



Connecticut Parkinson's Working Group Newsletter

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There are some interesting points to be made this newsletter: Part one of a two part article on different PD therapies, be they valid or not; an article in a recent newspaper in Oregon touting the benefits of a drug, already FDA approved for drug addiction, that seems to be at least neuroprotective in PD; a short article on why drinking green tea can be neuroprotective in the sense that it rescues nerve fibers the deadly plaque that deposits on the brains in so many diseases causing deterioration.

Again, I invite interesting article from anyone in the group; I will make every effort to include them Please, only send me proposed articles in electronic form, MS Word by far my first choice. Also, if you have any control, send your article "Text Only"—that is, with no formatting. We will do that.

DANCING WITH PARKINSON'S DISEASE

BROOKLYN Friday, April 25, 2008—For the millions of people who suffer from PD, life can be difficult. But a new, free program from a professional dance company is boosting people's spirits and their health. The Mark Morris Dance Group (MMDG) dances on many world stages; at their home studios in Brooklyn, there is a slightly different set of dancers!

The company holds free weekly classes for people with PD and their caregivers. The class is taught by MMDG faculty members and was initiated by Olie Westheimer, who founded the Brooklyn Parkinson Group. "There is no mention of PD or problems in this class," Olie Westheimer from Brooklyn Parkinson Group said. "It's just a dance class." It is a dance class that provides more than dance lessons.

Today's teacher Misty Owens says dance helps alleviate symptoms for many of the participants. "It helps them understand their body and relate to their body differently by taking the class," MMDG faculty Misty Owens said.

And always there's live music. "It's just wonderful," PD patient Donna D. said. "When people with PD hear the music, they can move when they can't normally move." Pamela Q. teaches a movement class on a different day of the week. She's a former professional dancer who herself developed PD. She's developed coping mechanisms based on her knowledge of dance and movement. She now teaches them to others.

"I find the body really responds to little challenges," Pamela Q. said. Studies say dance groups provide physical help, social and emotional support.

SOURCE: Eyewitness News (WABC) <http://abclocal.go.com/wabc/story?section=news/local&id=6104025>

Editorial Postscript: The CPWG is actively looking into getting a similar program instituted here in CT. We are not far enough along to say anything definite, but many threads are coming together, one of which reaches to Mark Morris and Brooklyn. If you are interested contact Stan; he is coordinating the several players that would make up the program, if it happens.

EDITORIAL COMMENT: *The following story provides an example of: a treatment for PD which, if successful, has an unknown cause; a drug that could be a life-saver for many people but has not gotten a clinical trial probably because of the profit requirement for big pharmaceuticals (I have been told that I might be somewhat cynical here—alas!); a drug that sounds like it should be much, much more widely known and is not, for reasons unknown; and finally, a case in allopathic (western) medicine that mimics homeopathy in the administration of lower rather than higher doses of its remedies. One wonders if many of us could be on lower doses of our medications and receive the same, or better, result. One is lead to ask: Who sets the dosage of a drug, and should this be an individual determination?*

N.B. *Please notice all the subjunctive references. I am aware that until proven otherwise, there is nothing but scattered anecdotal evidence to think that this may have some validity. Some might even think there are evil forces promoting LDN. Possible. I looked up Dr. Zagon; he certainly is a reputable physician and researcher from one of the top universities in the country. His endorsement means a lot.*

LOW DOSE THERAPY USING EXISTING DRUG A POTENTIAL SAVIOR FOR PWP

Mail Tribune (Oregon) March 10, 2008 6:00 AM When Destiny Marquez finds a good thing, she wants other people to know about it. These days she has been talking about a drug called Naltrexone (NTX). It is been widely used to treat opiate addiction. Marquez came across it while she was trying to help her father, Bentley Lyon, who's been struggling with PD for 18 years. His symptoms had been increasing, and he started to decline rapidly after suffering a stroke during surgery.

A friend had told Marquez that she'd heard some PD patients were getting relief from their symptoms by taking extremely low doses of NTX, Marquez and her mother, Elizabeth, balked. Although the drug had been tested and approved by the federal FDA for addiction treatment, it had never been tested for treating PD. They said "No".

