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A POTENTIAL ROLE FOR POLYAMINES IN CELL DIFFERENTIATION IN FIBRE-PRODUCING FOLLICLES

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Polyamines have been shown to have profound effects on cell division and differentiation in many metabolically active tissues (Pegg and McCann 1982) and are thus likely to have an important role in the regulation of cellular events within the wool follicle. Recent studies, designed to elucidate potential roles, have utilised highly-specific irreversible inhibitors of the polyamine biosynthetic enzymes to inhibit polyamine metabolism and perturb follicle activity (Reis and Hynd 1989).

In this study ornithine decarboxylase (ODC) was specifically inhibited by the structural analogue of ornithine, α-difluoromethyl ornithine (DFMO), via intravenous infusion (75mg/kg/day) for eight days in four Corriedale wethers. Measurements of cellular and molecular events involved in fibre production within the follicle were obtained pre-, during, and post-treatment (see table).

Parameters	Pre	DFMO	Post 1	Post 2
Fibre length growth rate (L) (μm/day)	460	359*	443	440
Fibre diameter (D) (μm)	24.5	25.6**	24.1	24.0
L/D	18.9	14.1**	18.5	18.6
Mitotic rate (mitoses/bulb section/h)	2.061	1.806*	1.718	1.711
Cortical cell volume (μm^3)	530	539	558	579
Area of fibre/area of fibre and inner root sheath	0.549	0.587**	0.561	0.561
% Paracortex	28.7	37.9**	23.6	24.9

*P<0.05, **P<0.01 in comparison to pre-treatment

DFMO caused a reduction in the mean fibre length growth rate (L) of 22% while fibre diameter (D) increased 1.1 μm, resulting in a considerable decrease in the ratio of L to D, which recovered rapidly post-treatment. Estimates of mitotic activity and cortical cell sizes post-keratinisation supported the findings of Reis and Hynd (1989), suggesting that cell differentiation rather than cell division or cortical cell size was being influenced by DFMO, thus providing a presumptive role for the polyamines in wool growth.

Further evidence for this potential role was supplied by a shift in cell commitment towards fibre production which occurred with a concomitant change in the proportion of cells producing ortho- and paracortex. For this to have occurred there must have been corresponding changes in gene expression in those cells. Preliminary experiments displayed a perturbation of keratinisation mechanisms with a subsequent change in keratin gene expression. The level of mRNA of an ultra high sulphur cortical keratin gene was elevated 4.5 fold and an intermediate filament gene 1.8 fold during infusion of DFMO (70mg/kg/day) into one sheep. Similar observations have been noted during cysteine infusion (Fratini unpublished) and may indicate a common pathway or an indirect effect of DFMO on sulphur metabolism rather than a direct effect of the polyamines on gene regulation in the follicle.

At present wool follicle cell mRNAs coding for a range of protein subfamilies are being used to detect changes in the molecular events in the follicle such as mRNA and protein synthesis during infusion of the inhibitor. It is envisaged that when combined with the above results a more complete understanding of the actions of DFMO on follicle "normal" functioning and the role of polyamines in cell differentiation in the follicle will be obtained.

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