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Armed Epstein Barr Virus Gene Therapy of Human Medulloblastoma Clinical Trial Phase-II (100% Powerful and Fully Treated Vaccine)

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Abstract

Sample of ten patients defected with medulloblastoma and rhabdomyomas are selected to treat by heavily armed vector (Epstein Barr Virus with catalase enzyme supported with long chain of phosphate group synthesized in self-funded laboratory with esterase enzyme).

Ten samples of patients were invited from Jordan University of science and technology university hospital and king Hussein cancer center of these ten samples five defected with primitive neuroectodermal tumors (medulloblastoma) and the other five defected with primary tumors in infants and children of heart (rhabdomyomas). Nine of ten were selected to expose to catalase enzyme of one to six genes of the vector capsid envelop protein and it takes seven days; the last is exposed to insertion of phosphate group chain inside tumor cells by stereotactic microinjection armed (EBV) by this group inside brain tumors (medulloblastoma) and primary heart tumors (rhabdomyomas),other ten exposed directly forward to acetyl esterase gene by viral vector instead of seven and eight genes which are defected genes for human as considered other expose to three stages with effectively potential Armed vector of medulloblastoma and rhabdomyomas.

This study showed significantly prolonged median survival time of 10 days for the first exposing of armed catalase enzyme in order to get catalysis procedure inside tumors itself when it reacts with c-AMP then to destroy both tumors (case of control inside tumor cells and the reagent is PCR) which can indicate the tumor controlling when the bands get the same size on gel electrophoresis 95 Kbp; the second case is using long armed chain p-group which allow to help catalase enzyme to get catalysis procedure inside brain and heart then it will react with c-AMP to destroy SHH and NOTCH genes in medulloblastoma in the brain and rhabdomyomas in the heart and it takes 25 days. The final result takes 27 days and it started from the beginning of consisting 3 factors which are 1-catalaseenzyme located from gene 1 to 6 of the vector 2-phosphate group inside tumor cells via vectors 3-estrase gene. all of these genes collected together in a single chain with 5–p-group to construct a strong-Armed vector to do as a surgical neurooncologist in the operating room of primitive neuroectodermal tumor and primary heart tumor in infants and children to remove fully seized of tumors in both cases which has 10 patients of them by acting as precursor of c-AMP to fully destroyed SHH and NOTCH genes without altering the expression of 5-p-group; catalase enzyme; esterase enzyme in the tumor cells.

We conclude that Epstein Barr Virus which Armed by catalase gene; 5 prime-p-group; esterase gene solved the biggest problem in the world medulloblastoma and rhabdomyomas in tumors in cerebellum and heart of infants and children without any toxic side effect of both diseases' treatment. The prolonged survival time for 10 samples receiving this dose by armed vector appeared that no neurological symptoms in both tumors brain and heart.

Keywords: Epstein barr virus • Medulloblastoma • Long chain of phosphate group • Esterase gene • Rhabdomyomas, *EBV-FUNJAN1* genes