When Bentley's condition continued to deteriorate, mother and daughter asked him to give LDN a try. By then they had done some research on their own, and learned that the drug was gaining favor not only with PWP but also as a treatment for other diseases, including multiple sclerosis and Crohn's disease. Marquez said her father started taking 3 mg a day late in 2004, far less than the 50 mg that's prescribed for addiction treatment. It was like a miracle," she recalled. Marquez said the plasticity in her father's left leg disappeared over several days, and his caregiver said he stopped complaining about back pain.

Speech is difficult for Bentley, 78, a former Marine and marathon runner who worked as a forester and wrote two mystery novels, but he said LDN "stopped the progression" of his symptoms. NTX apparently works by stimulating the body's own immune system, said Dr. Ian Zagon, a professor of neural and behavioral sciences at Pennsylvania State University. "It is simple," he said, "but it took a while to sort out."

See the file at which announces a clinical trial for LDN and Crohn's Disease in 2007: <http://www.medvission.org/mihpf/medinsight%20-%20ldn%20-%20Press%20Release%20-%20January%2030,%202007.pdf>.

Zagon said research over the past two decades indicates the body's immune system is orchestrated by its own naturally produced internal opioids. Large doses of NTX block the body's opioid receptors, eliminating the high derived from drugs. In extremely small doses, however, NTX seems to block the opioid receptors just long enough to prompt the body's hormone system to produce more of its own natural endorphins, which somehow encourages the immune system. "We're working with the body's own chemistry," Zagon said.

The drug's off-label use began to grow just as the Internet became a major source of information exchange. www.lowdoseNaltrexone.org an LDN home page, there is a Wikipedia entry, and forum pages where people share information and their own experiences with the drug.

NTX being appropriate for PD and other autoimmune diseases could be established by subjecting it to a new round of clinical trials, the same rigorous, expensive, time-consuming studies that were performed when it was approved for addiction treatment. Unfortunately, there's little incentive for drug manufacturers to spend the money. NTX has gone generic, and lost the patent protections that would make it a profitable drug for treating autoimmune diseases. "It doesn't behoove the pharmaceutical companies to develop it," Zagon said. As a generic drug, it's also cheap, costing about \$1 a day.

Zagon would like to see someone provide the funding for new clinical trials for LDN; however, some studies are already under way. The National Multiple Sclerosis Society has funded a study that will look at high- and low-dose NTX treatments in mice with a disease much like multiple sclerosis, and the NIH has funded a phase II trial using LDN in patients with Crohn's disease. Phase II trials involve as many as several hundred people, but they fall short of the randomized double-blind phase III trials in which some people get the drug and others do not.

Marquez has seen how the drug has helped her father; she hopes one day someone will do the research that will determine its efficacy. N "We're not the only family talking about this," she said. "We're trying to share this information because it buys you time. We've got to tell the world this drug is incredible."

The problem with off-label use is that there have been no randomized clinical trials to determine possible side effects or other problems, Ryan said. Internet sites provide all kinds of information, but there's often no way to validate its accuracy.

"You can at least be sure the trial process was reviewed by an uninterested party," she said. NTX is not suitable for all patients, even in extremely low doses, said Dr. Ian Zagon, a professor at Pennsylvania State University. People with liver problems, for example, should not take NTX, and there are other caveats. "People (who are considering NTX) should be under a physician's care," he stressed. If a physician rejects a request for low-dose NTX, the patient may want to look for another physician who may be more aware of new research, Zagon said.

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SOURCE: <http://tinyurl.com/2v5whw> The Mail Tribune of Southern Oregon

UNDERSTANDING THE RECENT ANNOUNCEMENT ABOUT AZILECT® AND ITS POTENTIAL TO SLOW THE PROGRESSION OF PARKINSON'S DISEASE

(06/20/08) On Monday, June 16, Teva Pharmaceuticals issued an announcement about the results of its Phase III clinical trial, ADAGIO, which tested the neuroprotective abilities of Azilect® (rasagiline), a medication already on the market for the treatment of the signs and symptoms of PD. PDF has issued a statement about this development, which appears below.

STATEMENT FROM THE PDF

Earlier this week, Teva Pharmaceuticals, the Israel-based company that manufactures Azilect® (rasagiline), an anti-PD medication, announced that it has applied to the US Food and Drug Administration (FDA) for approval to market Azilect for its potential to slow the course of the disease.

In 2006, the FDA approved Azilect as a stand-alone treatment for people with early PD and as a treatment in conjunction with levodopa for people with more advanced PD. If the FDA should approve the new request, this would be the first treatment to be marketed in the US for a disease-slowing property.

