Study of the human QKI gene, a susceptibility gene for schizophrenia disease

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Schizophrenia is a psychiatric disorder with a prevalence of 1% in the population characterized by delusions, hallucinations, reduced interest and drive, altered emotional reactivity, and disorganized behavior. A recent study at a single large family from northern Sweden has shown the quaking homolog, KH domain RNA binding (mouse) (QKI) gene to be involved in schizophrenia.

The QKI gene has been studied in the mouse and is thought to play an important role in myelination, regulating mRNA levels of different genes involved in myelin formation. Myelin is made of glial cell membrane that wraps around neurons, isolating parts of the axon from the extracelullar medium. In the central nervous system oligodendrocyte cells are involved in myelin production. Multiple studies support the idea that myelin abnormalities are involved in the schizophrenia disease.

The aim of this study was to study the QKI gene in human oligodendrocytes, promoving oligodendrocyte maturation (only mature oligodendrocytes produce myelin) and modifying QKI's expression in order to evaluate QKI's effect on other myelinationrelated genes. I modified QKI expressions using siRNA. siRNA is a small oligonucleotide which has a complementary sequence to an mRNA target for a particular gene, therefore binds to the mRNA in the cell inhibiting its translation. To promote oligodendrocyte differentiation I tested two different media, but both of them were unable to prove oligodendrocyte differentiation during a period of 7 days. Surprisingly the immature oligodendrocyte cells I were working with showed Myelin Basic Protein (MBP) expression although MBP is a gene expressed only in mature oligodendrocytes. QKI expression levels were decreased in immature cells and MBP mRNA levels were analyzed, suggesting that MBP expression increases in these cells. I also decreased GAPDH mRNA levels, showing that QKI mRNA levels dropped in a similar proportion. Since GAPDH enzyme catalyzes an important energyyielding step in carbohydrate metabolism it is possible that QKI expression could be hindered due to the metabolic stop in the cell.

The lack of success in oligodendrocyte differentiation hindered the progression of the study and therefore the goals that were established at the beginning could not be reached. I have made all the experiments in human oligodendroglioma (HOG) cells due to their ability to grow indefinitely, but they are very difficult to differentiate. The continuation of the present work should include further studies in HOG cells from a different source, another cell line or primary cells from rat or mouse.

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