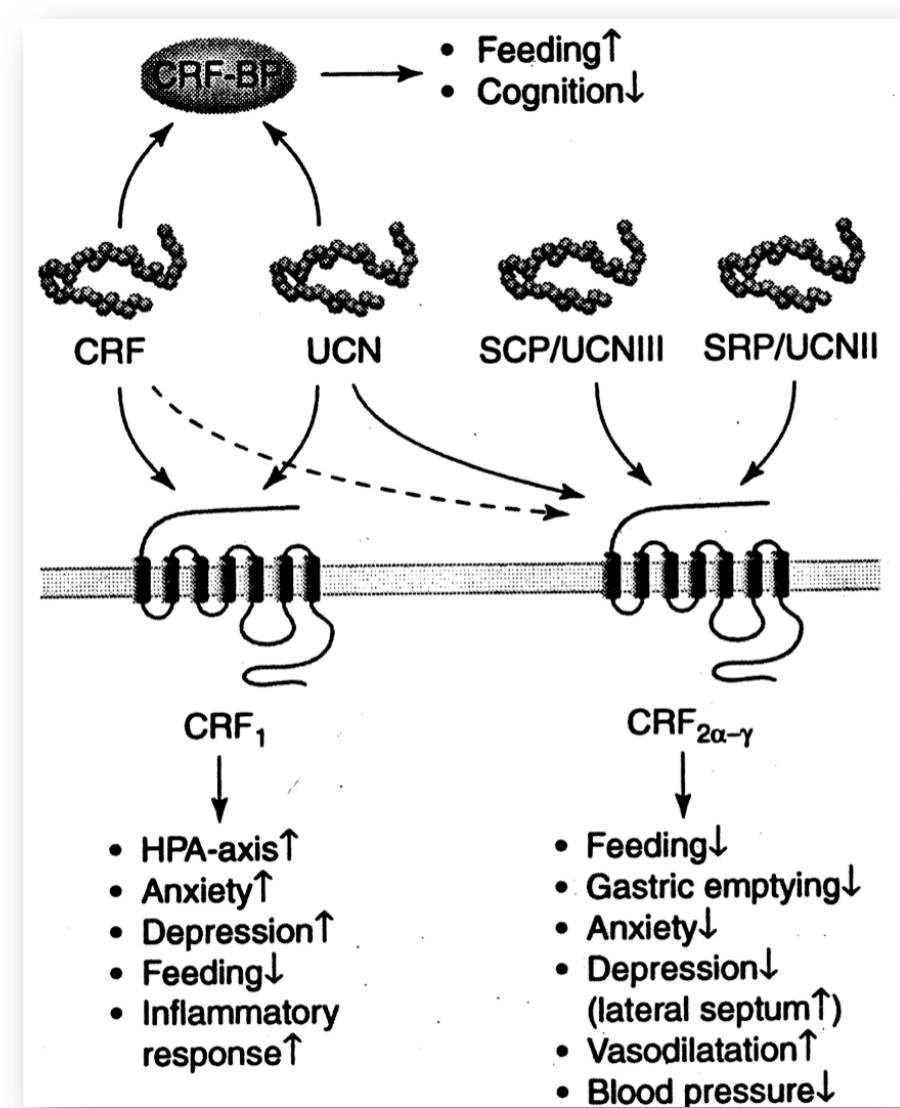


CORTICOTROPIN RELEASING FACTOR (CRF) NEUROPEPTIDES IN HUMAN FETAL LUNG DEVELOPMENT

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INTRODUCTION/ OBJECTIVE:

CRF, among other functions, regulates the secretion of ACTH by the pituitary and along with a series of homologous peptides (Urocortins I, II and III) and binding sites (CRF1, CRF2 and CRF-BP) constitute the CRF system. This system is fundamental for the maintenance and the homeostasis of an organism (Figure 1). There are only few reports concerning the detection of CRF system in fetal tissues of experimental animal models. The aim of the present study was to investigate the expression of CRF and its homologous neuropeptides in human normal fetal lung.

Figure 1: Role of CRF system

MATERIALS/METHODS:

Fetal lung tissues were retrieved from 17 archival, human, male normal fetuses (with no congenital or chromosomal anomalies and no signs of chorioamnionitis or other pathology). Fetuses were divided according to their gestational week, into pseudoglandular (7-16 gest. week, n⁰:5), canalicular (17-27 gest. week, n⁰:10) and saccular stage (28-35 gest. week, n⁰:2). The presence of CRF neuropeptides was evaluated with immunohistochemistry. Positivity was graded, in epithelial and mesenchymal cells, as follows: Grade 3 51-100 % positive cells in the total number of cells counted per field, Grade 2 18-50 %, Grade 1 < 18 % and Grade 0 absence of positively stained cells.

PEPTIDES	GRADE	STAGES					
		PSEUDOGLANDULAR (Total n ⁰ : 5)		CANALICULAR (Total n ⁰ : 10)		SACCULAR (Total n ⁰ : 2)	
		Epithelial n ⁰	Mesenchymal n ⁰	Epithelial n ⁰	Mesenchymal n ⁰	Epithelial n ⁰	Mesenchymal n ⁰
CRF	G:0	1	1	4	3	1	1
	G:1	2	2	3	4		
	G:2	2	2	3	3	1	1
	G:3						
Ucn I	G:0			1	1		
	G:1	1		1	2		
	G:2	4	5	8	7	2	2
	G:3						
Ucn II	G:0			2	2		
	G:1	1		5	4	2	2
	G:2	4	5	3	4		
	G:3						
Ucn III	G:0	1	1	4	3	1	1
	G:1	1	1	6	7	1	1
	G:2	3	3				
	G:3						

Figure 2: Results table.