According to the company's press release, Teva has new data from a large 18-month study known as ADAGIO that it claims supports a neuroprotective benefit for Azilect. Unfortunately, the data have not yet been released and so the PD Foundation (PDF) is not in a position to judge whether the claim is valid and how strong the benefit is, and therefore to what extent people with PD and their families should be encouraged by the news.

The value of Azilect as a treatment to ease PD symptoms has been well demonstrated over several years of successful use by thousands of patients. Its value as a neuroprotective has been suggested by an earlier, smaller study, but has not been proven. The new study—and the FDA's response to this—may help to clarify Azilect's potential in this area but we will not know for sure until the data have been released.

While PDF recognizes that companies are legally obligated to notify the public when they have information that may impact the price of their shares, we also believe that they have the same obligation, albeit a moral rather than a legal one, to extend the same opportunity to the scientists who run the trials and the patients who have the greatest stake in their outcome. We urge the research and regulatory communities to recognize this obligation, and to assure us all that in future, when claims of this kind are made public, that they be accompanied by the scientific data on which these claims are based.

PDF's Medical Policy Committee will be watching the situation very carefully over the next several weeks—beginning with monitoring the annual meeting of The Movement Disorders Society in Chicago, when there may be discussion of the treatment—to review the data and to evaluate its significance. As soon as we have something to report, we will place it on our website, www.pdf.org.

If you have any questions about this matter, please email your question to info@pdf.org or call our toll-free helpline at (800) 457-6676.

WHAT IS A VALID TREATMENT FOR PD? (PART 1)

Stan Wertheimer

If you are a PWP you are in a treatment (therapy, regimen). If you are doing nothing, that is still a treatment. I have been wondering how each of us chooses a treatment, because it is ultimately our personal choice. Our doctor can make suggestions, but we choose to accept them, or not. Like most PWP I have accepted some choices; I have also been presented with additional options that I rejected.

I would like to explore the central question of how we choose our treatments. Before doing that I will present a collection of choices that I have had over the past 18 years to give the central question a context. This is a personal recollection so it should not be treated as you would a journal article.

Since I rejected most of the described choices, the following may have a negative tone; it is not meant to be that. During the same period many positive advances were made in the treatment of PWP; I will mention some later.

I would like to share some of the thoughts I have had about clinical trials, alternative medicine, experimentation, working with my neurologist, and so on. I think we are at a point where some of the issues raised will, and should, be addressed by the entire PD community, especially our echelon of M.D.s I will use my own experience when it seems relevant. If I make a mistake, or my memory is not 100 percent, I will try to err on the conservative side. Some terms may seem obscure to you (COMT inhibitor, UPDRS, GDNF, gene therapy); you can look them up, or just assume what is implied by the context. If you do this I believe you will get my gist with out any loss.

Anti-oxidants: Since the early 1980s I have been on a regimen that includes regular, usually once every one or two days, consumption of antioxidants. I had read and heard enough by that time to convince me that powerful over-the-counter antioxidants would not harm me and more likely do me some good. I started with vitamins E and C, and beta-carotene. Over a few years I added selenium, alpha lipoic acid, and some others for

things like heart health (folic acid). Since I did not know that I had PD at that time it could not be deemed a PD therapy; since I found out about having PD (1990) I have considered it therapeutic, especially in light of the incontrovertible evidence that smoking protects one against PD; it is widely believed that it is the CO, or carbon monoxide, in the smoke that is responsible—it is a powerful antioxidant (carbon monoxide wants another oxygen atom in the worst way).

Datop: When I was diagnosed the PD world was optimistic about the results of a large long-term study, Datop that seemed to prove that the drug under consideration, selegiline, was neuroprotective. When supplemented with vitamin E, it was supposedly more so. I do not recall what burst the bubble; selegiline, commercially called Eldepryl or Deprenyl, was not the drug it was thought to be and its use dropped off. Was this a scam? Of course not—the drug went through all of the hoops; it just didn't live up to its hype. It is used widely today (generic available) as a minor supplement to other treatments. Recently a version that dissolves on the tongue, Zelapar, has come out. Zelapar is pricier than selegiline because the makers have exclusive rights by the law that grants these rights 17 years from the time the fit is submitted. There is another drug in the same class as selegiline—Azelect ; more on that later.