Introduction

Medulloblastoma is the most effective tumor in children and infants for more than 24 years in the past century [1]. As it effects cerebrospinal fluids of the midbrain it can cause several symptoms inside the body of patients like suffering in breathing; hard swallowing; seizure in the feel of patients; headache; diarrhea; pains in neurons; vomiting for few days and finally hard in extra features like extraction of fesses and urine [2]. In the past 2 years Prof Dr. J. Pilkington used acetyl esterase gene in therapy of glioblastoma by Baculo Virus (bcv) vector. And he had found that the deactylation of glioblastoma by esterase gene lead to apoptotic cell division of glioblastoma multiform which lead to improve survival time mean of patients with glioblastoma multiform to 5% of 720 cases per person. From this mean we found the esterase gene is the best factor with Epstein Barr Virus as a vector tool to make a reaction of acetylating procedure medium in finding a solution for treatment of primitive neuroectodermal tumors (medulloblastoma); and primary tumors in infants and children of the heart (rhabdomyomas). What we have is to find a fully treatment for both tumor diseases by Armed Epstein Barr Virus vector with acetyl esterase gene which sources from big animals' meat like cow; sheep; horse; and different species of plants. In our clinical trials phase Ⅱ medulloblastoma is fully treated by making medium inside tumors tissue of medulloblastoma and rhabdomyomas; this medium is consist from different enzymes; long chain of phosphate group; deletion of some genes of Epstein Barr Virus 7 and 8 genes which consider defecting genes for human like lymphoma Hodgkin s; Burkett s lymphoma; nasopharyngeal carcinoma and conditions associated with human immunodeficiency virus (HIV) such as hairy leukoplakia and central nervous system lymphoma. Other else is to build a series long chain of phosphate group in my laboratory at Jordan (see the procedure in material and methods); also to destroy both SHH and NOTCH genes in both tumors by catalase enzyme which found in (1 to 6 genes) of Epstein Barr Virus nucleosomes and has (520 bp) in length; other issue it can cause deactylation process by catalysis procedure enzyme which contained in (16 to 24) of procedure zone of double strands DNA of Epstein Barr Virus genome it was in length (1 × 103 Kbp); other thing is 5-p-group long chain synthesized in my laboratory in Jordan (6000 mcg) in shape which could be construct by 5 hydrogenase of being southern blotting technique in molecular biology laboratories anywhere in the world. The acetyl esterase gene done isolated from plants; animals and microorganisms; it will act as surgical neurooncologist in the operating room by catalysis helicase gene which located in (25 to 32) genes of nuclear envelop zone of Epstein Barr Virus vector and (810 bp).the acetyl esterase gene is (9000 mcg in shape and 510 kbp in size); what we have done is to insert it into capsid nucleosomes by phosphate electroporation procedure (region of 7 and 8 genes; genes of defective PD in human); and this is was the first study and

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discovery in my laboratory (if reach for this evidence please call 7 and 8 genes; *EBV-FUNJAN1*).acetyl esterase gene is large in shape (9000 mcg) and large in size (510 kbp); we can insert this enzyme in empty envelop (*EBV-FUNJAN1*) region. The ATA closed region of Epstein Barr Virus cosmid protein it contains (320 bp) in length and the most effective region in tumor diseases in human. Finally open medulloblastoma insertion sites the biggest in size and (504 × 102 Kbp) and long in shape (1 × 1011 mcg).

Approach

Cosmid construction

Cosmid become the most powerful vector for treating different brain tumor diseases like medulloblastoma and heart primary tumors in infants and children rhabdomyomas (soft tissue of both tumors). What we will have is to create a constructed cosmid of envelop protein of Epstein Barr Virus envelop protein and this result lead to isolate genes 7 and 8 (defective genes for human of Epstein Barr Virus to call them *EBV-FUNJAN1* gene); to put acetyl esterase gene instead of them by phosphate electroporation system. In this case we will include no pathogen diseases will come from this virus otherwise to select them as a potent of mine background.

Patients study

10 samples were selected from both Jordan university of science and technology university hospital and king Hussein cancer centre were tested in different procedure weighed daily and examined for clinical and neurological symptoms; of these samples we test 5 samples in neurological disorder like Epstein Barr virus defective genes 7 and 8 or *EBV-FUNJAN1* and we found that they are not defected by *EBV-FUNJAN1* so we are going to the second step which represented by CT (enhanced T1-weighted coronal and sagittal MR images) and no one defected with other tumors. Other tests like cystic fibrosis test were done to include no interaction when the results observed.

Samples preparation

Tissue samples were observed (medulloblastoma and rhabdomyomas) in immunohistochemistry and DNA samples test. After observation of tests we found both of tumor diseases appear roseate form in induction (medulloblastoma and rhabdomyomas and 75 Kbp in amplified PCR and 72 Kbp in rhabdomyomas; so we observed that no contamination in these samples.

Western blotting

In this issue we use western blotting to reach to 5 of genes which are 1-Helicase 2-estrase 3-catalase; the most important genes inside the vector (Epstein Barr Virus).

Northern blotting

In this case we use this technique to get heavy bands of tumors disease like Epstein Barr Virus 7 and 8 genes which I called them as *EBV-FUNJAN1* (27 Kbp for each one).

Southern blotting

It is used to discover catalysis procedure of mixture inside medulloblastoma which consisting of dehydrogenase gene which come from long chain of phosphate group (synthesized in my laboratory) and Armed virus by that chain (long series-6000 mcg in shape); with phsphodiester bonds (5 bonds in shape in the helix of the loop).

