



Building Blocks for the Future  
PILLAR III - HEALTH AND WELL-BEING

# Healthy Ageing

João Transmontano

ENTOGENEX EUROPE

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everythink



## About this white paper

This document aims to compile and summarize the speeches, thoughts and bold ideas shared during the Open Sessions of the 2021 Annual Event of the Business and Innovation Network, recording, for future reference, the contribution of a group of impressive people from all over the world who gathered in Porto to share, evolve and create knowledge and visions for the future of Humanity. This was a collaboration between BIN@ Network and Everythink, a design company.

## About BIN@ Business and Innovation Network

Business & Innovation Network (BIN@) is an international network of academic and industry partners engaged in supporting open innovation and the creation of sustainable forum for sharing good practices and opportunities in innovation. BIN@ promotes a set of activities ranging from brokerage events to softlanding opportunities for startups. BIN@ has currently around 4500 delegates worldwide and so far has held 14 international events in Portugal, UK, Brazil, Romania, Poland and one fully digital event. You can see more about our activities on the official website: [www.businessandinnovation.net](http://www.businessandinnovation.net).

## About Everythink

EVERYTHINK is an award-winning studio for creativity, design and innovation, established in 2008 in Porto. Through design, they put creative methodologies and strategic thinking at the service of companies' innovation, to create new services, products and experiences, impacting people in a positive, easy and happy way. Everythink's approach with customers, users, and stakeholders is key to create new products, services and experiences, with a positive impact on people's lives. The team works on different areas and outputs, offering diversity and experience in an effect of cross-pollination offering innovative insights, efficiency and time-to-market. Find more at [www.everythink.com](http://www.everythink.com)

# Healthy Ageing

A conversation with



**João Transmontano**  
*Entogenex Europe*

*João Transmontano worked in the pharmaceutical industry for over 25 years. He is PhD in pharmaceutical technology and drug delivery systems, postdoc on pharmaceutical medicine and MBA in marketing. He was guest professor in Southern California for global business strategy, leadership and ethics, which was pioneering in the 90s and a critical part of doing business globally nowadays. He has been active in most continents, developing innovative projects focused on wound treatment, mostly on elderly people improving their conditions of life.*

**As we eat healthier, medical treatment prolongs life of human beings. Looking back 100 years, people would rarely get older than 50 to 60 years old. In a century, our genetics did not change much, we are still the same people. What fundamental factors are responsible for a 20 years increase in the life period? Medicine is one of them, obviously. Food is another one, but food is catching up in a bad way. As the number of people living on the planet increases, more food is needed, and chemical substances that normally increase the food production also cause damage to the human health. This is where the medicine enters. We're seeing diseases like cancer, Alzheimer and Parkinson increasing. With less expression in the past, once we live longer, they got relevant and some of them are caused by what we ingest during our life period.**

**Medicine did a wonderful job keeping people alive, and we are not only living more, but with quality of life. The development of new products is incredible. Less invasive diagnostics are critical as people age, helping to diagnose situations that normally would not be detected on time. The doctor was a miracle man in the past. He had to identify or try to guess the problem. It was extremely difficult, especially if the patient was a child. Or even the veterinarians, where their patients don't speak. Nowadays, with all the diagnostics available, the doctor can really do a great job, because he has a lot of support. Diagnostic is a key issue, and then all those treatments that can help you extend life are great.**

We would normally say, “you are what you eat”, and a very important part of that is the quality of food. Food supplements contribute a lot, and their market is increasing worldwide. We do not get these kind of supplements in the normal food that we take every day. There is a huge food supplement industry and no price regulation, so they can charge whatever they want for the product. Meanwhile, medicines are highly regulated, you have to negotiate the price, especially in Europe and the United States, and the rest of the world tries to follow the reference prices of their countries of origin.

