Glioblastoma multiforme is one of the deadliest diseases affecting mankind with an average survival of 15 months despite aggressive, multimodal treatment. This dismal prognosis arises, at least in part, from an extensive migratory capability of GBM cells that disseminate throughout surrounding neural tissue. Our proposal focuses on mechanisms responsible for this migration. One of the genes that participate in this process is doublecortin (Dcx), primarily found in migrating neuroblasts in developing CNS. Several studies addressed its role in GBM cells' migration albeit their results as well as conclusions are contradictory. It is likely that these discrepancies relate to highly heterogeneous nature of GBM with a number of clones present within a single tumor that might significantly differ in their phenotypes. The majority of aforementioned studies were based on existing glioma cell lines that implies clonal selection and thus hampers the evaluation of Dcx role in GBM biology in vivo. Therefore in our project we propose a novel migration assay based on chicken embryos. It ensures more versatile microenvironment when compared to classical cell cultures and allows tumor cells extraction at a given time with high reproducibility of the results. Implementation of this model should also facilitate an evaluation of probable differences in migratory capabilities between genomic subtypes of GBM defined in The Cancer Genome Atlas (TCGA) study. This important initiative defined four different subtypes of GBMs: proneural, neural, mesenchymal and classic based on genome profiling. To our best knowledge our project is the first to date that addresses possible differences in migratory patterns of different glioma subtypes.

Results of our proposal should, first of all, allow a full characterization of a novel migratory assay that we propose. The implementation of the assay should result in detailed description of the relationship between migratory capabilities of GBM cells and Dcx expression and prove the foreseeable correlation between GBM genomic subtypes and migratory patterns of their cells. Moreover, the experiments put forward in our proposal might provide a theoretical base for development of a novel biomarker of tumor's cells migration into surrounding brain tissue. It should in turn facilitate stratification of brain tumor patients into therapeutic subgroups with more targeted therapeutic protocols (personalized medicine).