Title	Functional characterization of liver-enriched transcription factor CREB-H (poster 1989)
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and tissue-specific events, which optimize the glands for their highly demanding function. The latter is attained through a series of transient bouts of activities which enrich the gland's protein synthesis machinery. The processes are reproducible in terms of their timing and also relative intensities. The earliest of these events, one of considerable magnitude, provides the glands with a variety of small RNAs: two isoforms of 5S rRNA, a tissue-specific alanine tRNA, and members of the U subset of small RNAs which constitute the spliceosome complex. Isoforms of U1 and U2 generated have been proven not to be intermediates of RNA processing. The second event, which generates the fibroin template, is followed by an event of rather limited magnitude which attains selective enrichment of the gland's tRNA population by generating the tRNAs cognate to the fibroin's predominant amino acids: glycine, alanine and proline; an adaptive tRNA population shift. The last of the transient events, and one of considerable magnitude, attains the culmination of the elicited process through the massive production of the full size fibroin. Of special interest is the generation of a tissue-specific alanine tRNA of considerable intensity. Although its function is not, as yet, known it is a feature in the fibroin production strategy of the silkworm *Bombyx mori*.

1987

Detection of HLA-E and HLA-G Expression in Human Placental Tissue

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Nonclassical MHC class Ib human leukocyte antigen E (HLA-E) and HLA-G molecules differ from classical ones by specific patterns of transcription, protein expression, and immunotolerant functions. HLA-G can be expressed as four membrane-bound (HLA-G1 to -G4) and three soluble (HLA-G5 to -G7) proteins upon alternative splicing of its primary transcript. In this study, we used a set of monoclonal antibodies (mAbs) called HCA2, 4H84, MEM-G/1, -G/9, MEM-E/2, and -E/6 recognizing HLA-G or HLA-E. The patterns of reactivity of these mAbs were analyzed on transfected cells by Western blotting and immunocytochemistry. MEM-G/1 recognizes (similar to the 4H84 mAb) the denatured HLA-G heavy chain of all isoforms. MEM-G/9 mAb react exclusively with native HLA-G1 molecules. MEM-E/2 and -E/6 mAbs bind the denatured and cell surface HLA-E molecules, respectively. These mAbs were then used to analyze the expression of HLA-G and HLA-E on cryo-preserved and paraffin-embedded serial sections of placental tissue. Single and double-immunolabeling with the respective mAbs revealed the presence of HLA-G and HLA-E in extravillious cytotrophoblast. In comparison, however, the levels of HLA-E expression seem to be much lower than those of HLA-G. In addition, we found a strong expression of HLA-E in endothelial cells using mAb MEM-E/2. The presence of HLA-G and HLA-E in specific cell populations of the placenta suggest an interacting functional role of these molecules in maternal-placental immune recognition.

1988

Cdx2, Gata-4 and Hnf-4α Lead to Expression of an Intestinal Epithelial Phenotype in Fibroblasts

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The intestinal epithelium is an excellent model to study the molecular mechanisms during cellular differentiation. The epithelial stem cells located at the bottom of the intestinal crypts constantly divide to generate cells that will differentiate into four cell lineages. This differentiation is tightly regulated during cellular migration up to the villi. Literature supports the idea that restricted expression of many intestinal specific gene in differentiated cells is due to the specific combination of transcription factors. However, little is known about the exact molecular mechanisms that ultimately lead to intestinal epithelial cell differentiation. In the light of recent observations, we followed the hypothesis that Cdx2, Gata-4 and Hnf-4α could act as a transcriptional complex and induce cells to specialize into intestinal epithelial cells. To test this hypothesis, we first generated fibroblastic cell lines (NIH-3T3) that can conditionally over-express different combinations of Cdx2, Gata-4 and Hnf-4α transcription factors. We then characterized these inducible cell lines by Western blot analysis. NIH-3T3 cell lines that showed the best controlled expression for each factors were chosen to further investigate. RT-PCR analysis revealed that the combination of Cdx2, Gata-4 and Hnf-4α resulted into the induction of expression of the intestinal epithelium specific genes intestinal-fatty-acid-binding-protein (IFABP), intestinal trefoil factor 3 (ITF3) and apolipoprotein A-IV. We also found by electronic microscopy that NIH-3T3 with combined expression of Cdx2, Gata-4 and Hnf-4α changed morphology with the increase in cellular dimension, appearance of microvilli and beginning of polarization. In conclusion, our results suggest that ectopic combination of HNF-4α, Cdx2 and GATA-4 can initiate a program of intestinal epithelial cell determination within the mesenchymal context. Further studies will be necessary to document the targets of these transcription factors during the acquisition of the intestinal epithelial phenotype.

1989

Functional Characterization of the Liver-enriched Transcription Factor CREB-H

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We have previously characterized transcription factor LZIP/CREB3 to be a growth suppressor targeted by hepatitis C virus oncoprotein. In search of proteins closely related to LZIP, we have identified a liver-enriched transcription factor CREB-H/CREB3L3. LZIP and CREB-H represent a new subfamily of bZIP factors. CREB-H activates transcription by binding to cAMP responsive element, box B, and ATF6/UPRE-binding element. Interestingly, CREB-H has a putative transmembrane domain and it localizes ambiently to the endoplasmic reticulum. Proteolytic cleavage that removes the transmembrane domain leads to nuclear translocation and activation of CREB-H. CREB-H activates the promoter of hepatic gluconeogenic enzyme phosphoenolpyruvate carboxykinase. This activation can be further stimulated by cAMP and protein kinase A. CREB-H transcript is exclusively abundant in adult liver. In contrast, the expression of CREB-H mRNA is aberrantly reduced in hepatoma tissues and cells. The enforced expression of CREB-H suppresses the proliferation of cultured hepatoma cells. Taken together, our findings suggest that the liver-enriched bZIP transcription factor CREB-H is a growth suppressor that plays a role in hepatic physiology and pathology.

1990

Characterization of Two New Members of the *XK* Gene Family: XPLAC and XTES

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XK, a putative membrane transporter, is a component of XK/Kell complex of the Kell blood group system. The substrate of XK is unknown but