Dehydrogenase enzyme catalysis

In this issue the Epstein Barr Virus Armed with phosphate group can make catalysis procedure by effecting Helicase enzyme and this is the first phenomena in surgical neurooncology field because it looks like surgical neurooncologist in his made when the reaction inside medulloblastoma tumor cells react with phosphate group; in this case phsphodiester bonds will act as seizure by reacting with helicase enzyme (interfering between H-bonds and covalent bonds at the level of electrons in the orbits lead to destroy H-bonds in helicase enzyme then it will create a medium inside tumor cells without any reaction of side effects.

Dehydrogenase reagent procedure

In this case the medium will act as neurosurgeon inside surgical neurooncology operating room and we can indicate this reaction medium by enzyme histochemistry and it was the hydrogenase in soft tissue of defected cerebellum (medulloblastoma) and primary tumor of heart (rhabdomyomas).

Histological evaluation

The tumor size was calculated using formula for an oval $A = \frac{1}{4}\Pi r1r2$, with r1=length and r2=width of the tumor in one slice. Necrotic areas in the mass lesion, abnormal vessel spread and cell migration into surrounding brain tissue were examined by a neeuropathologist blinded to the therapy and scored semi quantitatively. The amount of confluent necrosis in the tumors was assessed by a score from 0 to 3 (0-no confluent area of necrosis, 1-mild amount, and 2-moderate, 3-marked. Vasculature abnormalities included endothelial proliferation of small vessels or increased vessel density, microhemorrhages and dilated vessels [2] red blood cell pooling [3] similarly scored. Tumor cell spread was also described from 0 to 3, evaluating spheroidal growth, uneven tumor boundaries [1], perivascular cell cuffing [2] and invasion into CSF compartments or leptomeningeal spread [3]. The mitotic division figures were counted in two 200x power fields of a viable tumor area; the results were averaged and reported as number per field.

Monoclonal antibody

This technique was used to as a reagent to find different expression of enzymes of inserted genes in the vector by immunostaining of these enzymes which are; 1-catalase 2-hydogenase 3-helicase 4-actyel esterase gene. All conditions were performed in my lab at Jordan.

Statistical analysis

Survival and symptom-free survival estimates were computed using the Kaplan-Meyer method.

Results

EBV-FUNJAN1* new call for genes 7 and 8 defective genes of Epstein Barr Virus

EBV-FUNJAN1 new call for genes 7 and 8 defective genes of Epstein Barr Virus In this issue we estimate that genes 7 and 8 of Epstein Barr Virus is causing genes of human diseases (lymphoma Hodgkin's, burkitt's lymphoma ,nasopharyngeal carcinoma and conditions associated with Human Immunodeficiency Virus (HIV) such as hairy leukoplakia and central nervous system lymphoma); for that purpose we isolate these genes by southern blotting; by phosphate electroporation we insert acetyl esterase gene in construction cosmid envelop protein.

Epstein barr virus cosmid of image

In this phenomena we construct some genes inside Epstein Barr Virus in order to get acceptance for neurooncologist surgery room of operating; important factors is catalase gene with phosphate group long chain which incubate tumor cells in a medium (please see the material and methods).

Epstein barr virus as a vector tool of phenomena

In this phenomena the vector during his react with human medulloblastoma inside brain it will act as surgical neurooncologist by reaction 3 types of chemist basic units which are 1-catalase 2-hydrogenase 3-acteyl esterase gene. All of these basic units will act a cerebrospinal fluid medium by long chain of phosphate group and esterase gene with catalase will act as seizure by making a catalysis procedure inside medium of tumor cells zone after expression of these genes inside of defected cells by medulloblastoma and rhabdomyomas; in other case it would act as neurosurgeon in operating room.

Prolonged survival of human treated with vector viral gene therapy

10 patient human samples were exposed directly to Arm Epstein Barr Virus vector injection it in patients in operating room for 25 days. After one month we got these results. No need for median Kaplan-Meyer curve because the probability is p=0 in significant and no need for statistical analysis (the samples out of 20) there is no neurological symptoms after get the treatment. No need for tumors necrosis alpha due to it seems 1-no necrosis 2-no vessels score 3-no spread 4-anywhere no mitotic division were mentioned.

