Integrated transcriptomic and metabolomic analysis shows that disturbances in metabolism of tumor cells contribute to poor survival of RCC patients (Article) (Open Access)

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Abstract

Purpose Cellular metabolism of renal cell carcinoma (RCC) tumors is disturbed. The clinical significance of these alterations is weakly understood. We aimed to find if changes in metabolic pathways contribute to survival of RCC patients. Material and methods 35 RCC tumors and matched controls were used for metabolite profiling using gas chromatography-mass spectrometry and transcriptomic analysis with qPCR-arrays targeting the expression of 93 metabolic genes. The clinical significance of obtained data was validated on independent cohort of 468 RCC patients with median follow-up of 43.22 months. Results The levels of 31 metabolites were statistically significantly changed in RCC tumors compared with controls. The top altered metabolites included beta-alanine (+ 4.2-fold), glucose (+ 3.4-fold), succinate (− 11.0-fold), myo-inositol (− 4.6-fold), adenine (− 4.2-fold), uracil (− 3.7-fold), and hypoxanthine (− 3.0-fold). These disturbances were associated with altered expression of 53 metabolic genes. ROC curve analysis revealed that the top metabolites discriminating between tumor and control samples included succinate (AUC = 0.91), adenine (AUC = 0.89), myo-inositol (AUC = 0.87), hypoxanthine (AUC = 0.85), urea (AUC = 0.85), and beta-alanine (AUC = 0.85). Poor survival of RCC patients correlated (p < 0.0001) with altered expression of genes involved in metabolism of succinate (HR = 2.7), purines (HR = 2.4), glucose (HR = 2.4), beta-alanine (HR = 2.5), and myo-inositol (HR = 1.9). Conclusions We found that changes in metabolism of succinate, beta-alanine, purines, glucose and myo-inositol correlate with poor survival of RCC patients. © 2016 Elsevier B.V.
Author keywords

Beta-alanine  Metabolism  Myo-inositol  RCC  Renal cell carcinoma  Survival

Indexed keywords

EMTREE drug terms: adenine  beta alanine  glucose  hypoxanthine  inositol  purine derivative  succinic acid  uracil  beta alanine  inositol  transcriptome

EMTREE medical terms: Article  cancer patient  cancer prognosis  cancer surgery  cancer tissue  cohort analysis  controlled study  correlative study  diagnostic test accuracy study  follow up  gene expression  gene targeting  hazard ratio  human  human cell  human tissue  kidney carcinoma  major clinical study  mass fragmentography  metabolite  metabolomics  polymerase chain reaction  priority journal  protein folding  protein metabolism  receiver operating characteristic  sensitivity and specificity  survival rate  transcriptomics  tumor cell  uninephrectomy  female  gene expression profiling  gene expression regulation  genetics  genomics  kidney tumor  male  metabolism  metabolome  metabolomics  renal cell carcinoma  survival analysis

MeSH:

beta-Alanine  Carcinoma, Renal Cell  Female  Gas Chromatography-Mass Spectrometry  Gene Expression Profiling  Gene Expression Regulation, Neoplastic  Genomics  Humans  Inositol  Kidney Neoplasms  Male  Metabolic Networks and Pathways  Metabolome  Metabolomics  Survival Analysis  Transcriptome

Chemicals and CAS Registry Numbers:

adenine, 22177-51-1, 2922-28-3, 73-24-5; beta alanine, 107-95-9; glucose, 50-99-7, 84778-64-3; hypoxanthine, 68-94-0; inositol, 55608-27-0, 6917-35-7, 87-89-8; succinic acid, 110-15-6; uracil, 66-22-8; beta-Alanine; Inositol

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