

Influence of Chemotherapeutics on Brain Cancer Cells using DNA Microarray
Gene Expression Monitoring
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Genetic disease is often caused by genes which are inappropriately transcribed -- either too much or too little -- or which are missing altogether. Such defects are especially common in cancers, which can occur when regulatory genes are deleted, inactivated, or become constitutively active. The earliest and most common known genetic event in a special type of brain tumors, so called astrocytic gliomas is the mutation of the

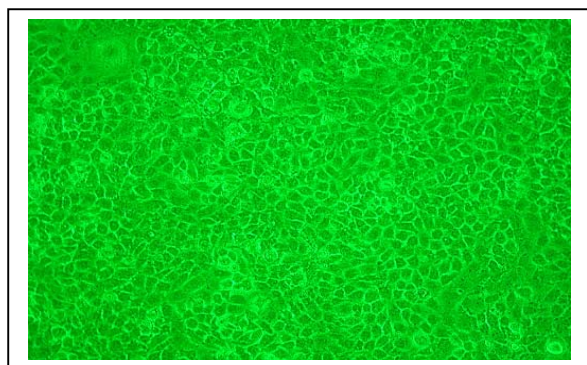


Fig 1: Cell culture of LNZ308.

tumor suppressor gene *p53*, which leads to the production of aberrant p53 proteins that have lost tumor suppressor activity. This kind of mutation is represented in the cell line LNZ308 whereas LN443 is *p53* wild-type. We examine the different gene expression patterns of these cell lines to get a clue of the possible regulatory role of the tumor suppressor gene on the other genes and in addition to that we examine the influence of different anti-cancer drugs on these glioma cells reflected by their gene expression patterns.

While the commonly used cisplatin

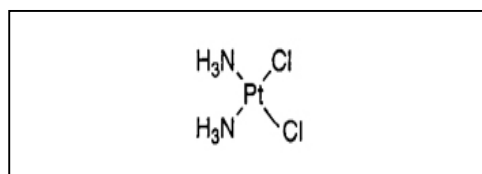


Fig 2: Molecular structure of Cisplatin.

as a chemotherapeutic agent showed some clinical promise in the treatment of glioma, the problems encountered with delivery and

toxicity among others have meant that it is no longer a drug of choice for this disease.

A novel platinum compound, BBR3464,

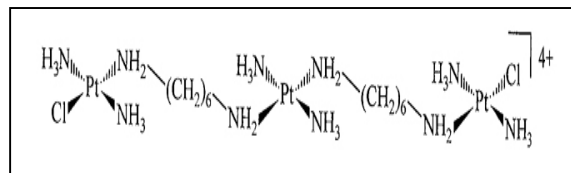


Fig 3: Molecular structure of BBR3464.

which is based on a trinuclear structure, causes different types of DNA interactions than cisplatin, and also has vastly superior efficacy and pharmacological characteristics. In order to determine the molecular nature of the different cellular responses observed with different chemotherapeutics, we are studying the gene expression profiles of treated LNZ308 and LN443 cells using DNA microarrays.

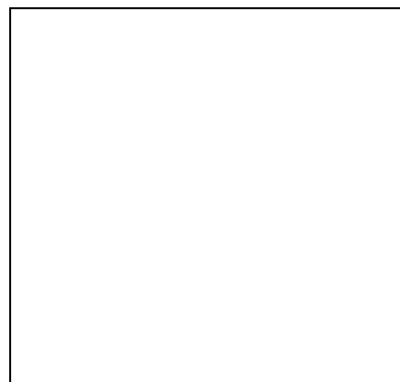


Fig 4: Scanned image of a DNA microarray.

DNA microarray technology allows the simultaneous determination of the expression level of tens of thousands of genes. There are several different varieties of DNA microarrays. Basically they are small glass slides on which we spot thousands of genes in a regular array or layout. The genes are present as small gene fragments known as oligonucleotides. The particular chip that we use is the C3B 10k Microarray, where each gene is represented by a 50-base oligonucleotide and there are 10,000 genes in duplicates represented on the chip.