Glioblastoma (GBM) is the most aggressive and deadly form of brain cancer, known for its rapid growth, diffuse infiltration into healthy brain tissue, and resistance to conventional treatments. Under the microscope, GBMs reveal a chaotic architecture composed of poorly differentiated astrocytic cells exhibiting nuclear atypia, high mitotic rates, necrosis, and microvascular proliferation. Despite intensive treatment, including surgery, radiotherapy, and chemotherapy, median patient survival remains dismally low—typically no more than 16 months. This sobering statistic reflects the profound complexity of GBM biology.

A central challenge in GBM research is the incomplete understanding of the molecular mechanisms which drives tumor growth and resistance to therapy. One emerging factor of interest is *hypoxia*, that is low oxygen level within the tumor. Hypoxia is more than a passive consequence of rapid tumor expansion—it actively shapes tumor behavior. By triggering pro-survival and pro-angiogenic pathways, hypoxia reprograms glioma cells to adapt, invade, and resist treatment. Importantly, it drives the transition to the mesenchymal GBM subtype, which is associated with enhanced aggressiveness and worse prognosis.

Within the hypoxic tumor microenvironment—an intricate network of cancer cells, immune infiltrates, signalling molecules, and structural components—cells begin to remodel the extracellular matrix (ECM). An underexplored feature of this adaptation is the secretion of *collagen*, a major structural protein, by specific tumor cell populations. Collagen not only reinforces the physical architecture of the tumor but also promotes the formation of new blood vessels (micro-angiogenesis), creating a vicious cycle of tumor expansion and therapy evasion.

The proposed project addresses a critical knowledge gap by focusing on the role of *COL family genes*, which encode various types of collagens in hypoxia-driven GBM progression. Although early studies have implicated genes such as *COL1A1* and *COL6A3* in hypoxic GBM cell lines, we lack a detailed map of how collagen-secreting cell populations function within real tumors—especially at the single-cell level. Using cutting-edge transcriptomic technologies, this research will identify the gene expression signatures of collagen-producing cells under hypoxic stress and explore how they contribute to the malignant transformation of glioma cells and the reorganization of their microenvironment.

The results of this study aim to transform our understanding of GBM. From a biochemical perspective, it will provide valuable insights into how the ECM remodeling impacts the fundamental behavior of tumor cells. Clinically, it may lead to the identification of new molecular targets for therapies designed to disrupt the tumor-supporting ECM—potentially improving treatment outcomes for patients with this devastating disease. Furthermore, by integrating transcriptomic data with knowledge of tumor biology, the project supports a shift toward precision oncology, where targeted interventions are guided by the molecular profile of each tumor.

This research represents a promising step forward decoding the biological intricacies of glioblastoma and offers hope for more effective and individualized therapeutic strategies.