Metabolism of tay sachs disease

Since evolutionar, time living organism have always strives to maintain survival capability that further prolong their lives. Build in internal environmental surveillance, known as homeostasis had always enhance the organism ability to detect any damage and fix, the mistake before any substantial amount of damage can occurs. Normal function of this system is always under threat from pathogen and cell defects within the system that lead to condition that is characteristics as disease. The state of disease call Tay-sachs will be explored from the metabolic aspect of recurrent, to the medical or clinical events.

According to literature, Tay-sachs disease is known as “ congenital ” neurodegerative disease that is cause by malfunction of lipids synthesis during cellular respiration or metabolism. In a normal cell lipids synthesis occurs in two functional states that alternate between degrading and synthesis of lipids. Changes to this particular normal cell programs is the results of a lipids condition that is called lipidose or diseases cause by the accumulation of lipids molecules in the body. From the biochemical stand point Tay-Sachs disease is causes by a number of enzymes, cell and metabolic activities that are no longer capable of performing their function that would have otherwise be present had it not been dysfunctionality of these specific enzymatic reactions. The enzymatic cells known to have involved in path way leading to creation of Tay-Sachs disease slightly varies but overall their cellular activities are the similar. According to (Beutler, E), article entitle “ The Biochemecal Genetics of the Hexosaminidase sytem in man”. Two members of carbohydrates sugar from a complex cell of glycolipids had been known to have causation of Tay-Sachs disease

metabolic enzymes. The two carbohydrates are labels as ” N-acetylgalactosamines and N-acetyl-neuraminic acid” the two branches of sugar are the terminal point of gaglioside phospholipids in the cells. Both N-acetylneuraminic and N-acetyl acetyl galactosamines under normal circumstances are fill with abundance of enzymes that cleave the terminal points of the gangliosides molecule of “ N-acetylneuraminosylgalactol-glucosylceramide”. The lack enzyme to catalyze the reaction with the above respective enzymes can results in “ ganglioside accumulation” in the brain of the individual with any of the deficient enzymes. In the article entitle “ Biochemical characterization of the GM2 gangliosidosis B1 variant” the metabolic characteristics of the of the Tay -sachs disease is dictate by action of the different enzyme preferably called “ Beta hexosaminidase” or (Hex). Lysosomal or isoenzymes Beta hexosaminidase, according to (tutor, J. C) comes in two conformational parts the “ hexosaminidase alpha, beta and hexosaminidase that contain two beta subunits”. The system of the four different subunits contain within the hexosaminidase are the content of the enzymatic activities of the cell metabolism to catalyzed the reaction. So under normal animals’ body physiological, homeostasis internal check points and catalytic enzymatics reactions, the Isoenzymes beta N acetylhexosaminidase will break down or hydrolyzed the reaction of the gaglioside activities.

This can result in disappearance of this nerves cell lipid that would have increase its byproducts at the level of the nervous system. Because isoenzymes beta N acetylhexosaminidase is divided into two subunits of enzymes mention early as beta, alpha and beta, beta subunits, each

member of the enzymes is deploys to perform it respective function, given that system is operating under normal circumstances. For example isoenzymes beta N acetylhexoaminidase level a or containing subunits a will “ participate” in the action of “ degradation of the following molecules glycoproteins, gylcolipids and glycosaminoglycan” this will results in the breakdown of “ Beta gylcocidic links of betan N acetylgulocosamine and beta N acetlygalactoamines”. Within the subunits of the isoenzmes beta N acetylyhexosaminidase, subunits apha and beta contain polarity charge that gives them the ability to bind to specific types of the cell, therefore leading to a desirable cell performance outcome. For instance, the lpha subunits contain an “ active side that is negatively charge”, and small amount of “ neutral charge”, but the beta subunits contains only “ neutral charges”. The variants that is cause by the polarity, determine the side of the lipids cell each subunits will bind to resulting in the activation of isoenzyme beta N acetylhexosaminidase at the time of catalytic reaction events. In the case of alpha a subunit, which has a minus or negative charge, according to (tutor J. C) the “ gaglioside bind alpha a subunits causing hydrolyzes of gaglioside” during enzymatic catalasis, at the same time the subunit beta does not bind to any of the gaglioside, because there is no attractive charges that would cause the two to bind to each other. The properties of the beta subunit liberate beta subunits from the causing any type hydrolization even when alpha subunit is not present.

