



March 19, 2024, Update

Preface

Vika and I have just returned from the British Virgin Islands (BVI) where we were supporting our test subjects in Cohort #22. As always, the volunteers were outstanding and wonderful people. Again, there were no adverse events from the dosing of FGF-1 and there seemed to be small positive events that occurred with test subjects. Ultimately, we had a good start for these new “Lab Rats” on their journey of discovery to potentially answer the question: Can dosing with FGF-1 enhance their recovery from Parkinson’s disease?

Vika is now managing the redosing of our test subjects who have reached the 6-month and 12-month thresholds since their first dosing with FGF-1 in the BVI. Zhittya is sending these patients additional doses of FGF-1 to learn if “continual dosing” with FGF-1 enhances their recovery from Parkinson’s disease. Read Vika’s section of this Update for the emails we have received from test subjects about their improvements. We have seen enhanced improvements at 9 months, 15 months, etc., which implies the additional dosing of FGF-1 into the brain has a

positive effect on those people. How long is continued dosing with FGF-1 needed? We have no idea. Some people are reporting that their neurologist is shocked over how much they have improved over 12 or 18 months and have stated that their doctors have said to them, that if they did not know that they had Parkinson's disease, they could not tell. Is that victory? No, not yet! We do not know if 6 months later those test subjects will relapse and start to decline again. We do not know that if after 5 years of decent health, their Parkinson's disease will return. We have to monitor these people and learn more about the long-term effects, both good and bad.

I am always amazed when someone shows me a negative posting on what Zhittya is conducting. I am amazed how an uninformed person comments with such confidence on what we are doing, when they do not know anything about us. I am disappointed when these pundits bravely comment, "Ah, Zhittya admits it does not know about this or that". Obviously, these people have no idea of what the concept of "**Discovery**" is all about. Discovery is attempting to learn what you do not know. No one discovers what they already know. Dr. Jacobs was in the lab where the structure of FGF-1 was first determined in the late-1970's (when he was very young), and since then, thousands of research studies have been conducted by some of the world's leading research organizations about what FGF-1 is and what it might be able to do in humans. Zhittya's ignorance about FGF-1 in the brain has given us our newest realization on "**The Mystery of the Vanishing FGF-1 in the human brain**". Zhittya is being forced to look into the unknown (again) and attempt to learn where all of our FGF-1 molecules in the brain are vanishing to? Again Dr. Jacobs, Vika and others are diving into any research that

can help explain why our mathematical calculations of how much FGF-1 is getting into the brain and what it should be accomplishing are so far off.

Question: Where is all the FGF-1 that we put in the brain vanishing to?

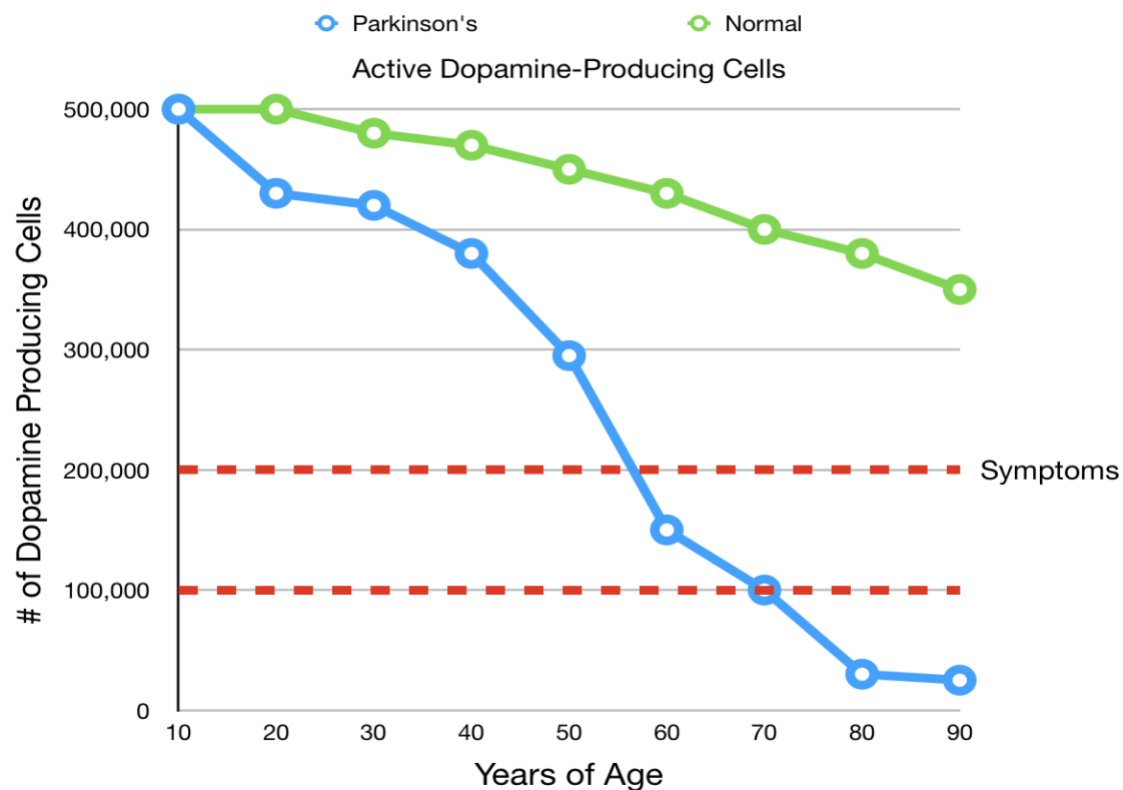
We started our journey with FGF-1 25 years ago, based upon medical studies from Germany, which showed FGF-1 grew new blood vessels in the human heart, thereby treating coronary artery disease - the number one cause of death in the world. This research was published in the peer-reviewed journal, *Circulation*, published by the American Heart Association, the most respected authority on circulation diseases in the world. In Germany two heart studies were conducted, with zero adverse events, new blood vessels growing and being seen in angiograms, and heart function improved materially in test subjects. Then, in 2004, Dr. Jacobs would lead and manage a USA FDA Phase I cleared trial utilizing FGF-1 to treat patients with severe coronary artery disease. Here is a clip from ABC Nightly News showing we grew blood vessels in the human heart from that clinical trial. You can see that video here:

https://youtu.be/!Ptv_0LWK4k

Of the over \$170 million USD I have expended on this project so far; my guess is over \$100 million of that money was spent on the heart effort. The math calculations behind using FGF-1 to treat heart disease was easy. When you inject an amount of FGF-1 into an ischemic area, permanent blood vessels would appear ~2 months later. In terms of calculations, it was easy to potentially treat the number one cause of death in adults in the world and we demonstrated a potential treatment to extend the lives of millions of people.

There is a similar story with peripheral artery disease (PAD), which affects about 10 million Americans. The math calculations were simple: when we injected a certain amount of FGF-1 into the legs of patients with PAD, permanent blood vessels would develop in the legs of these individuals. Even diabetic foot ulcers (DFUs) proved to be a similar story, where we could easily calculate the amount of FGF-1 needed to treat DFUs and once again showing no adverse events and 100% success in healing major diabetic foot ulcers with FGF-1.

But in the brain, there is a mystery: What happens to all the FGF-1 that we introduce to the brains of Parkinson's disease sufferers? Below is a chart which shows what is generally believed to cause Parkinson's disease.



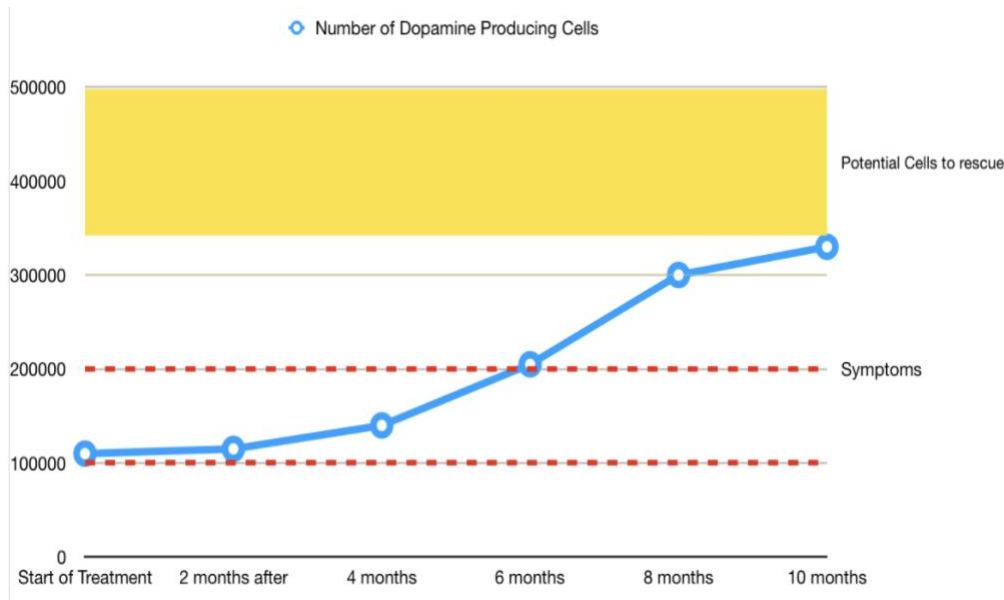
From this chart you can see that it is estimated that a normal healthy person only has about 500,000 dopamine producing cells at birth, which is a very small number in a brain with hundreds of billions of cells. The green line is the anticipated normal decline of these dopamine-producing cells, as a healthy person ages. These people lose dopamine neurons as they grow older, but they do not develop Parkinson's disease.