Tasmar: My first experience with a clinical trial came in 1992 or 1993 when I joined the first group to go through Phase III trials for tolcapone, a COMT inhibitor. Roche was competing with another drug company who were in Phase III with entacapone, another COMT inhibitor. In essence, these drugs inhibit the enzyme COMT that consumes levodopa, thereby making more available for use by neurons. The trials went on for about eight weeks (plus pre-trial testing). At the end of that time participants were given the option of remaining in the open study until the product went on the market; here everyone got the drug. I chose to remain on the drug, since it gave me an extra 30-45 minutes of on-time per dose of Sinemet. It was soon after

it went on the market that three people were found to have suffered severe liver damage (I believe all three died), possibly due to tolcapone, now called Tasmar. Many doctors stopped prescribing Tasmar, Canada banned it (and still does), and those that continued were required to have liver function tested every month. I did this for a while and then stopped; I had been on Tasmar for over two years with no liver problems and all of my doctors said that I had nothing to worry about. I understand that most drugs involve the liver in their absorption.

Was Roche pulling a fast one? Was there evidence of liver problems before approval? I cannot imagine it; they were the big losers. It is only recently that Tasmar has received a clear bill-of-health. The right to make it has passed to Valeant, and they raised the price from a healthy \$2.50 per dose to a lofty \$3.

Imaging: At the time of the Talcapone Study, I was part of an imaging study at Yale run by Dr. Marek. We were imaged once a year after being injected with a radioactive tracer (iodine), which migrated to the striatum, which I think of as the carburetor for dopamine distribution. This went on for eight or nine years, at least in my case. The objective was to see if there was a correlation between dopamine availability in the striatum and PD symptoms as measured by a modified UPDRS, which was also administered. During these years I learned a lot about PD, PD medications, and other aspects of PD mostly from discussions with Ken Marek. Perhaps the most surprising thing I learned was that there was little correlation between the level of dopamine in the striatum and your score on the UPDRS. We were given the option of seeing our scans, which I always rejected. I saw no benefit. I do not know what happened to the data that was collected. If nothing, it was still a valuable experience for me.

Foot Trauma: Also at this time, or a little after, I agreed to consider participating in an experiment fostered by a woman in California who maintained that all PD was the result of a trauma to the foot; if one followed her regimen a cure was in your future. She wrote copiously on both the rationale for her methods and its implementation. She claimed many cures. I bowed out rather quickly. To her credit, she made some good points (side effects of PD meds often mimic the symptoms they are supposed to alleviate, for example). I knew people who visited her clinic and who were following her advice. She was characterized by everyone as a sincere, intelligent, well-meaning person. I did not doubt that. Of course there were no clinical trials, merely her anecdotal

evidence. Was she a charlatan? I doubt it. I think she really believed what she was doing was the right thing. I know of at least one person who suffered dreadfully because of following her therapy, however. Does this mean we should never consider a therapy that has not gone through the clinical trial system? We will consider this again.

Glutathione: I was also introduced and urged to take part in a therapy being touted by a Dr. Perlmutter in Florida using intravenous doses of glutathione and a supplement of antioxidants, and other supposedly beneficial over the counter compounds. I thought of this, from reading and verbal evidence, yet another approach to getting more on-time; it was expensive and difficult to implement, but it seemed to work for many who tried it. Was the doctor a scam artist? I don't know, but, after reading his book, I felt that he was another person on a mission that didn't fit the accepted procedures. I believe he still vigorously practices medicine in Florida, perhaps not his therapy for PD.

Exercise: In 2000, or 2001, I joined a group of about 15 PWP in the Mystic/New London area that were the first cadre in what was to become a well-established PD Exercise group sponsored by L&M Hospital. I dislike formal exercise; I had always had a goodly bit of strenuous activity in my life: you might say that exercise was "built-in". As the group coalesced over time it became more than an exercise group; people cared about one another and it became an effective support system. I continue this therapy.

Cervical Vertebrae: Another therapy that I became familiar with through a friend who tried it was that of having the chiropractor that had developed this technique manipulate your cervical vertebrae to remove pressure on your spinal cord at this crucial location. My friend had limited success. Was this person pulling a fast one? I imagine there were many who got relief of one form or another, which could easily be mistaken as symptomatic relief.