The beta subunit property explains the lack of gaglioside breakdown in the present state of beta subunits. The present of Tay-Sachs disease will result from two variables, according to the literature studies showen the two

variances are label as “ B and B1 variant”. Variable letter B is going to be deficient in isoenzyme beta N acetylhexosaminidase, meanwhile letter b with one is going to have isoenzyme beta N acetylhexoaminidase that lack a “ cataylix or mutated isonzyme”. The mutation will cause a non functional side chain of the acetyhexosaminidase from reaction with gaglioside side of negatively charge groups. In addition the mutation will specifically act on the “ gaglioside activator proteins” preventing the activator protein from binding to the substrate of side of the isoenzyme. The general consequence, action of this protein, added with behavior of both gaglioside products and isoenzyme beta N acetylhexosaminidase results in biochemistry path way of gaglioside not being hydrolyzes by the enzyme resulting in a condition called the Tay-sachs disease.

Because the biochemical reaction that result in gaglioside build up is known, one is left to asked why would alpha and beta subunits of the isoezyme beta N acetylhexosaminidase would cause enzymatic catalytic deficiencies? From the genetics stand point this question can be answer base on nucleic acid genetics or genes component. According, to inherited health web side article, a person is bone with type two type of gene that are responsible for enzymatic catalysis of” beta-hexosaminidase genes call hexa”. The main altermate goal for the hexa genes in the cells, during cellular differentiation is to direct the hexa genes to produces or turn into beta hexosaminidase isoezymes. The actions of the hexa genes is comprise as a results of the mention in the cells, the mutation “ disrupt” the cellular machinery of the hexa genes from performing their normal cell functions. So the question a rise, how do someone get the hexa genes that is the causation for the lack of

hexosaminidase enzymatic deficiency in the cells? Given that mendellian genes flow dictate how genes are passed from one generation to the next generation, this question can be explained by following basic mendel, theory of inheritance. According to mendel theory of inherit ant of gene, for the individual to receive defective hexa genes deficient in hexosaminidase enzyme catalytic activities. Two events must occur in order for the organism to inherent the genes. Both parents of the organism mother and father must be a carried of the defective genes, for the gene to be passed on to the offspring or progeny. Which mean that both parents were heterozygote for the copy of the mutated gene and each must passed the bad gene or mutated gene copy of the gene to the child resulting in autosomal recessive alle. The inherent recessive alles copy of the gene is now present in two copies in the cells of the progeny organism. Because the gene pattern of inherent is directly in control, of the type cellular function, each genes is suppose to do in the cell, this is the reason the mutation of hexa genes is important in lysosomal enzymatic activities. So the question is how does a mutation that have cause a defective in the hexa gene lead to or related to Tay-Sachs disease? According to the article on Genes and disease from the nation center for biotechnology information, there is a direct correlation relationship between mutation on the hexa genes and neurodegerative disease that result in Tay – Sachs disease. Research showed that it is the hexa gen that “ code for the alpha subunit of the enzyme beta-hexosaminidase A”. During normal condition “ Beta-hexosaminidase a help to degrade a lipid called GM2 gaglioside, but in tay-sach individuals the enzyme is absent or present only in very reduce amount, allowing excessive accumulation of the GM2 gaglioside in neurons”. In addition research,

showed that the three component that are involved in tay sach disease are “ alpha subunit, beta subunit and G activator” it is believes that lack or low functioning of the alpha subunit of the “ hexosaminidase malfunctions leads to a toxic build up of the Gm2 gaglioside in the lysosomes” organel compartment of the eurkayotic cells.

The condition of Tay-Sachs disease as it related to the two form of organism both prokaryote and Eukaryote has not been indentify between these two organism. Either because there has not been any research done on prokaryote organism, regarding the present or the absent of the tay sach disease concerning the availability of tay sach in this population of organism, prokaryotes. Other plausible explanation, because prokaryote lack compartmentalized organelle that house content such as lysosomes , may just simple not present with this group. Since the pathway of the disease is dictate by the enzymatic breakdown of the in the lysosomal organelle prokaryote will not have this condition. In Eukaryotes within the organism, other than human, in mice the same type of GM2 gaglioside lipid that cause high level of lipid build up in human, was also indentify in mice. The “ activator proteins ” in mice is defective, therefore mice is not able to hydrolyzed fat storage in their systems resulting in neurological characteristics similar to those observed in human, however the condition is not called Tay-sachs. On the contrary, the conditions in mice also exhibit some differences with those condition observed in human. For example the lipid “ storage in mice is in the cerebellum and developed defects in balance and motor coordination”. The differences in mice and human are the results

of “ Gm2 gagliosidoses are species specific differences in the gaglioside degradation pathway”.