The blue line in the graph above depicts a more rapid decline of these specialized dopamine producing cells to below 200,000 cells, at which time the symptoms of Parkinson's disease start to occur. As the number of dopamine producing neurons continue to decline, the symptoms become worse as the lack of dopamine leads to greater movement issues. Zhittya believes that disruption of blood flow to those dopamine neurons causes their dysfunction and leads to the reduced performance of dopamine neurons, the hibernation of dopamine neurons, and, ultimately, to the death of dopamine neurons.

Zhittya's management believes that if the FGF-1 can stimulate new blood vessel growth (a process known as angiogenesis) thereby leading to the regeneration of dopamine producing neurons, that those neurons will recover. Secondly, a person's own neuronal stem cells will regenerate dopamine producing cells if there is sufficient blood flow there to provide those stem cells with the energy they need to prosper. This is what was witnessed in animal studies in the brains of rodents and monkeys, which had been given experimental Parkinson's disease.

Below is a chart of Zhittya's targeted objective for its FGF-1 treatment in the area of the brain where the dopamine neurons exist, an area called the substantia nigra. The goal of our therapy is to create 100,000 to 200,000 new dopamine

producing neurons to increase the functional dopamine-producing neurons back above the 200,000 level, and thereby, in theory, reversing the symptoms of Parkinson's disease.



This was Zhittya's original math when we started this Parkinson's disease project back in May of 2022, namely, to potentially regenerate 200,000 new dopamine producing neurons. The monkeys had the FGF-1 injected directly into their brain via a surgical hole. Instead of that approach Zhittya decided to utilize a nasal spray to introduce the FGF-1 molecule into the brain via transfer into the brain's cerebral spinal fluid (CSF) via two main nerves in the nasal cavity: the olfactory nerves and the trigeminal nerve. Zhittya had animal studies conducted that verified that this method of delivery was a safe and viable pathway to introduce FGF-1 into the brain.

How many FGF-1 molecules are needed to accomplish this task of reinvigorating 200,000 dopamine producing cells in the substantia nigra? Prior research indicates that ~10,000 FGF-1 molecules must be captured by the upregulated

FGF-1 receptors on the surface of a stressed cell to start the process of growing new blood vessels. This biological process of sprouting new blood vessels from an existing stressed cell is called creating a new “foci” of blood vessels. A foci that creates new blood vasculature can be seen in heart angiograms. In the heart, the new field of blood vessels is impressive, reaching thousands to millions of heart muscle cells.

In the brain, we were more cautious and estimated that a new foci of blood vessels would only reach 10 dopamine-producing neurons (not like in the heart where a foci reached thousands of muscle cells). To create an additional 200,000 new dopamine-producing neurons in the brain, we figured we would have to trigger 20,000 foci (200,000 neurons divided by 10). To trigger 20,000 foci requiring 10,000 FGF-1 molecules each, would total 200 million FGF-1 molecules that were needed in that region of the human brain. This was similar to the math of FGF-1 needed in the monkey’s brain to reverse Parkinson’s disease. Great math so far.

Every patient’s nose is different, with variations in shape, nasal membranes, etc. From Zhittya’s animal work we estimate that 1 to 3% of the FGF-1 we spray into the nose enters the cerebral spinal fluid (CSF) of the brain. Zhittya estimates that with each daily dosing regimen, the nasal application delivers around 3 trillion FGF-1 molecules into the cerebral spinal fluid (CSF) **every day**. The original dosing regimen was 6 days in a row, thereby equaling around 18 trillion FGF-1 molecules delivered in 6 days. If you divide 200 million (the amount we believed we needed) into 18 trillion FGF-1 molecules given, you get 90,000 times more FGF-1 introduced into the brain than was theoretically needed to create the new

dopamine-producing neurons we wanted. When we started in May 2022, we saw improvements in Parkinson's disease patients from their one-time dosing for 6 days, however not the 100% improvement as we had hoped. More interestingly, over time patients reported a number of changes including that their sense of smell had come back, their drooling reduced, their sleep was better, their cognitive functions enhanced, their short-term memory had improved, and even long-term memories started to return. None of those improvements were on Zhittya's original target list, but they were a wonderful surprise for all of us.

Realizing we did not accomplish the primary objective of completely reversing Parkinson's disease, we modified the Protocol and we are now on what we refer to as Protocol #17, which delivers about 36 trillion FGF-1 molecules to the brain spread out over six months. We know that for FGF-1 to work successfully, the FGF-1 cell surface receptors on stressed cells have to be increased or upregulated, so the brain cells can grab the FGF-1 and not let the drug simply run out through the kidneys. Many people think dosing with FGF-1 every day would be better and we believe that they are wrong. The FGF-1 receptors have to be reset for the biological process to occur.