GDNF: Several years ago I consulted with a neurologist whose opinion I value; it was about a clinical trial involving GDNF in Philadelphia. I first read about GDNF in 1990 in an article in Science magazine (AAAS). It "cured" monkeys that had had their substantia nigra wiped out by MTPT, a compound made for hallucinogenic purposes. My consultant said that the group I was talking about had been trying different approaches of using GDNF and always wound up making no headway; the advice was to forget it. I did,

and was glad because they again made no progress. Was the group being less than professional? In light of the latest successes using growth factors in gene therapy, I must say that they were going down the wrong road but were in the right neighborhood.

Low Dose Naltrexone (LDN): Then there is the article about LDN: what can one make of it? We haven't talked about the placebo effect; it can be the strongest effect in a trial. There are cases, I am told, of this effect lasting as long as a year—the person got NO drug but became symptom-free for a year. The PE is especially strong in PWP so any trial that ignores it is suspect. One must agree. However, I'll take the PE if it will make we feel better! I imagine many of the anecdotal stories of improvement are due to the PE. This raises another question: So what if the PE is triggered and the patient feels better after what would prove to be an ineffective treatment? The specific patient doesn't care, even though the treatment cannot be approved as beneficial. If LDN works because of some unknown mechanism (as do some of the widely accepted PD drugs and procedures (e.g. amantadine and DBS) what is wrong with that?

Azilect: My last example is characterized by the article on Azilect and Teva's announcement that it is neuroprotective. They gave the conclusion, but not the supporting data. Any neurologist, hearing the conclusion would immediately recommend to all her clients that they start Azilect. Now, suppose that three or four weeks after the announcement, or more, the data is presented; it shows that Azilect is neuroprotective in that

it can slow the rate of deterioration of the dopamine producing neurons by one-fourth percent a year. For a person in his forties this amounts to a saving of five percent of his neurons in a twenty year period. This may be the right thing to do, at least as far as his neurologist is concerned, and of course Teva, but other considerations (cost, side effects, contraindications) may keep him from taking the drug. I think it is only natural to think that if the data on neuroprotection were presented with the conclusion, some doctors might not be so quick to suggest a patient move to it (not very neuroprotective), or insist vigorously that the patient take the drug (clearly an effective neuroprotector).

Some positive results: During these 18 years the drugs Mirapex and Requip were tested and brought to market, as was Parcopa, rasageline (Azelect), Zelapar, and Deep Brain Stimulation replaced pallidotomy and thalamotomy as surgical procedures, with much better results. Ceregene-120, although still in Phase II trials, shows great promise as a gene implant. The appreciation that PD is a whole body disease as opposed to simply (!!) a movement disorder was an important step in directing research for a cure, The MJ Fox foundation has become a boon to the research community looking for fast turn around time for proposals leading to a potential cure.

This ends part one of this discussion. Next time I will address the question: What therapy (therapies) do you follow, and why? Do you try some that your doctor does not know of? approve of? As we saw above, there are many therapies available, not just those requiring drugs.

ANECDOTE (HAVING TO DO WITH GREEN TEA AND FOLDING PROTEINS): In the late 19th century a mathematician, Reimann, got his PhD from a German university after presenting his research on some obscure geometry; he always felt that he was lucky because the work could never lead to anything useful.

In the early 1900s a young patent clerk in Zurich who was also a physicist had hit a dead end in his research; then he read the results of Reimann, and he was able to use it to finish his work. The clerk, Einstein, published his Theory of Relativity as a result.

Editorial Comment: *I have included more than you want to know in the following. I had better have a good reason, right?! The reason is to point out that basic research often doesn't sound like it has much to offer to the average (almost everyone in this case) reader. Only by knowing WHY the scientists are investigating EGCG and folding proteins can you see the use.*

Why couldn't the scientist say to the unwashed, Drink green tea and you will form less plaque in the brain, or better yet, and your disease will progress more slowly. We would then have to go through a cascade of questions because we know enough not to accept a drug for no reason, and the scientists are treating green tea like a drug. After enough questions we arrive at the reason to do the basic research. In the meanwhile, those of us who don't understand keep drinking Coca Cola, while those that expend the effort to see the links will switch, if they like

green tea as well, or feel that it benefits them to do so. The basic research that seemed so obscure and unfathomable finally made sense and you were convinced that the statements about green tea are valid.

