Characterization of 1-ACBP, B-ACBP and PBR in Oesophageal Cancer

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ACBPs (Acyl co-A binding proteins) vary from 86-103 residues and are found to be conserved among different eukaryotic species. There are at least five ACBP subgroups and the two isoforms being focused on in this study is B-ACBP (brain specific) and 1-ACBP (found in nearly all tissues). The principle function of ACBPs is acting as intracellular carrier-proteins for medium to long chain acyl-coA, mediating fatty acid transport to the mitochondrion for -oxidation. ACBPs are also believed to be putative ligands of PBR (Peripheral Benzodiazepine Receptor), and bound to this receptor facilitates mitochondrial membrane permeabilization giving the notion that it favors apoptosis. PBR arouses great interest because of its association with numerous biological functions including the regulation of cellular proliferation, immunomodulation, regulation of steroidogenesis and apoptosis.

Oesophageal cancer in South Africa has been found to be the most prominent among black men and the second most common cancer among all men combined. Oesophageal cancer is a multifactorial disease; no single agent has been identified thus far as the cause of this disease. The known important risk factors for cancer of the oesophagus included poor socio-economic conditions, tobacco and alcohol and a diet lacking in vitamin A, C and zinc.

Aim: The purpose of this study was to establish the expression patterns of 1-ACBP, B-ACBP, and PBR in oesophageal cancer and to characterize their roles in this disease.

Methods: Paraffin-embedded sections of normal and malignant oesophageal tissues were utilized for the localization studies. RNA probes were synthesized complimentary to PBR mRNA and to the 5 and 3 regions of the ACBP mRNAs to increase specificity. These probes were labeled using Digoxigenin for colorometric and fluorescent detection during the *in situ* hybridization (ISH) technique. ISH was performed to localize the mRNA and determine the expression patterns between normal and diseased tissue.

Results: All three genes showed upregulation within the malignant tissue sections compared to normal oesophageal sections, within the lamina propria, muscularis mucosa, submucosa, connective tissue and longitudinal muscle layers. All three transcripts localized specifically to lymphocytes in diseased and normal tissue sections, with a substantial increase in diseased tissue. In the normal tissue sections localization of B-ACBP and PBR were restricted to neutrophils in connective tissue, whereas 1-ACBP mRNA localized to neutrophils and lymphocytes in the connective tissue, lamina propria and muscularis mucosa. In the diseased tissue B-ACBP mRNA and PBR also localized in the nucleus of stratified epithelial cells, and also in between the oesophageal mucous acini glands in the muscularis mucosa, but no localization was found in between these glands in normal tissue sections. 1-ACBP mRNA showed no localization in between the oesophageal glands in diseased tissue, but was highly expressed in the normal tissue sections.

Discussion: All three gene transcripts have been localized mostly to lymphocytes in the oesophagus. Lymphocytes help create antibodies that attack the invaders and mark them for destruction by the neutrophils, monocytes and macrophages. Lymphocyte production increased with the transformation from normal to diseased tissue, therefore suggesting that these three genes play a role in combating the progression of cancer cells, since all three genes are expressed in the lymphocytes and are upregulated in cancer cells.

Conclusion: These results show that 1-ACBP, B-ACBP and PBR play a role in the pathogenesis of oesophageal cancer. Further experiments are still required to determine the function of these genes and the role they play in apoptosis and oesophageal cancer.