

Role of neuregulin-1 β in dexamethasone-enhanced surfactant phospholipid synthesis in rat fetal type II pneumocytes *

G KING,¹ G L MAKER,^{1†} D BERRYMAN,¹ R D TRENGOVE,² & M H CAKE¹

¹ School of Veterinary and Life Sciences, Murdoch University, Murdoch, WA 6150, Australia.

² Separation Science and Metabolomics Laboratory, Murdoch University, Murdoch, WA 6150, Australia.

[†] Corresponding author ✉ G.Maker@murdoch.edu.au

Surfactant production is known to involve a cellular communication between lung fibroblasts and the type II pneumocytes. Glucocorticoids induce the production of a peptide by lung fibroblasts, fibroblast-pneumocyte factor (FPF), which sequentially acts on type II cells to enhance the synthesis of surfactant phospholipid. Our findings show that fibroblast-conditioned medium (FCM), generated in the presence of dexamethasone, not only enhanced surfactant phospholipid synthesis in type II cells but also contained an elevated concentration of neuregulin-1 β (NRG1 β). Even though it has been earlier proposed that leptin has many of the characteristics of FPF, recent research has revealed that NRG1 β also has many similar attributes. In the current study, exposure of the type II cells to a commercially available form of NRG1 β (heregulin-1 β) directly stimulated by more than three-fold the rate of phospholipid synthesis ($p < 0.05$). Although similar in magnitude, the effect of heregulin-1 β appeared to require a longer time of exposure to that

reported for leptin. There was no increase in the gene expression of NRG1 β when lung fibroblasts were exposed to dexamethasone, irrespective of the concentration of dexamethasone used, or the time of contact of the cells to the steroid. Thus the glucocorticoid-induced increase in the level of NRG1 β in FCM was not the result of enhanced expression of the NRG1 β gene. The inability of dexamethasone to induce a significant increase in NRG1 β gene expression in lung fibroblasts suggests that the elevated concentration of NRG1 β might be the result of enhanced cleavage of the membrane-bound neuregulin precursor. In summary, these findings not only support but significantly extend the concept previously promoted that NRG1 β plays an essential role in the differentiation and maturation of the lung in the later stages of gestation. Moreover, together these studies suggest that FPF may be a complex mixture of agents capable of motivating surfactant synthesis.

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