

I'm a Mortal Episode 6: Luigi Fontana – Diet, Metabolism, Medical Research

Speakers: Luigi Fontana (Guest), Sufal Deb (Host), Marvin Yan (Host)

[MUSIC - I'm a Mortal Theme]

Luigi Fontana 0:27

I'm Luigi Fontana. I'm a Professor of Medicine and Nutrition at the University of Sydney and Leonard P. Ullman Chair in Translational Metabolic Health, Director of the Healthy Longevity Program, and a clinical academic at the Royal Prince Alfred Hospital. Before moving to Sydney almost three years ago, I was a Professor of Medicine at Washington University in St. Louis in the US, and the Director--the Co-Director of the longevity program, and I also had a journal appointment with the University of Brescia where I was a Professor of Medicine.

Sufal Deb 1:08

Thank you so much for coming to Luigi. To begin, our podcast is called Im a Mortal, a little bit of a play on the word immortal. What does the word immortal or immortality mean to you?

Luigi Fontana 1:18

Immortal means eternal life.

Sufal Deb 1:22

Is that all you feel? If you got the opportunity, would you like to be immortal?

Luigi Fontana 1:26

We are immortal.

Marvin Yan 1:29

Oh, what do you mean by that-- immortal.

Luigi Fontana 1:33

We mean that our physical life is just one of the many transitions that our body, our atoms-- they are what we are made of-- go through. It's like if you see a piece of ice, and you say, "Now that it's getting warmer, and the ice is melting, it doesn't exist anymore." No, it does exist. It is transforming into the water and then into vapor and then as vapor and water, it goes somewhere else. It becomes a plant, an animal, a human, a cell. It is an immortal transformation of energy and matter into different forms. I think we are immortal, it's just a wrong perception of how the universe works.

Marvin Yan 2:21

Okay, that's a very creative answer. I don't think we've ever had an answer like that. Normally, we follow this up with "Would you want to be immortal?" But I guess you don't really have a choice in this case, right? We're just atoms.

Luigi Fontana 2:30

Yeah, we are immortal. It's just, again, it's a wrong interpretation of how the universe works. I think we are immortal.

Sufal Deb 2:42

I just wanted to ask a quick question. Can you tell us a little bit about your journey toward becoming the Director of the Longevity Research Program?

Luigi Fontana 2:48

Yes. Look, I got my degree in medicine in Verona in Italy. A beautiful town in North Italy. I don't know if you have ever been there, it is fantastic. Beautiful, old Roman so you can see there is a Roman amphitheater, and there are medieval buildings. Beautiful. Anyway, I did my medicine there. Then, I did my residency in internal medicine in Verona. I spent one year in London at King's College. And then I started my Ph.D. in metabolism. And as I was practicing medicine as a specialist in internal medicine, I didn't like what I was doing. I said I cannot do this job for the rest of my life. I cannot go to the emergency room and put some bandages on someone who comes in with myocardial infarction or stroke or cancer, knowing that many of these diseases and the suffering linked with these diseases are preventable. I said, "Look, I want to understand if we can prevent all this pain and discomfort and suffering and disability."

Luigi Fontana 3:56

I started to look into what we knew back in 2001, what was known about longevity and health and the only data available were from animals. We knew that if you take animals, experimental animals and you reduce calories by 30-40%, these animals will live 50-60% longer. Not only will they live longer, but many chronic diseases, like cancer, cardiovascular, kidney, dementia, and many others, are either totally prevented or hugely delayed. All these animals, at any age, are much younger, metabolically and physiologically, than the ad libitum-fed animals, eating ad libitum, and it was really fascinating and fantastic. There is a biological program that is working on mammals, so what about humans?

Luigi Fontana 4:59

I started to search and I found out that there was this [doc] professor at WashU [Washington University School of Medicine] called John Holloszy, one of my best friends, who just died three years ago, that was studying exercise and calorie restriction. I wrote an email to him and said, "Look, I'm interested in what you're doing. That's my interest." He replied back to me in a few days, and said, "Your interests are my interests, why don't you join me?" So, I packed my luggage and went to WashU, and I stayed there for 17 years. And so I had this beautiful journey with him, where we started to work on the effects of calorie restriction in humans, comparing calorie restriction with exercise, and then we moved into fasting, protein restriction, and the

quality of diet, Mediterranean diet, just to dissect how nutrition and exercise are able to modulate some of these important molecular pathways, metabolic molecular pathways that are essential to health and longevity.

