EG-10. LONG NON-CODING RNAs IN GLIOBLASTOMA
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Glioblastoma (GBM) is the most common, aggressive and incurable primary brain tumor in adults. Genome studies have confirmed that GBM is extremely heterogeneous with many genetically different subgroups. Consequently, there is much current interest in epigenetic drugs that may be active across genetically distinct tumors. In support of this, some epigenetic drugs has recently shown efficacy against several cancers including glioblastoma. Much recent interest has also been devoted to long non-coding RNAs (lncRNAs), which can modulate gene expression regulating chromatin architecture, in part through the interaction with epigenetic protein machineries. To date, however, only a few lncRNAs have been studied in human cancer. We therefore embarked on a comprehensive genomic and functional analysis of lncRNAs in GBM. Using the Helicos Single Molecule Sequencing platform glioblastoma samples were sequenced resulting in the identification of hundreds of dysregulated lncRNAs. Among these the lncRNA HOTAIR was found massively increased in GBM. This observation parallels findings in other cancers where HOTAIR’s increased expression has been linked to poor prognosis due to metastatic events. Interestingly, here we show that in glioblastoma HOTAIR does not promote metastasis, but instead sustains the ability of these cells to proliferate. In fact, we demonstrate that HOTAIR knockdown in GBM strongly impairs cell proliferation and induces apoptosis in vitro and in vivo. Further, we implicate HOTAIR in the mechanism of action of certain epigenetic drugs. In summary, long noncoding RNAs (newly discovered epigenomic factors) play a vital role in GBM and deserve attention as entirely novel drug targets as well as biomarkers.