The big difference between medical devices and medicines is the way the substance acts. Medicines normally have a chemical interaction with some receptors in the body, while medical devices have a physical action. Just like an ointment, a gel, or an injection of hyaluronic acid in a surgery to give the structure of the eye. Medical devices are also not subject, until now, to price controls. We realized that one of the best products to treat and to prevent amputations, being basically the last line of defense is based on a product occurring in nature and known for quite a long time. The last thing that could prevent you from getting a member amputated, is using honey based products. Honey is a great product, a highly concentrated sugar product

that removes the water from the bacteria causing the microorganism death.

But sometimes honey also has some spores of a microorganism that can produce botulinum toxin, a very powerful toxin that can cause human death specially if applied on the wound. You need to make sure that your honey is free of contaminated biological agents that can kill the patient. This was done with highly energetic gamma radiation. And in one of the side conversations on the BIN@ event, we found that professor Adriano Carvalho, from the Faculty of Engineering at the University of Porto, had a specific technique to treat the chestnuts with electric current and ultra-sounds, that can be extremely effective and may have huge applications in other areas in food processing. We also use some biopolymers that can be reabsorbed by the body, and so you can even treat deep wounds, neutralize the bacteria, apply the product there, and those materials will be reabsorbed by the body. If this confirms the potential, we might have a very nice line of products that reduce the time of cicatrization up to 50% of difficult wounds that usually take 4 to 6 months to close.

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*with João Transmontano*

It's a huge cost saving! It took longer to find some honey suppliers with production capacity and eco certificates, but now we have suppliers for the long term with a quite good product.

I do envisage the future with people paying more and more attention to food supplements, and to products from rain forests and natural areas on the planet, where the production is not being affected by the pollution or by these modern substances to promote the growth and increase the crop production. One product that is very common now in Europe, is Açai. It's a Brazilian product, from the Amazon region. It is actually a very rich product with great properties. The quality of the water that you drink also helps drive the extension of your lifetime. A lot of people spend money buying bottled water. Now we also have relatively good tap water. 100 years ago it was not always the case, water quality was quite variable.

Then, there is also a well established need for movement, walking and doing sports, exercise, and open air. And we see one slight danger here is the sun exposure that people do not always take care of. Skin problems are one of the largest threats that we will probably see in the next 10 to 20 years. The sun exposure has increased maybe 20 to 30%, when compared to 50 years ago.

On the other hand, this is the dawn of a new

age, with diagnostic methods that identify diseases all the time, and innovative treatments. And the question is, how much is that going to cost and who is going to pay? Health insurance has been increasing year on year, where do you put the cap on that? It's a big challenge for the health systems, especially in those highly financed by the state, like in Europe. Brazil has the largest government health system in the world, probably more than 220 million people within a unique system. But also private insurance for around 30 to 40% of the population, where growing costs are becoming higher than the monthly salary of some families. The United States is another country where you have health insurance but a lot of people cannot afford it.

**If you don't have  
money, you don't  
survive? Where do  
you draw the line?  
You see all these  
systems collapsing.**

**Health for all**

Brazil has threatened a couple of times to break patents related to AIDS products in the past, because they had the largest system in the world that provides free treatment to AIDS patients. They use that kind of negotiation tactics to lower the prices, because Brazil has a very large market. When it comes to biological medicines, the situation changes a lot. Let's say, they break a patent of RNA vaccine for COVID. It would take years for Brazil to get the facility built, train the people and make it happen. This is not something that you just go to an existing factory, do a tablet, mix the powders and get the batches going on. This is more complex. And there are not many facilities in the world that can do cell culture, or produce these kinds of products. So breaking the patent, without the assistance, the know-how, it's not that simple.

There was a project we tried to do with the Belgians in the past, to build these small factories that would be assembled inside a container, and could move around the world, to produce the vaccines locally where they are needed. But this was cell culture. This was a more simple approach. Now, India is a very interesting example. It's an exception, because India has the capacity to produce vaccines in large scale. Why are they not getting vaccines for their population? There might be some interest there, as they produce for other companies and those

vaccines are being distributed in South America and other areas. AstraZeneca installed a huge manufacturing plant there.