Epithelial cells: bronchus, bronchiolus and endothelial cells

Mesenchymal cells: stromal cells

RESULTS:

Both epithelial and mesenchymal cells were positive for all 4 neuropeptides during the pseudoglandular stage, except one fetus for CRF and one for Ucn III. In the canalicular stage: 6/10 and 7/10 (epithelial and mesenchymal cells respectively) fetuses for CRF, 9/10 (all cells) for Ucn I, 8/10 (all cells) for Ucn II and 6/10 and 7/10 (epithelial and mesenchymal cells respectively) for Ucn III were positive. Finally, during saccular stage, 1/2 (all cells) fetuses was positive for CRF and Ucn III, while 2/2 (all cells) fetuses were positive for Ucn I and II. Staining was Grade 1 or 2 in all cases (Figure 2,3).

CONCLUSIONS/ DISCUSSION:

CRF and its neuropeptides were present in the majority of fetuses, during all three stages, in both epithelial and mesenchymal cells. Our results, in combination with functional data from experimental animals, imply an important role of the CRF system in fetal lung development.

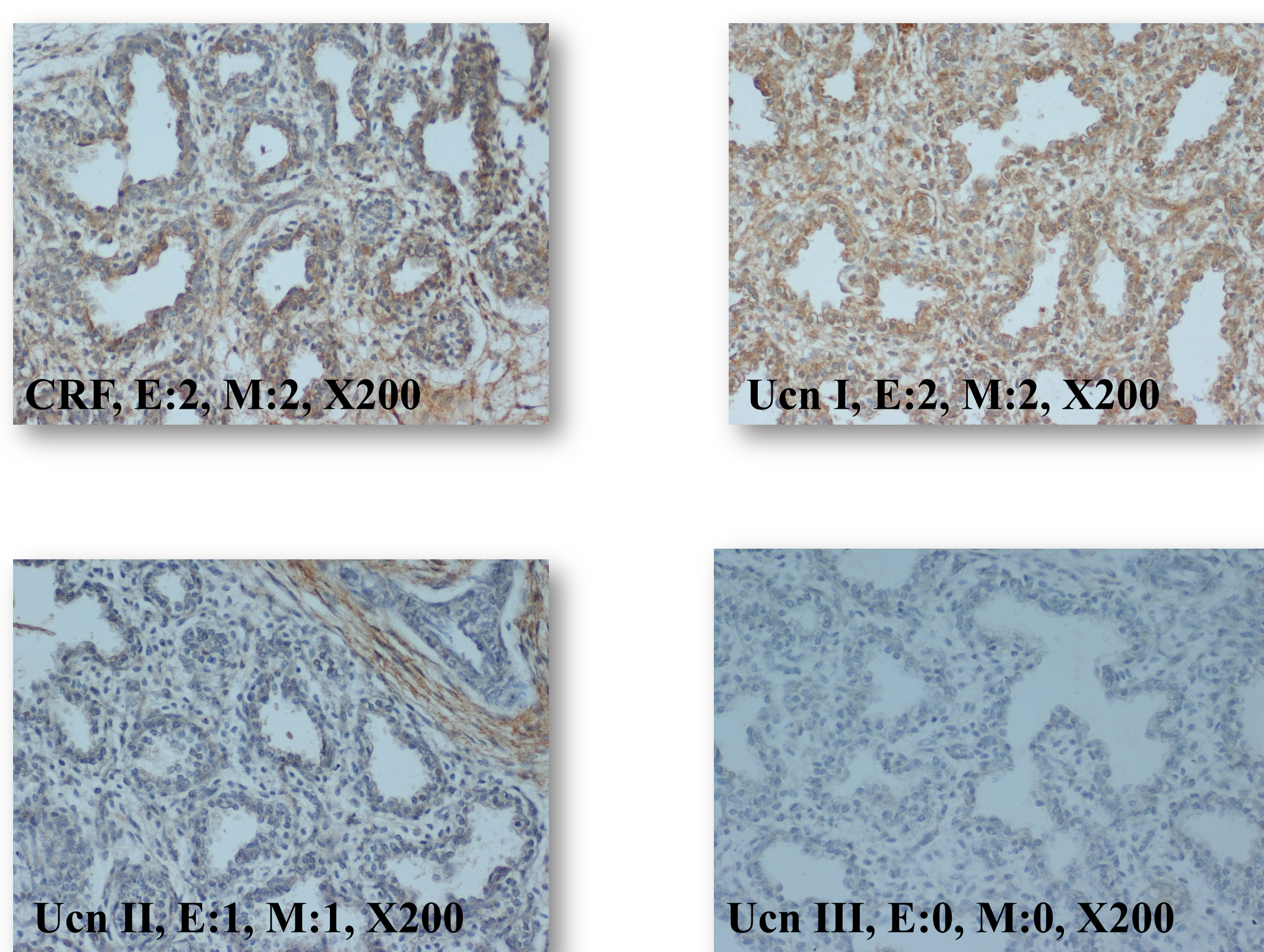


Figure 3: Fetus 28w, male