Hepatocellular carcinoma (HCC) is one of the leading causes of cancer-related deaths worldwide, and its development is closely linked to chronic inflammation. This cancer is characterized by significant biological heterogeneity and a clear gender disparity—it occurs much more frequently in men than in women. Despite progress in diagnostics and treatment, the mechanisms underlying the initiation and progression of HCC, as well as the variability in patient responses to immunotherapy, are still not fully understood. The aim of the project is a comprehensive molecular, metabolic, and immunological analysis of the process of liver carcinogenesis, with a focus on identifying the impact of chronic inflammation on cancer initiation and development. In this research, we will use a mouse model of chemically induced liver cancer, in which neoplastic changes develop with histopathological features similar to those observed in humans. Analyses will be performed at different time points, allowing for the identification of key stages of tumor transformation and the assessment of sex-dependent differences. During the project, transcriptomic analyses at the single-cell level (scRNA-seq) and spatial gene expression profiling (spatial transcriptomics) will be performed, enabling the assessment of cellular heterogeneity, plasticity of cellular states, and interactions within the tumor microenvironment. Subsequent stages will involve analyzing the effects of chronic inflammation on DNA repair mechanisms and epigenetic modifications, to identify signaling pathways and transcription factors critical to carcinogenesis. We will also investigate liver cell metabolism during tumor progression, as well as the immune response—including immune cell infiltration, activation, and cytotoxic function. The final stage of the project will evaluate the effectiveness of immunotherapy with immune checkpoint inhibitors (anti-PD-1 and anti-CTLA-4), depending on the stage of cancer progression and sex. This project aims to provide new data on the molecular mechanisms of HCC development and to identify potential biomarkers and therapeutic targets for liver cancer treatment.