Let's look at the last 40 years. We know that a virus pops up once in a while. There is a yellow fever outbreak every 10 years. We had AIDS coming in the 70s, then we had SARS somewhere around the beginning of the 21st century. Now we get this COVID twenty years later. And we believe that in the next 10 years, there'll be another one. So, shouldn't we make an effort to have some plants prepared to produce these vaccines strategically placed in different parts of the world? We have a flu every year, actually in the Northern Hemisphere, around April, Southern hemisphere around October, on a current basis. Now we have a flu that has the capability to affect more people and eventually to increase the rate of death by a few percentage points. So this is something as a new market, we got to live with these, there will be more.

The real pandemic is not the COVID, it is the people that are dying because of lack of treatment and attention. When you turn on the TV and see how many people died of COVID today, why aren't there other lines, with oncology, heart attack, and so on? There's a political use to keep you busy, to control your movements, your complaints, just to try to blame everything on COVID. We know the death toll is set to 4%, depending

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on your age, but we already vaccinated many people. These viruses don't go away. If you look into the past, to get rid of a disease normally takes decades. You may say we eradicated this and that, but you keep monitoring because sometimes it pops up somewhere. Let's not underestimate the problem, but also not overestimate it. And this is highly done around the world, with countries blocking everything. Definitely, going like that is just going to make another 30% of people poor and jobless, and then you have a really huge pandemic.

**Food as preventive medication**

The quality of the food obviously contributes tremendously to your health, because it is something you take every day. And what we see today is that a lot of food brings traces of pesticides. There are no new pesticides in agriculture, everything we use has been developed in the last century. This is one of the few industries in the world that has not changed in the last 40 years. And there's one reason for it. The methods of detection have improved very much, and the capacity of detecting small traces of these pesticides increased tremendously, so less products are allowed. Also science advanced and started to link some of the substances used to some specific disease conditions (cancer, Parkinson, Alzheimer, etc), like glyphosate, paraquat and other. The governments are aware that most

interfere with human processes, at normally causing diseases, and they raised the bar requiring products to have less content of these potentially damaging compounds.

Two years ago, the United States looked at about 50 brands of corn cereal, and they found that most of them contained well above the accepted limits for glyphosate. Science analyzed the continuous use of glyphosate during several years, and started seeing people developing leukemia, and that was considered proof beyond doubt. That's when the punitive charges led by the courts affected the manufacturing company. The Fiocruz foundation in Brazil has been monitoring the farmers around big plantations that use these large quantities of toxic products sprayed by airplanes. Invariably, they all get sick, they develop cancer, it's tremendous!

When people treat the wine grapes and have some beehives around, normally there is a decrease in the population of bees by 30 to 50%. Now, the bees are the key element for pollination. Without insects, we won't live, that is as basic as that. It all goes around. If it goes to nature, it gets back to you. And once you kill an insect with a poisonous molecule that is not easily degraded, like an organophosphate, that insect stays there and he's eaten by a rat or a snake. Birds as the American Eagle eat them, the Eagle started to become more rare and almost disappeared. As the symbol of the US nation it finally triggered some action.



Photo by Heather McKean on Unsplash

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It is like the landmine that you never get rid of. It's amazing that in the 21st century we still tell the farmers to apply poison. And, please wait 30 days, hopefully that the sun and the rain might dilute that a little bit, before harvesting the fruit. But the economics will lead the farmers to do the harvesting as soon as possible. This is the balance, healthy aging is totally linked with healthy food. You bring poison everyday into your body. If we could avoid that little extra poison in every bite on an apple or on a carrot, that would be wonderful. All these pesticides block enzymes responsible for essential processes in our body.

As common people become more aware, we are seeing an exploding market in biologics, foods produced in organic ways that do not use those pesticides. This was about 2.5% of the world market one or two years ago, but I do expect that to increase exponentially to 10% to 20% in a short time. Products that can be used to treat pests without bringing those kinds of diseases or conditions have a huge future. We have developed some innovative products and we do know that the world market of pesticides is worth about USD 80 billion, and is growing.

