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Metabolic profiling of renal cell carcinoma tissue using gas chromatography metabolomics

Filipa Amaro [1,2,*], Márcia Carvalho [1,2,3,†], Carina Carvalho-Maia [4,5], Carmen Jerónimo [4,5], Rui Henrique [4,5,6], Maria de Lourdes Bastos [1,2], Paula Guedes de Pinho [1,2] and Joana Pinto [1,2]

[1] Associate Laboratory i4HB – Institute for Health and Bioeconomy, University of Porto, 4050-313 Porto, Portugal
[2] UCIBIO – Applied Molecular Biosciences Unit, Laboratory of Toxicology, Faculty of Pharmacy, University of Porto, 4050-313 Porto, Portugal
[3] RISE-UFP, Faculty of Health Sciences, University Fernando Pessoa, 4200-150 Porto, Portugal
[4] Cancer Biology and Epigenetics Group, Research Center (CI-IPOP), Porto Comprehensive Cancer Center (P.CCC), Portuguese Oncology Institute of Porto (IPO Porto), 4200-072, Porto, Portugal
[5] Department of Pathology, Portuguese Oncology Institute of Porto (IPO Porto), P.CCC Porto Comprehensive Cancer Center, 4200-072, Porto, Portugal
[6] Department of Pathology and Molecular Immunology, ICBAS-School of Medicine and Biomedical Sciences, University of Porto, University of Porto, 4050-313 Porto, Portugal
[†] Current address: LAQV/REQUIMTE, University of Porto, Porto, Portugal

* Correspondence: up201608003@up.pt

Abstract

Background: Renal cell carcinoma (RCC) is marked by dysregulation of angiogenesis, energy metabolism, and nutrient sensing pathways [1]. This diversity is an obstacle to achieving long-term responses to treatment, notwithstanding progress in targeted and immunotherapeutic drugs. **Objective:** This study aimed to characterise the metabolic dysregulations that occur in RCC tissue using a metabolomics approach. **Methods**: Tumour and non-tumour kidney tissues were collected from 18 patients who underwent nephrectomy at the Portuguese Oncology Institute of Porto (IPO-Porto). Ethical approval (238/2018) and written consent were obtained. Tissues were homogenised, and metabolites were extracted using a methanol-water technique. Metabolites were then analysed by gas chromatography-mass spectrometry (GC-MS) analysis. Statistical methods and pathway analysis were used to interpret potential dysregulations associated with RCC. **Results**: RCC tissue showed a significant reduction in amino acid levels (including alanine, asparagine, aspartate, serine, tyrosine, among others), except for β-alanine and glutamate, which exhibited significant elevated levels. Perturbations in organic acids were observed, with a significant decrease in fumarate and gluconate levels and an increase in 3-aminobutyrate, citrate, and lactate. Increased levels of glucose and maltose were also found in RCC tissue, whereas sugar derivatives such as *myo*-inositol and *scyllo*-inositol showed decreased levels. Pathway analysis suggested dysregulation in amino acid, energy (TCA cycle, pyruvate metabolism), sugar, and glutathione metabolism pathways in RCC tissue. **Conclusions**: These results reveal the metabolic reprogramming related with the development and progression of RCC. Understanding these alterations provides important insights for improving RCC treatment strategies.

Keywords: renal cell carcinoma; tissue; metabolic reprogramming; metabolomics

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