Marvin Yan 6:01

As a follow-up question, when I first heard of your research, in my head, it didn't make sense, we're all built so we want to eat more and yet we live a shorter life. Is there a particular reason why calorie restriction ends up prolonging lifespan? Because logically if you tell someone it doesn't make any sense.

Luigi Fontana 6:21

Right. Yeah, so basically, what we think is going on--because you know the phenomenon that calorie restriction without malnutrition, with all the vitamins and minerals is extending lifespan, is very well known. Now we have data on monkeys. My studies in humans strongly suggest many of the metabolic molecular preventative actions are also happening in humans. The question is, why? So in nature, animals--and humans are animals-- we are designed to procreate. Our main task is to transmit our genes. In nature, animals don't live long. As soon as they are middle-aged and they lose their strength, they are killed by other younger animals or some very normally harsh death, they don't live long.

Luigi Fontana 7:23

The job is to procreate. Because food is not always available in nature, there are times when there is scarcity, where there is a reduction because there is a flood, there is a drought, and where there is any natural phenomenon that can occur, the food is less. When food is less, procreation is not possible. One of the physiological functions that immediately stops when there is food scarcity is reproduction. And what is interesting, what we are finding is that when food is scarce, these molecular pathways within our cells--they are sensing how much food is available for growth and in procreation, they shift into maintenance -- instead of growth and reproduction into maintenance. They keep the body younger. Why? The idea is that when food is available again, your body's younger, and therefore can reproduce, have less DNA damage, and less aging. It gives time for the body to get food again for reproduction.

Luigi Fontana 8:36

If you take animals on calorie restriction -- a mouse on average lives two and a half years long. Let's say you calorie restrict the animals for two years, and so chronologically they are in menopause. But if you refeed them, if you start to feed them ad libitum they are able to reproduce, even if chronologically they are in menopause. You are delaying the fertility period of life. That's powerful. I mean the effect of these dietary restrictions on physiology and metabolism and hormones is huge. It is a huge program and that's the reason. The reason is that contrary to belief, you think "The more I eat, the stronger I am, and the longer I live." Instead of -- it is the opposite because, within the limit, if you go below a certain level, then it is starvation or you're going to die. Or if you are eating an unhealthy diet without all the vitamins and minerals you are going to die. But within limits, like 30-40% restriction with all the nutrients. You are switching your cells from a growth and reproduction mode to a survival, protective, maintenance mode. You're investing energy to keep

yourself younger and more efficient.

Sufal Deb 9:59

You just went through a lot of how eating less keeps you younger and healthier. How is it that eating extra calories, eating excessive calories -- how does that accelerate aging?

Luigi Fontana 10:07

Well, there are several mechanisms, but the most important -- so what we discovered in the last 15-20 years is that there are certain pathways and in particular one is called the insulin IGF-1 mTOR pathway. That is one of the most important ones, it's not the only one because there are many that are working together. But this insulin IGF-1 mTOR pathway, based on all the studies we did with genetic manipulation of some of these molecules along this pathway, and with drugs, like rapamycin, we are able to extend lifespan in all model organisms that we have started. The insulin IGF-1 pathway is a pathway that is stimulated by the binding of insulin and IGF-1 to the insulin receptor and the IGF-1 receptor. So, why do you have high insulin? You have high insulin when you are becoming insulin resistant. If you have excess abdominal fat, these adipokines produced by this excessive abdominal fat are inhibiting the insulin signaling and you become technically what we call insulin resistant. When you have peripheral insulin resistance, you have compensatory hyperinsulinemia. The beta cells of the pancreas, they are producing more insulin to try to overcome this resistance. This excessive binding of insulin to the insulin receptor is triggering this insulin IGF-1 pathway. And the trigger of the insulin IGF-1 pathway by inhibiting FOXO translocation, for example, and activating mTOR is causing a reduction in DNA repair pathways, it is inhibiting autophagy, it is inhibiting antioxidant pathways like SOD2 and catalases, it is promoting cell proliferation -- more cell proliferation, more random mutation, more cancer, more cell senescence, and it is also inhibiting apoptosis.