**Starving the insects**

These large pesticide companies are no longer innovative, they are just huge

machines to develop products from a laboratory bench into a commercial product. Innovation for their size is rare, as 90% of the innovation is done in very small groups. But they have the money and experience, and this is fundamental (similar situation happens in the pharmaceutical industry). And so far, they've been trying to block any newcomers. But smaller companies that use some biological products to treat the food crops are now moving and possibly getting into the market. Eventually, the large companies will start looking for these small companies, acquiring them, or making deals with them. They have the power to bring them worldwide, but need to change their own mentality as they will normally give preference to the internal projects and miss the opportunity. If they purchase something from outside, it means that some of their people feel threatened (they fear for their jobs). So they need to resolve this dilemma internally.

Let us establish here a connection between oncology and pest control. In oncology we mostly focus on killing the cells, removing them physically by surgery, poisoning them with chemicals or bombarding them with radiation. But, understanding the mechanism of cancer, we may eventually let the cells die on themselves, if we are able to unblock the normal death process called apoptosis. So, instead of using toxic molecules that kill the

insects, why don't we interfere in the processes by stopping their digestion and allow them to starve and die?

**It's a change of attitude. Understanding the process instead of simply destroying it, using it in your favor, like swimming following the current in a river instead of swimming against it.**

Science today makes this possible. We have this project – Biostarv - we try to block enzymes in insects that are critical for the digestion and energy generation. If somehow we could block this production, then the insects cannot perform digestion, they don't get their energy. Basically, they stop attacking the crops.

This is a project that we are doing with INIAV, the National Institute of Agriculture and Veterinary Research in Portugal, the Center of Biological Engineering in Braga and the Faculty of Sciences of the University of Coimbra, all in Portugal. A similar project is being carried out with Embrapa (Brazilian Agricultural Research Corporation from the Minister of Agriculture) in Brazil targeting

different crops. We are trying to identify modulators that may block the biosynthesis of those critical enzymes for digestion in the insects, and there is one particular enzyme – trypsin - that is transversal to mosquitoes and insects, which are the pests of agriculture.

Our objective is to identify at least one product that may be used as a target oriented pesticide, non toxic and biodegradable, which would be a peptide that would block the receptor responsible for the activation of the biosynthesis of the main enzyme in digestion - trypsin. All insects synthesize this enzyme and this is triggered by a receptor activated in the gut. They start producing the trypsin enzyme and the food is then processed to generate eggs for procreation and energy,. If you block the biosynthesis of trypsin, the insects cannot process the food.

The olive fruit is one of the targets chosen. There is a fly that bites the olive and feeds on the fruit, starting to make some little tunnels. Obviously this reduces the value of the fruit and of the olive oil. It's something you don't want to happen and we are trying to identify the way to block the production of trypsin on this fly. We spray the tree with a water suspension, so when the fly bites the olive surface it ingests an yeast containing that specific peptide. We need the yeast to protect the peptide from being destroyed in the gastrointestinal tract of the fly, because it's acidic and the acidity destroys peptides.

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Eventually the peptide is released in the gut blocking the production of trypsin, and the fly does not feed anymore on the olive. She flies around and eventually dies, and will be eaten by other insects, but there are no toxic products. After all, it's just yeast containing a peptide. In Brazil we target cotton, sugar cane, soy beans, maize and coffee.

**The mosquito**

That's the basic principle, not to kill but to let die. This along no toxicity to other insects, animals and humans and additionally, the product is biodegradable. This idea is behind the project we are developing. With the mosquito, we already have a product that works, and that's already a huge thing. With other insects, we've seen in the laboratory moths and flies being affected by some of our developed peptides, they won't feed on the leaves that they normally feed on. After spraying the leaves, they start biting the leaves, then they stop eating, they move around and then become inanimate and eventually die. And that's all we want to do, just to make sure that they don't feed in there and go eat elsewhere, trying to not affect the balance of the ecosystem. Reducing the level of crop destruction in a specific plantation from 50% to 10% is already wonderful. Very recently we got results that may represent the proof of concept we were hoping to achieve by 2026. Our partner Embrapa encountered extremely significant activity in