Now for the mystery: If over a 12-month period, a patient gets 72 trillion FGF-1 molecules into their brain and it only takes 200 million molecules to regenerate 200,000 dopamine producing cells, what happens to the other 71.9998 trillion FGF-1 molecules? Maybe 50% of the FGF-1 never gets captured by an FGF-1 receptor on the cell's surface and they are flushed out the body. If that is the case, that implies 36 trillion molecules remain in the body, so subtract 200 million

FGF-1 molecules (for regenerating the dopamine producing neurons), that still leaves 35.9998 trillion FGF-1 molecules unaccounted for.

Okay, some FGF-1 must have been captured by a stressed cell in the olfactory nerve or olfactory bulb to regenerate the sense of smell again. Some FGF-1 must have been captured by the neurons handling drooling, balance, thinking, forming short- and long-term memories - yet still trillions of FGF-1 molecules cannot be accounted for, unless the brain is consuming FGF-1 for its biological and functional processes. If billions of brain cells are consuming small quantities of FGF-1 for their biological processes, does that explain the mystery of the vanishing FGF-1?

Dr. Jacobs and Vika have been studying the question of why patients are showing us improvements which have nothing to do with dopamine producing cells? This has led to an intense study by Zhittya of neuroplasticity and the role of FGF-1 in this process. Neuroplasticity is one of the most amazing functions of your brain. Dr. Jacobs in his section will provide you a brief introduction to this amazing topic. When people reported to us that their long-term memories were coming back, I was personally shocked. I thought if the cells that held the long-term memories had died as a result of a lack of blood flow, that those memories were gone forever. Yet countless patients have discussed their long-term memories recovering. Then the thought was that the neurons with those long-term memories may have been hibernating and with new blood flow, they awakened, reviving memories.

When studying neuroplasticity, we observed that neurons communicate with each other by reaching out with their long arms (dendrites) to touch other cells.

We learned that an undernourished neuron to survive deprivation will withdraw its dendrites back to conserve energy to survive. This would then cause the neuron to break its communication with other cells. Is this what causes the loss of memory? Does FGF-1, by reestablishing blood flow, nurse the damaged neuron back to health, allowing it to extend its dendrites out again, touching its neighbor neuron and reestablishing a memory? We do not know!

What we believe is there is a lot more damage in the brain than we ever guessed and that includes someone who thinks they have a healthy brain. We have seen that it is taking us longer to develop dopamine producing neurons in the brain of a Parkinson's disease sufferers than we thought, however, along the way the FGF-1 was most likely repairing many problems and many unknown issues in the brain, including such things as leaky blood vessels and micro-strokes.

Why in a young monkey's brain, who was given Parkinson's disease, did it take so much less FGF-1 to grow new blood vessels and reverse their Parkinson's disease than our aged humans? Are the cells in the brain of a 70-year-old human so worn out, so stressed in many unseen ways; that their brain swallows up FGF-1 to repair and rejuvenate their functions? We can believe a young monkey has no memory loss. We can believe the young monkey has a movement disorder but otherwise a healthy brain. Does the 70-year-old have leaking vessels in their brain that need repair? Does the 70-year-old have billions of brain cells that are not functioning properly and they just do not know it?

Yes, we are in the dark about exactly where all the FGF-1 molecules that go to in to the brain have gone. We still have a lot to discover, but it is a very exciting

process for us! Stay tuned for our next chapter in the mystery of vanishing FGF-1 molecules in the human brain.

Important!

HEALinc Future Health Innovation Summit in The Bahamas

April 28th – 30th

Zhittya Genesis Medicine is a sponsor of the HEALinc Future Health Innovation Summit, a major conference being hosted at the Atlantis Hotel in Nassau, The Bahamas from April 28, 2024 – April 30, 2024. This conference will bring together over 30 speakers from around the world to discuss the future of regenerative medicine in a multi-day conference focusing on innovations in the field. On top of this medical conference, Zhittya Genesis Medicine will be hosting a Cardiovascular Regeneration Symposium on Zhittya's innovation into the treatment of coronary artery disease and severe heart disease with therapeutic angiogenesis on April 30, 2024.

At this symposium, Zhittya Genesis Medicine will focus on Zhittya's breakthrough angiogenesis treatment in the ischemic heart, with the potential to treat over 16,000,000 people worldwide, who die from coronary artery disease every year, with Zhittya's new medicine to regenerate their blood vessels by using our medical breakthrough treatment. Zhittya has developed FGF-1 to treat severe coronary artery disease by growing blood vessels around blocked arteries. FGF-1 has the capability to grow new blood vessels, as shown in past USA FDA and German Clinical trials where this treatment was proven to be safe and effective. In previous human studies on patients suffering from coronary artery disease,

Zhittya was able to lessen their heart pain and extended their lives by upwards of 15 years. Zhittya Genesis Medicine has plans to restart this program in 2024 in The Bahamas for individuals suffering from severe heart disease.