Luigi Fontana 12:19

Apoptosis is a process where when there is damage within your cell that cannot be repaired, the cells go -- it causes suicide. That's what we are finding, of course, this is the main one, but then there are other pathways like the [unintelligible] proteins, NFKB [Nuclear factor kappa B], MIC [macrophage inhibitory cytokine], and there are many other ones that are working together and keeping ourselves younger, more efficient in getting rid of dysfunctional proteins, dysfunctional organelles, increasing DNA repair, antioxidant, and so on and so forth. And the beauty is that, only 50 years ago, we didn't know anything about it. We knew calorie restriction was extending lifespan, but it was a black box, we didn't know why. Because of all these experiments by using animal models, simple model organisms and rodent studies, by knocking down genes or overexpressing genes, now we have a clear understanding of what's going on.

Marvin Yan 13:29

Now that you've outlined one pathway for us. I don't think we need to go through all the pathways. Like you mentioned --

Luigi Fontana 13:33

It was just an example of how science by using technology has discovered the secret, the cellular

mechanisms.

Marvin Yan 13:41

Okay so now that we know a little bit more about how a diet relates to longevity. I think the current record right now, for the longest time has ever lived is 122-ish. Let's say you could start everyone on the ideal diet since they were a kid. How long do you anticipate the maximum lifespan is with the ideal diet?

Luigi Fontana 14:04

Well, we don't know. But let me put it this way, based on several lines of research, including the homozygous twin studies, twins that are genetically identical. We know that around 30% - 25% of your probability of living a longer or shorter life is due to the genes that you have inherited from your parents. 75% is due to environmental factors. Even in centenarians that are studied by Sebastiani and Pearls at Tufts showing that 40% of the lifespan in centenarians is due to genes and the rest is due to environmental factors.

Luigi Fontana 14:49

Let me put it this way. If you're born in a family where your parents are unlucky, and on an average lifestyle, they live 65 years. If you're smoking, overdrinking, if you're obese, or not exercising, you're going to die when you're 50. If you do everything right, if you do everything well, you're probably going to make it to 80 or 85. But if you're born in the family of Calment, the woman who died at 122-- and she didn't do calorie restriction exercises, she was not doing anything. Probably, you can make it to 140-150 with her genes, with her background. Instead of-- if you do everything wrong, if you're smoking and taking drugs, and that, probably you're going to die when you are 90.

Marvin Yan 15:41

Okay. Pretty much the rule is that we should still aim to all be healthier, even if we're not Jeanne Calment.

Luigi Fontana 15:47

Yeah, it's like Espinosa says, people, they think they are free. In reality, we are not free, there are certain constraints that are genetically determined, even in mice, they live two and a half years, but they will never live for 80 years. Maybe, their life is going to become four years, five years, but not 80 years. Monkeys, rhesus monkeys, on average, live for 27 years. The longest-lived monkey was the monkey who was nicknamed Sherman, who lived 44 years, on calorie restriction. This is one of the monkeys of the NIA calorie restriction study. She lived for 44 years. If you do it in an equation it is 135 years for a human being. But I doubt that a rhesus monkey is going to live for 80 years.

Marvin Yan 16:43

Okay, that's fair. That's fair.

Sufal Deb 16:45

I'm going to jump into a little bit of a demographic type of question. Various countries have various diets

and lifestyles, which countries, as of now in 2021, are good lifestyle examples and have longer living populations due to diet and exercise?

Luigi Fontana 16:59

Well, if you look at the data, the Japanese right now have the highest number of octogenarians, nonagenarians, and centenarians, in the world even if things are changing, because the lifestyle in Japan has changed quite dramatically lately. But I will say Japan, and then Spain, Italy. And then you have Switzerland and Scandinavian countries. But many of these improvements are due to major improvements in public health. We went from 45 years on average lifespan in 1850, to 80 and 84. 84 for men and 84 for women in 2020, in many developed countries. But this is because we drastically improved public health and hospitals and medications. We have a number of people that are living longer, but they are not living healthier.

Luigi Fontana 18:02

The US is a good example where they spend a fortune, I think, on the budget of NIH, it was like 3.3 trillion last year. They spent \$3.3 trillion on health. The results are poor. The life expectancy of Americans is a few years shorter than Italians, or Japanese because of the super unhealthy lifestyle of many Americans. The epidemic of obesity now is really appalling, 40% of men and women in certain states of the US are obese. If you put obesity and overweight together, we are now close to 75% which is a disaster. It is a disaster. In fact, in some countries lifespan is going down for the first time in the last 50 years instead of increasing lifespan, the lifespan is coming down.

Marvin Yan 19:00

Wait, can I ask, is the main reason that lifespan is going down in some countries purely because of diet or -- what's the reason that we're seeing this change only now?

