A Prognostic Signature of Brown Fat-Associated Proteins in Colorectal Cancer

Colorectal cancer is a common type of malignancy with a relatively poor outcome and is one of the main contributors to cancer related deaths. Brown fat phenotype/proteins have been implicated in tumour growth and metastasis. Therefore, the aim of this study was to characterise the expression of brown fat-associated proteins cell-death-inducing DNA fragment factor 45-like effector A (CIDEA), elongation of very long fatty acids 3 & 5 (ELOVL3 & 5) and uncoupling protein 1 (UCP1) in colorectal cancer. Monoclonal antibodies to these protein targets were developed with short peptide immunogens which were selected using a range of bioinformatic tools. To select each peptide, the structural and physicochemical properties of each protein were analysed. The antibodies were used to profile the expression of proteins by immunohistochemistry in a discovery cohort (274 primary colorectal cancers) and in a validation cohort (549 primary colorectal cancers). Unsupervised hierarchical cluster analysis was used to examine the overall relationship of proteins expression with overall survival and based on this identify a protein signature associated with prognosis**.** Cluster analysis of all proteins identified a cluster that was significantly associated with patient survival in the discovery cohort (HR=1.574, 95%CI=1.037-2.390, χ^2=4.658, p=0.031). Cluster analysis of the validation cohort also showed that the pattern of expression was significantly associated with patient survival (HR=1.691, 95%CI=1.284-2.228, χ^2=14.405, p<0.001). Multi-variate analysis confirmed that the cluster group was prognostically independent of clinically-established prognostic parameters (p=0.03).

This study showed that novel targets CIDEA, ELOVL3, ELOVL5 and UCP1 are overexpressed in colorectal cancer. A prognostic signature of these proteins has been identified in colorectal cancer.