There will also be a variety of other applications discussed at this symposium beyond Zhittya's potential treatment for severe heart disease, such as Multiple Sclerosis and Parkinson's Disease. Those in attendance will include members of Zhittya Genesis Medicine's team, Cross Border Medical Tourism's team, as well as Bahamian Government officials. Our speakers include the CEO of the HEALinc conference, Dr. Desirée Cox; The Honorable Minister of Health, Dr. Michael Darville; members from the National Ethics Committee; and medical and community leaders such as Dr. Conville Brown, Zhittya's partner in our clinical efforts in the Bahamas.

The conference is also available via the internet for people who cannot travel to The Bahamas. To register for either the in-person or online conference visit here: healincsummit.com

The schedule and speakers for our April 30, 2024 symposium is as follows:

- **1:00 PM**: Welcome by Dr. Desirée Cox, CEO and Founder of HEALinc and Chair of the Joint National Stem Cell Ethics Committee and National Medical Ethics Committee of The Bahamas.
- **1:15 PM**: Dr. Desirée Cox introduced Honorable Minister Dr. Michael Darville, the Minister of Health of The Bahamas.
- **1:30 PM**: **"Therapeutic Angiogenesis: A new Potential Breakthrough Treatment to Regenerate Health and Extend Life"** by Dan Montano, CEO of

Zhittya Genesis Medicine, will be presenting on why Zhittya's medicine could extend a person life, by deferring their death from the cause of death for 65% of all people, insufficient blood flows to a tissue or organ.

- **2:00 PM: "Utilizing Therapeutic Angiogenesis to Reverse Major Diseases in the Heart, Brain, and More"** by Dr. Jack Jacobs, President and Chief Science Officer of Zhittya Genesis Medicine. Dr. Jacobs will introduce the medical science of the FGF-1 medicine and show examples of human success in reversing these deadly diseases.
- **2:30 PM: "Development of New Therapies in The Bahamas for the Benefit of Both International Patients and Citizens of The Bahamas"** by Dr. Conville S. Brown the Founder, President, and CEO of the Medical Pavilion Bahamas. Dr. Brown will present his plan to implement his clinics to provide Medical Research to heart patients, Parkinson's Disease patients and more in The Bahamas.
- **3:00 PM:** Break
- **3:15 PM: "How to Identify, Gather, and Deliver Regenerative Medicine Therapies to Medical Tourists Traveling to The Bahamas for Treatment"** by Sam Cross, President of Cross Border Medical Tourism. Mr. Cross will explain the critical component of finding patients, screening patients and bringing them to The Bahamas for treatment.
- **3:45 PM: "Is Therapeutic Angiogenesis a Potential Treatment for Multiple Sclerosis"** by Viktoriya Tamlenova-Montano, Vice President of Strategic Innovations and Women's Health Issues. Mrs. Montano will speak about

the new medical breakthrough in Multiple Sclerosis which shows that MS is a vascular disease and the FGF-1 could be able to reverse it.

- **4:15 PM:** “**Summation of the Regenerative Medicine Opportunity for The Bahamas**” by Dan Montano, CEO of Zhittya Genesis Medicine. Mr. Montano will be speaking on how Regenerative Medicine can enhance the economic development of The Bahamas and its people.
- **4:45 PM:** Closing Remarks by Dr. Desirée Cox, CEO and Founder of HEALinc and Chair of the Joint National Stem Cell Ethics Committee and National Medical Ethics Committee of The Bahamas
- **5:00 PM:** Reception and Cocktail Party hosted by Zhittya Genesis Medicine

We encourage anyone interested in learning more about Zhittya Genesis Medicine’s potential treatment for heart disease, Parkinson’s disease, and various other neurodegenerative diseases to join us in this conference and meet our team! For more information and to register for this conference visit

healincsummit.com

Vika’s Patients’ Comments Section:

Here are a few emails I have received over the last month from our test subjects. I only picked a few, otherwise this entire Update would be patients’ comments!

#1) Hello Vika, this is Joe from cohort 11. I wanted to share some good news. If you remember in our last video chat, I was not showing much improvement and was almost worse in some aspects. A few weeks after finishing the last treatment you sent us, I noticed some changes, as did my partner and my brother. I had been suffering from leg freeze, imbalance,

difficulty in turning to face a different direction, among other things. One day I was getting in the car to go somewhere, and my partner could not believe how quickly and easily I sat down. Another day I was putting dishes into the dishwasher and did not realize, until after a few movements, I was turning to face the other direction with ease. Also, my brother has a large dog that loves to be under foot. When I was there, he would constantly be directing his dog to a different part of the room, so that I didn't trip over him. This day, though the dog was in the way, but I just stepped sideways over the dog without stumbling or losing my balance. My brother just looked at me and disbelief and said look at you! Since then, the imbalance has almost disappeared, I have not had any instances of leg, freeze, I am getting in and out of bed with much more ease than I used to, I can get out of the chair more easily, and I can go shopping at the store without being exhausted once I am finished. These are not the only things that have improved and I do still have symptoms, but they are manageable. I can tell you that I would say I have had at least a 50% improvement in my symptoms, and for the first time in a long time, I am experiencing more hope than dread about my future. I want to thank you for your continued efforts, and I hope you still plan on follow up treatments. I look forward to our next video chat so you can see the improvements for yourself. Thank you and God bless!