So, I have included the article for us in the simplest of terms announcing the results of the research in its most useful form; the abstract of the article, for the research community, announcing the nub of what is actually going on, which is meaningless until you know the context. So, in a nutshell: Be willing, from time-to-time, to attempt something you know will be confusing if it has the potential of setting your mind at ease about an important issue.

NOTE: Researchers of the Max Delbrueck Center for Molecular Medicine (MDC) Berlin-Buch, a national research laboratory of the Helmholtz Association in Germany have made this discovery in the test tube and in cell models. The research of Dr. Dagmar Ehrnhoefer and Dr. Jan Bieschke of Professor Erich Wanker's laboratory in Berlin-Buch has now been published in the journal Nature Structural and Molecular Biology* (<http://dx.doi.org/10.1038/nsmb.1437>).

GREEN TEA PREVENTS DEATHLY PLAQUE FORMATION IN PARKINSON'S AND ALZHEIMER'S FIRST RESULTS IN THE TEST TUBE AND WITH CELL MODELS

May 2008—The substance EGCG (Epigallocatechin-3-gallate) from green tea can redirect the deadly process which leads to the accumulation of protein aggregates in Parkinson's and Alzheimer's disease. EGCG modulates a cascade of protein mis-folding in such a way that the formation of deadly plaques is interrupted, and harmless protein structures emerge instead. They made this discovery in the test tube and in cell models. It has now been published in the journal Nature Structural and Molecular Biology.

EGCG binds directly to unfolded proteins at a very early stage and thus prevents their conversion into toxic aggregates. Instead non-toxic, unstructured round aggregates of a new type are formed, presumably by an alternative folding cascade. *"These new aggregates are harmless"*, Dr. Bieschke is convinced. He said that to show this they treated the result with an antibody that recognizes toxic aggregates. This antibody is unable to bind to the newly formed protein aggregates that occur after EGCG treatment.

Now the MDC-researchers want to know exactly how EGCG interferes with the "do not bind" proteins. They collaborate with researchers from the neighboring Leibniz Institute for Molecular Pharmacology (FMP) using NMR-spectroscopy to identify the structure of the new type of aggregate.

The mis-folding of proteins is a complex, multi-step process that eventually leads to the accumulation of dangerous insoluble aggregates. These aggregates are toxic for nerve cells and cause their death. They are associated with a number of disorders, including Parkinson's and Alzheimer's, and also Huntington's disease.

EGCG binds to several proteins that are causative for various protein mis-folding disorders. Therefore, the MDC researchers consider EGCG or similar substances to be suitable for the development of drugs to treat neurodegenerative diseases and other amyloid diseases, connected to the formation of toxic plaques.

NOW HERE IS THE BASIC RESEARCH CRUCIAL TO THE ABOVE ANNOUNCEMENT.

Article abstract: Nature Structural & Molecular Biology 15, 558—566 (2008) Pub: 30 May 2008

EGCG redirects amyloidogenic polypeptides into unstructured, off-pathway oligomers

Dagmar E Ehrnhoefer, Jan Bieschke, Annett Boeddrich, Martin Herbst, Laura Masino, Rudi Lurz, Sabine Engemann, Annalisa Pastore & Erich E Wanker

ABSTRACT The accumulation of beta-sheet-rich amyloid fibrils or aggregates is a complex, multistep process that is associated with cellular toxicity in a number of human protein misfolding disorders, including Parkinson's and Alzheimer's diseases. It involves the formation of various transient and intransient, on- and off-pathway aggregate species, whose structure, size and cellular toxicity are largely unclear. Here we demonstrate redirection of amyloid fibril formation through the action of a small molecule; resulting in off-pathway, highly stable oligomers. The polyphenol (-)-epigallocatechin gallate efficiently inhibits the fibrillogenesis of both alpha-synuclein and amyloid-beta by directly binding to the natively unfolded polypeptides and preventing their conversion into toxic, on-pathway aggregation intermediates. Instead of beta-sheet-rich amyloid, the formation of unstructured, nontoxic alpha-synuclein and amyloid-beta oligomers of a new type is promoted, suggesting a generic effect on aggregation pathways in neurodegenerative diseases.

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DISCLAIMER:

Articles in this newsletter are for information only.

Any questions of treatment should be discussed with your physician.

Write your Representatives in Congress!

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