/7	the perfused mammary gland	mammary explants
95 & 96	(reverse panels for Figures 4.1 and 4.2)	
99/7	Figure 4.4	data not shown
108/Table 5. 1	Insulin	Bovine insulin
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## LIST OF ABBREVIATIONS

ADG	Average daily gain
AIB	Aminoisobutyric acid
ALS	Acid-labile subunit
AUC	Area under the curve
b	Bovine
BP	Binding protein
BrdU	5-Bromo-2'-deoxyuridine
CB154	Bromocriptine
CP	Crude protein
DM	Dry matter
FCR	Feed conversion rate
h	Human
hp	Human pancreatic
GH	Growth hormone
GHR	Growth hormone receptor
GRF	Growth hormone-releasing factor
IGF-I	Insulin-like growth factor-I
IGF-II	Insulin-like growth factor-II
IGFBP	Insulin-like growth factor binding protein
i.m.	Intramuscular
K	The fractional decay constant
LTD	Laron-type dwarfism
LW	Liveweight
MCHC	Mean corpuscular haemoglobin concentration
ME	Metabolisable energy
MG	Mammary gland
MJ	Megajoules
M-6-P	Mannose-6 phosphate
NE	Net energy

NEFA	Non-esterified fatty acids
NSILA	Non-suppressible insulin-like activity
o	Ovine
p	Porcine
PL	Placental lactogen
PRL	Prolactin
PCV	Packed cell volume
r	Correlation
RIA	Radioimmunoassay
SE	Standard error of the mean
SRIF	Somatotropin release inhibiting factor (somatostatin)
ST	Somatotropin
TRH	Thyrotropin-releasing hormone

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