Sincerely, Joe, cohort #11

#2) Dear Dan and Vika,

I was inspired by the February newsletter to send some updates.

First, thank you voluminously for taking Jacque and I, "under your wings" during our return trip from BVI. It meant a great deal to us and cemented your kindness in our hearts! Also, I have gotten phone numbers from our local Rock Steady Boxing facilities in the greater Reno area. There are three of them, and I'm endeavoring to contact them. I have also enrolled in a continuing education course to recertify my LSVT Big certification in June. Moving toward the business of opening the facility in the Reno area to help regenerate those with Parkinson's,

Here are some definite improvements since receiving my dosing in the BVI and then again, at our home outside Reno, NV three weeks later:

- 1) I am noticing a 50% improvement with using my left hand for typing during my daily documentation as a Doctor of Physical Therapy, an essential skill!
- 2) My thinking and speaking are 80 % improved since receiving FGF 1, essential for ministering and teaching. I just taught a seminar in Oregon where I taught 3, 30 to 40-minute sessions in one day!
- 3) I'm buttoning and unbuttoning my shirts with 80% improved ease now.
- 4) My facial expressions are nearly back to normal now.
- 5) Left hand tremors are 50 – 60% reduced now, and no resting tremor anymore.

I am grateful to God for Him bringing Zhittya Genesis Medicine to our attention to help bring my healing to pass! I'm grateful for both of you and the Zhittya team for being and doing what you do!

God's mighty blessings in the name of Jesus Christ,

Ed, PT, DPT

#3) Good Morning Vika, Craig and Annie

Hope you are doing well today. The Update was exciting. Can't wait for my 6 months check-up.

I found an app "PD Pro" a student doing research turned me on to. It rates your PD by asking you to rate your symptoms. I had a survey done on June 15, 2023. I did another survey Feb. 2024. Big improvement. proof the treatment works! Remember I was in Cohort 16 done in Sept. 6-11. I have attached the reports for your review.

#4) Here is one more: from a daughter of a patient from South America, from slightly over one year ago. From her daughter's translation: **We truly appreciate, because [the patient] feels like she has no Parkinson's.**

Upcoming Events

April 28 – 30: 2024 HEALinc Future Health Innovation Summit in the Bahamas

At Atlantis Resort | Paradise Island | Bahamas

At the HEALinc Future Health Innovation Summit, Dr. Jacobs will be giving a presentation. As noted above in this Update, Zhittya will also be hosting the following symposium:

Zhittya Cardiovascular Regeneration Symposium, which will be held on April 30, 2024, from 1 pm to 6 pm, Eastern Standard Time.

To learn more about this symposium, go to: <https://www.zgm-heart.com>

Cross Border Medical Tourism

Cross Border Medical Tourism services those people who want to be considered for Zhittya's future clinical trials or its current Medical Research Studies. Cross Border's focus is to fill all available slots in the Medical Research Studies in the British Virgin Islands (BVI), while we wait for other clinics to come online.

Cross Border is working on filling the available slots for the next BVI Medical Research Studies (intranasal FGF-1 for Parkinson's disease) on the following dates:

Cohort #23: April 5, 2024 – April 10, 2024

Cohort #24: May 17, 2024 – May 22, 2024

Cohort #25: June 7, 2024 – June 12, 2024

Please contact Sam Cross at Cross Border Medical if you wish to be considered for a slot in one of these BVI cohorts. Sam's email address is:

sam.crossbordermedical@gmail.com.

In addition, if you are interested in participating in the brain scan studies, which will take place at Washington University in St. Louis, please let Sam know. There are a finite number of slots for the imaging studies.

Dr. Jack Jacobs

Dan in his comments above has brought up the concept of the “vanishing FGF-1” molecule after it is intranasally administered to our Parkinson's disease sufferers. Literally, trillions of FGF-1 molecules cannot be accounted for, and Dan speculated that perhaps billions of brain cells are consuming small quantities of FGF-1 for their everyday metabolic processes, which may explain, at least partly, the mystery of the vanishing FGF-1. Let me first address this issue of the “vanishing FGF-1” and then I will go on and discuss the topic of neuroplasticity in the brain.