Discussion and Conclusion

The present study identifies 100% powerful vaccine of human medulloblastoma and rhabdomyomas by Armed Epstein Barr Virus gene therapy. We have got 10 samples of patients from both Jordan University of Science of Technology university hospital (JUST) and King Hussein Cancer Center (KHCC) diseased by both medulloblastoma and rhabdomyomas to treat them by Armed Epstein Barr Virus on 3 steps. By self-defending treatment against itself by delay genes 7 and 8 from its genome otherwise to construct a tumor inside virus itself because genes 7 and 8 contain capsid structure of Epstein Barr Virus and we have the following result:

The structure contains some genes affect the virus itself like helicase especially in gene 7 and gene 8. In this test if we delay these 2 genes we can get capsid without helicase (the reason of causing tumors of Epstein bar virus). Other thing is to create long chain p-group in tumors like medulloblastoma and rhabdomyomas and arrange between Epstein Barr Virus (without helicase gene)and the long chain of p-group inside tumors (medulloblastoma and rhabdomyomas) of human patients (infants and children).in this way we get and show these results. No capsid were performed in medulloblastoma and rhabdomyomas that containing self-defending virus (without 7 and 8 genes of Helicase). The p-group is acting as a complimentary strand with capsid (without 2 genes) genes of helicase. In this case the virus will act as a macrophage with T associated cells of immune system of the brain (microglia cells). the catalase of Epstein Barr Virus contain in 1 to 6 genes of the capsid protein envelop and he can do a catalysis of tumors in different ways; it can be elimination process of tumors cells by c-AMP, and SHH, NOTCH in this way it could do as precursor for elimination process and the step as follow: When the virus injected inside tumors of the brain and heart (medulloblastoma and rhabdomyomas)it will act as precursor of these tumors especially NOTCH and SHH and this will react the C-AMP to make a catalysis process of tumors even in brain or heart and this will delay both NOTCH and SHH genes and stop them from acting itself in new necrosis or vessel score or spread or mitotic division (it will not eliminate the tumors but the tumors will be destroyed fully 100%) in this step we will include no signs , no symptoms ,no criteria's of tumors diseases. by this way we can get healthy samples without test for another steps. and this is was the first stem of elimination both medulloblastoma and rhabdomyomas. after the catalysis procedure we will insert acetyl esterase gene to tumor cells inside brain and heart by injection a genetic engineered virus (EBV) contain this gene as it follows in this procedure; when we delay genes 7 and 8 from Epstein Barr Virus by southern blotting way [4-10] we cover these region by armed acetyl esterase gene by northern blotting [10] in this way it will be genetically engineered vector contains acetyl esterase gene, catalase genes and long chain of p-group inside the tumor cells.

When acetyl esterase gene reach by vector to tumor cells it can be act as neurosurgeon (scalpel) in this way it will remove all tumor cells of medulloblastoma and rhabdomyomas by the following way; at the beginning it control the tumors growth by manipulated capsid and measure how we have of these tumor cells from signs by PCR we can know how he is control then once we get equal lane this is mean we control the growth. When the virus reach manipulating zone which supported by p-group it will act as seizure by the way it will act as surgical neurooncologist by it seizure but how we can explain this procedure.

When the vector insert itself to tumor cells his genetic code let the acetyl esterase gene to do an acetylation mechanism supported by phosphate group chain (synthesized in the lab after that the reaction will give negative results for tumor cells by the mean it will remove all the signs of tumors growth; also it will act as precursor for phosphate group to give highly top reaction give the acetyl esterase enzyme its ability to do surgical neurooncology operating room. it can be done when it react with catalase enzyme (genes of 7 and 8 of EBV vector)as complimentary surgical neurooncologist like nurses or other equipment but how this reaction work? the catalase will activate the process of acetylation with the armed p-grou acetylation will react with c-AMP which will act as precursor then it will damage SHH and NOTCH for that reason no signs will appear and this will be diagnosed by western blotting. This article based on Epstein Barr Virus which Armed by long chain of phosphate group; acetyl esterase gene; catalase enzyme; hydrogenaze enzyme; *EBV-FUNJAN1* gene instead of harmless genes 7 and 8 of (EBV) can solve the biggest problem in tumor of the brain, medulloblastoma, and heart tumor in infants and children, and rhabdomyomas which could be consider like vaccine for both diseases that I hope to produce this type of drug in companies and victories.

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