Tipo	Periódico
Título	Metabolomics of 3D cell co-culture reveals alterations in energy metabolism at the cross-talk of colorectal cancer-adipocytes
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Programa/Curso (s)	Programa de Pós-Graduação Stricto Sensu em Ciências da Saúde
DOI	10.3389/fmed.2024.1436866
Assunto (palavras chaves)	Cocultura, Metabolômica, Neoplasia, Reto, Bioinformática
Idioma	Inglês
Fonte	Título do periódico: Frontiers in Medicine ISSN: 2296-858X Volume/Número/Paginação/Ano: 11, 1436866.
Data da publicação	10/2024
Formato da produção	Digital
Resumo	Colorectal cancer (CRC) is the third most incident and the second most lethal malignant tumor. Despite the recognized association between obesity and CRC, further clarification is necessary regarding the lipids that are overexpressed during CRC development. In this scenario, the combination of metabolomics and a three-dimensional (3D) co-culture model involving CRC tumor cells and lipids can enhance the knowledge of energy metabolism modifications at the cross-talk between colorectal cancer and adipocytes. This study aimed to screen potential metabolites in the 3D co-culture of CRC and adipocytes by investigating the metabolome composition of this co-culture released into the extracellular space, known as the secretome. Pre-adipocyte cells (3T3-L1), human colon carcinoma (HT-29), and the 3D co-culture (3T3-L1 + HT-29) were cultured for secretome obtention. Then, ultra-high-performance liquid chromatography coupled with high-resolution mass spectrometry (LC-HRMS) was employed to analyze the metabolomics of each secretome. Overall, 3,731 molecules were detected independent of the cell culture. When comparing the three cultures, 105 molecules showed a statistically significant difference in abundance between groups. Among these, 16 were identified, with a particular emphasis on six lipids (PG 20:0, octadecenal, 3-hydroxytetracosanoyl-CoA, 9,10-dihydroxy-octadecenoic acid, palmitoleic acid, and PA 18:4) and one amino acid derivative (acetylglutamic acid), which presented significant scores during the partial least-squares discriminant analysis (PLS-DA). Although it is too early to determine the possible impact of these molecules in a CRC microenvironment, these results open new avenues for further studies on energy metabolism at the cross-talk between colorectal cancer and adipocytes.
Fomento	CNPq (408680/2021-0) / APC Solicitado Pagamento USF