It is estimated that the adult brain contains 100 billion neurons and all of those neurons contain relatively large numbers of cell surface receptors for FGF-1. Decades of research has established that FGF-1 is constantly at work in the brain, helping maintain the normal metabolic functioning of neurons, but also in processes that are unique to the brain, including functions involving memory, learning, emotions, and language. In certain brain disorders, such as chronic depression, it is known that brain levels of FGF-1 are significantly reduced. Zhittya has written a White Paper on this issue and would be happy to send it out to interested parties.

Apart from chronic depression, there is also general acceptance among researchers that as we age the levels of FGF-1 in our brain decreases. With this in mind, we hypothesize that the brains of our older Parkinson's disease patients are in need of additional FGF-1 molecules, and not just in the substantia nigra region of the brain where the dopamine neurons are located. This would be in billions and billions of other brain neurons that would literally "soak up" the FGF-1 molecules as they enter into the brain. In fact, we have heard back from many of our patients that their mood is elevated after dosing with FGF-1 and that they feel less depressed. This most likely reflects FGF-1 acting directly on neurons outside the substantia nigra region which are involved in mood and emotion control in the brain.

The FGF family of proteins (including FGF-1) has been shown to be intimately involved in the ability of the brain to form and reorganize nerve connections (called synaptic connections), especially in response to learning, new experiences or following injury. This phenomenon is known as **neuroplasticity**. The adult brain is not entirely "hard-wired" with fixed neuronal circuits. There are many instances of rewiring of neuronal circuits in response to training as well as in response to injury.

Neuroplasticity: Strengthening of Nerve Connections Through Learning



What is Neuroplasticity?

Neuroplasticity is the brain's ability to change and adapt in response to new experiences, learning, and injury. It means that the brain is not a static, unchanging organ but a dynamic and constantly evolving one. This process occurs at the cellular level, as neurons form new connections and strengthen existing ones in response to stimuli.

When a particular synapse is used frequently, it becomes stronger, while synapses that are not used weaken and may even be eliminated. It is the basis for learning and memory. When we learn something new, our brain forms connections between neurons, strengthening the synapses involved in that particular task. Over time, with continued practice and repetition, these connections become stronger and more efficient, making it easier for us to perform the task.

Neuroplasticity also occurs in response to traumatic events or injuries. For example, after a stroke, the brain can rewire itself to compensate for the damage, allowing the individual to regain lost function. As shown in the Figure below, we have seen in an animal model of stroke that giving these animals FGF-1 can “boost” the animals response to brain injury allowing for a more complete recovery in the animals.