The actual illness, expression of the tay sach disease condition can be very debilitating, not only does the Tay-Sachs cause severe neuron damage but the segment of the population that effected tend to be young children. The national library of medicine and genetic reference home page define tay sach disease as “ a rare inherited disorder that progressively destroy nerve cell or neurons in the brain and the spinal cord”. Some the symptoms associated with the above definition, that result from the action of the tay sach disease include, ability of decrease in motor function such as running, walking sitting and jumping. Most of the above symptoms can be observed in children, particularly infant groups. As the child grow in age the prognosis of the disease stage, begin to progress at higher speed rate, the child develops symptoms such as “ seizures, vision, lost of hearing mental retardation and eventually paralysis”. This condition will result in loss of life for the individual person that is affected by the disease. Tay-Sachs disease is not only prevalence in the young or the infant group but can be observe in other groups such the adolescent to adult and the severity of the disease varies from the groups to and groups. The symptoms similar those observed in children are also observe in adults, specifically the “ weakness in muscles coordination characterizes as “ ataxia”. According to the research, Tay-Sachs disease is found to be less common in overall population of the society, but at the same time it is common with specific group of the populations. The availability of the disease with sub category of the population is attributes to genes behavior, since genes are passed on from one generation to next

generation. The literature agrees on the most common segment of population that Tay-Sachs disease is the most prevalence, members of “ Ashkenaki eastern and central European Jewish ancestry”. Also the other groups were the members of the “ north western Spain and northern Portugal”. It is important to mention that those group mention above are not the only affected groups but instead, region where a higher than expected incident rate can be seen. It is worthwhile to note that all human population of the world have case of the Tay-Sachs disease, except that symptom varies with within subpopulation.

Following, the present of the Tay-Sachs disease symptoms and diagnosis or testing must be carried out from the clinical point of view to determine the cause of tay sach symptoms or for any other disease for that matter. Base on the article entitle ” hexosaminidase deficiency” testing is apply to confirmed or disprove the present or absent “ beta hexosaminidase A enzymatic activity in the serum or white blood cells of the a symptomatic individual in the presence of normal or elevated activity of the beta-hexosaminidase B isoenzyme”. Lack of the normally high level of beta hexosaminidase in the blood or present in small amount would indicate the present of Tay-Sachs disease. This particular type of testing is sometimes refer to as “ biochemical testing” because the expert is searching for the level of the damage or inefficient enzymatic chemical processes. Other type of testing that is used some time would be “ carrier testing” and the testing is perform on groups, whom their one or two members of their family is known to be the carrier of the mutated gene in other heterozygote. Both

tests are effective in identifying the gene or the disease with the exception of each testing being specific to each condition.

Treatment and management of Tay-Sachs disease is difficult to apply due to lack of the therapeutic drugs to cure Tay-Sachs disease. Some of the expert recommendation is gear toward things like proper nutrition and large amount of fluid to keep the body from dehydration. Symptoms such seizures can be management by providing the patients with anticonvulsant prescriptions drugs, such as" benzodiaxepines, phenytoins or barbituarate". These drugs are use to maintain or manage the seizure part of the Tay-Sachs disease. Psychiatric drugs can be used for individual that are having metal episode these can drugs like antidepressant. According to the literature some treatments have showed a promising outcome, such treatment with " lithium salts and electroconvulsive therapy has been reported to be beneficial, at least in amenliorating for the period of the episode of psychotic depression".

Currently according to the literature there are some neuronal procedure being, investigate to find the cure for Tay sach disease. Some of the experimental produce included " central nervous system enzyme replacement therapy". The idea would be to find synthetic enzymes that will mimic the activity of the hexosamidase isoenzyme taking over the place or natural enzyme. In addition to genetic engineering of the organism cell such as mice can also be utilizes to treat " innovative treatment modalities". Other recent invention, such blocking the enzymatic biosynthesis activities of " glycoshingolipids of a GM2 gaglioside. Research indicates that these

ongoing experiment and successive result have not been achieved at this point.

Conclusion

Given that organism is bone with internal mechanism to fight out infectious, diseases once cannot estimate the important of knowledge base skill to solved problems. Although currently Tay-Sachs disease does not have therapeutic prevention, because of many research studies devote to this disease one hope, that there will be cure in the future. Because the resilience and persistence character of human being far out weight any challenges faces society. This was a interesting topic, which have result in learning some of the biochemical aspect of the disease from biochemistry at a cellular level.