two insects that represent the major menace to two crops in Brazil (sugar cane and cotton). If confirmed on the field, this is the breakthrough we were hoping for – the change of paradigm in agriculture. In the long term, you know these insects have been here for millions and millions of years. If you manage to block the synthesis of trypsin they will develop another enzyme, maybe not so effective, but they have the genes there. So they will eventually mutate and go around this. But if you monitor that, if you understand the genome and the receptors, if we crack the code, we hope that we can just keep up with the level of transformation.

The mosquito is a very interesting animal. I learned a lot about it in the pharmaceutical industry, as I worked with malaria. They live from two up to four weeks. Only the females bite and they normally ingest 2 to 3 times their body weight in blood. That's why they lay low in the house, usually in the humid and dark toilets. They immediately start producing trypsin to digest the blood and generate amino acids to produce eggs, they produce around 150 eggs every time. But they have an autoregulation mechanism. So we're using a natural peptide that occurs in the female mosquito. The ovarian follicle starts to produce a decapeptide normally 10 to 20 hours after the ingestion of food, and this decapeptide blocks the receptor responsible to activate the biosynthesis of



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trypsin. At that moment, the female gets the signal that she should take off and go lay the legs around, close to the water. Those eggs are viable for up to two years, and when they meet some humidity, and heat, they within seconds generate a larva. And that larva has a voracious appetite and feeds on everything that's organic. In Europe and in the Americas, 8 to 10 days after she undergoes a metamorphosis and generates an adult, while in Asia, the mosquito has already mutated and only spends about 3 to 4 days on the water. Because that's the most critical and fragile period of its life cycle.

These mosquitoes have been around for about 100 million years. In perspective, the dinosaurs left 63 million years ago. So, the mosquitoes survived the dinosaurs. And we humans came into the equation only 400,000 years ago, and 10,000 years ago we started to have less air in our body surface. We became a very good food target for the mosquitos, so the female lives around us.

Once you kill a mosquito, and you see the blood in your hands, you have that decapeptide that blocks the receptor also in there. What was done was to isolate that decapeptide, sequence it and reproduce its genetic code, then put it into a yeast genome and then ferment the yeast, kill the yeast with heat, generate a powder, disperse it in water and apply that in the form of a spray into nature. The larva prefers this yeast because it

is one of their favorite foods, ingests the yeast which liberates the decapeptide into the larva gut and that blocks the production of trypsin. That's how the larva does not develop, and does not generate the energy needed to do the metamorphosis into an adult mosquito. We targeted three mosquito types that transmit over 30 known diseases: Anopheles transmits malaria, Aedes aegypti in America, and Aedes albopictus in Africa, Asia, and in the south of Europe. This is the Tiger mosquito that transmit 27 known diseases among those zika, dengue, chikungunya, yellow fever, Japanese encephalitis, Nile virus fever, you name it. And then the Culex quinquefasciatus that we have all over the planet, that transmit filariasis. One mosquito kills a person every 30 seconds, and this means about 1 million humans per year. So it's a pandemic every year. No vaccine. But it was until now a poor people's disease. With climate change on the planet, we need to get ready. We were a couple of months ago in Murcia, Spain, and one of the huge problems they have is the Tiger mosquito. They're already endemic in the region, and if they make the way to Alcáçer do Sal in Portugal they will become endemic there, too (in ancient times they were endemic there). They are aggressive, and if they bite somebody who is infected and they spread the disease, then we have a huge serious problem, we don't get rid of them very easily.

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Translating Systems Thinking into Public Health Innovations Terry Huang – CUNY  
Human-centered Design for Living and Ageing with Data Ana Correia de Barros – Fraunhofer Portugal  
Healthy Ageing João Transmontano - Entogenex

**Building blocks for the future**

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Júlio Martins, João Petiz