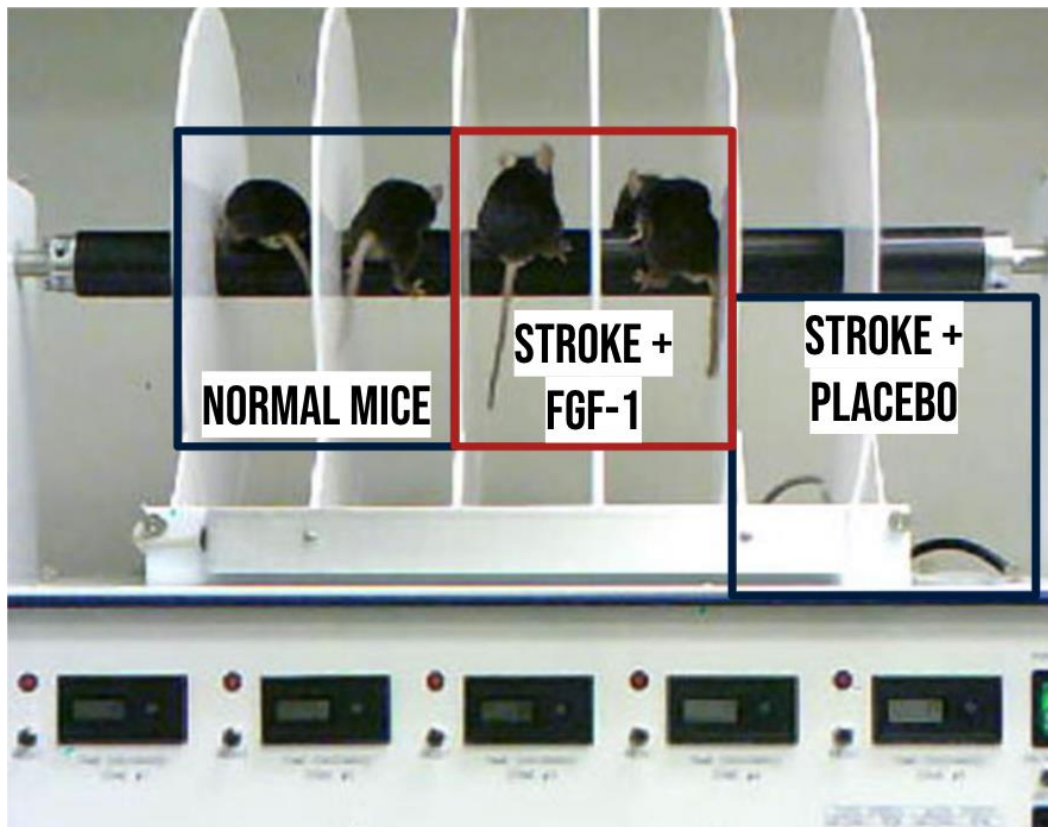


Figure 1. FGF-1 Stimulates Neuroplasticity Following Stroke

Animals given a stroke and treated with FGF-1 relearned motor skills. In this test, the mice are placed on a rotating bar and the normal response is for the animals to grab on and hold themselves on the bar.

In addition, our brains may become less adaptable as we age, making it harder to learn new skills or recover from injury. However, while genetics and age can play

a role, there are many things we can do to enhance neuroplasticity. One of the most essential factors is environmental enrichment. Studies have shown that exposure to a stimulating and challenging environment can promote the growth of new neurons and strengthen existing connections. Additionally, lifestyle factors such as diet and exercise can also influence neuroplasticity. A healthy diet rich in omega-3 fatty acids, antioxidants, and B vitamins can promote brain health and function. Exercise has also been shown to enhance neuroplasticity by increasing blood flow and oxygenation to the brain.

Genes that play central roles in synaptic plasticity were the most significantly affected by age, generally showing reduced expression over time. There was also a marked increase in cortical DNA damage, likely oxidative DNA damage, with aging. Neuroplasticity was once thought by neuroscientists to occur only during childhood, but research showed that many aspects of the brain can be altered (or are "plastic") even through adulthood.

A study that took place in England documented changes in the area of the brain responsible for memory and learning (the hippocampus) in taxi drivers who had to acquire the knowledge of London's layout and road systems. The study documented an increase and enlargement of hippocampal gray matter (neurons important for cognition) in London taxi drivers compared to controls. This work on hippocampal plasticity not only interested scientists, but also got the attention of the public and media worldwide.

There are many other examples of neuroplasticity in human development. For example, researchers looked at the effects of musical training on neuroplasticity, and found that musical training can contribute to structural changes in the brain

based on learning experiences that are unique to an individual. It was shown that changes in the brain of children could be seen in as little as 15 months after musical training began.

Aerobic exercise increases the production of neurotrophic factors such as FGF-1 that can promote growth and survival of neurons. In one study, exercise-induced FGF-1 effects on the hippocampus were associated with measurable improvements in memory tests. Another study showed that consistent aerobic exercise over a period of several months raises FGF-1 levels in the brain and results in marked clinically significant improvements in executive function and increased gray matter volume in multiple brain regions, particularly those that give rise to cognitive control (prefrontal cortex and hippocampus regions of the brain).

Finally, brain injury or stroke leads to increased neural plasticity in the spared, healthy regions of the brain. This allows the neurons in these regions to take over the sensory or motor functions that had been performed by the damaged areas. This remapping of function (indeed similar to drawing a new map) is critical in the recovery of function. According to a 2020 study of nearly 90,000 stroke survivors, 64% of individuals experience communication problems after a stroke. It was documented that recovering speech after stroke required creating new neural pathways in the brain, sometimes in areas that were not wired to perform the complex process of language. This is neuroplasticity in action, the brain's ability to create new pathways and strengthen old ones – and FGF-1 is an important and central figure in facilitating this critical healing process.

Conclusion by Dan Montano

Vika and I just returned from the British Virgin Islands where we supported the treatment of our “lab rats” in cohorts #22. As I have mentioned many times in the past, we learn so much from each new cohort of Parkinson’s disease patients and each cohort advances our knowledge on what is working and what is not. It raises our spirits that we seem to be on a good path towards reversing devastating brain diseases, such as Parkinson’s disease.

Zhittya has many projects advancing, and I am more confident than ever that we are close to proving our hypothesis that FGF-1 taken intranasally can reverse neurodegenerative diseases. I firmly believe that if FGF-1 is safe in the brain for patients with Parkinson’s disease, then it should be safe in the brain for patients with stroke disabilities, Alzheimer’s disease, autism, traumatic brain injuries, ALS, dementia, MS and more, and we are now beginning to treat patients with these disorders. If we learn that the simple and relatively easy delivery of FGF-1 into the brain via the intranasal route is safe and results in material medical improvement in patients with these devastating illnesses, God will have answered my prayers.

Zhittya thanks all of you who have supported us and guided us along this journey of medical discovery.

As we attempt to discover where the FGF-1 in the brain is going (vanishing) we will keep you posted. It seems wherever it is going, it's good for the test subjects and that is what matters most.

Dan Montano, CEO

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