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Introduction: Cutaneous melanoma is currently considered the most severe skin neoplasm due to its high metastatic potential, with the lungs being one of the organs most commonly affected. The lungs, as an organ constantly receiving blood to facilitate gas exchange, are more susceptible to circulating tumor cells. Additionally, the lungs receive specific signals from the primary tumor, preparing and forming a pre-metastatic niche. It is well known that metastatic foci begin to form even before tumor cells acquire the ability to circulate within the body. A variety of proteins and enzymes act at the site to prepare the microenvironment, making it conducive for the arrival and growth of tumor cells. **Objective:** To obtain primary cultures from the explantation of lung tumor tissues in mice previously injected with B16F10 tumor cells; to establish a matrix that represents the proteome of lung tissue for affinity chromatography assays using the conditioned medium from the primary culture; to evaluate the proteome of the conditioned medium from the primary cultures as well as the proteome of proteins interacting with the matrix; and to obtain the set of proteins representing the interaction between lung proteins and tumor-secreted proteins at the metastatic site. **Methodology:** Using the B16F10 metastatic melanoma cell line, lung tissue was extracted from both control and inoculated mice (1×10^6 cells) to produce matrices with tissue extracts and secretome generated by the primary culture cell line. To obtain proteins interacting with the lung extracts, affinity chromatography was used, eluting the secretome proteins. SDS-PAGE was performed for protein identification, and mass spectrometry will be conducted. **Results:** It is expected to identify secretome proteins from the primary culture that have a higher affinity for metastatic lung proteins compared to healthy lung proteins. **Conclusion:** This study aims to provide insights into how the primary tumor interacts with pre-metastatic lung tissue and identify the proteins involved in the formation of metastatic foci in the lungs caused by cutaneous melanoma.

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