Luigi Fontana 19:10

Because the epidemic of obesity is increasing. If you look at the 1980s, the number of obese and overweight people was a fraction of what it is now. Every year there is an increase in the number of obese and overweight people in the US. We think that obesity is a major driver of this phenomenon. There is an explosion of obesity in the US. Obesity and all the other related -- there is obesity, unhealthy food, overdrinking, smoking, and a sedentary lifestyle.

Luigi Fontana 19:50

If you watch a movie from the 1980s and you look at the characters, they were much, much leaner than now. If you look at a movie now, you look at the people around you, you can immediately see that people were much leaner than they are now. I lived in the US for 17 years, if you go to my -- to the cafeteria of my university, which is one of the top medical schools in the US, it is appalling, the number of super-obese individuals. It's normal. I was abnormal! I was the abnormal guy, the majority of people were overweight, obese, or super obese. It's terrible.

Marvin Yan 20:32

Okay, I know, there's a lot of misconception and you pointed out a bit earlier how the Mediterranean diet is looked up to as a good diet to possibly follow. But, at the same time, I feel like, one, there's a lot of countries around the Mediterranean and two, a lot of people have misconceptions like, "Oh, Italy, that means pizza", and they're like, "No, that's not what it means." Could you describe what an actual Mediterranean diet consists of that would help prolong longevity?

Luigi Fontana 20:56

Look, I wrote a book called *The Path to Longevity* where I summarize -- I mean, this is like 350 pages, so to summarize, in one hour all of these concepts are going to be difficult. But let me try to answer your question. The Mediterranean diet, as you said, is just something that is impalpable. What does it mean, a Mediterranean diet? As you said, there are 22 or 24 countries. And yes, they have some commonality, if you compare the food of the Mediterranean countries compared to the food of Germany or England, or Sweden, but it's not mechanistic enough. The concept is that if you're eating less animal food -- what is the typical Mediterranean diet, at least the one that Ancel Keys described in 1950 when he moved to Italy. The story is that this professor of Minnesota, Ancel Keys, was studying why, in the US after World War II, there was a huge increase in myocardial infarction. There were a lot of young, middle-aged individuals who were dropping dead because of myocardial infarction, and they didn't know why. In 1950 we didn't know that cholesterol, blood pressure, glucose, and signs of obesity, were respective to myocardial infarction, we didn't know. He met with a guy, with an Italian professor at a conference in Rome, about the food of the fowl, and he said look, in Naples, we don't have myocardial infarction. He (the guy) said, "I don't believe it. Keys said, "Come and see me." He was lecturing in Scotland, or any way in the UK, and he drove his car from the UK to Naples. Then he spent many years there, and he studied the Mediterranean diet, and he found that at that time in Naples after World War II, people were eating meat once every 10-15 days.

Luigi Fontana 23:05

Most of their diet was homemade, minimally processed, bread and pasta. With whole grains, not refined grains, lots of legumes, lentils, chickpeas, fava beans, borlotti beans, navy beans, very, very beautifully done. My grandma is from South Italy, as I tell in my book, and they were super experts in creating these very tasty recipes, full of flavour, spices and some olive oil. They would drink one glass of wine per meal. They were eating lots of vegetables and local fruits and some fish, nuts, and seeds. This is the Mediterranean diet that Ancel Keys found to be linked with a very low risk of cardiovascular disease. Cardiovascular disease, myocardial infarction, and stroke were unknown in Naples after World War II.

Luigi Fontana 24:13

But as you said, the Okinawans that do not eat a Mediterranean diet, that were living on Okinawa Island, which is south of Japan, also had very low cardiovascular cancer, diabetes, and stroke. They had a higher number of centenarians in the same historical time because again, after World War II, the Americans occupied part of Okinawa, where they still have a military base. They did -- the doctors of the army, did the survey, and they were looking at what the Okinawans were eating. The Okinawans were eating a diet that was very rich in unrefined carbohydrates. Instead of wheat grains, the Okinawans, they were eating sweet potatoes, the

local sweet potatoes that were very rich in -- the purple one in all these -- very rich in carotenoids. Carbohydrates from sweet potatoes were the main staple food with some tofu, soybeans and legumes, lots of local vegetables, and some fish. Meat was very rare. Once in a while they had local fruits. This was the diet of the Okinawans, that is not the Mediterranean diet, but has the same principle. Very low animal products, some fish, lots of legumes, complex carbohydrates, not refined not white sugar, white bread, white rice, but complex carbohydrates rich in phytochemicals and vitamins, some nuts and seeds. That's the diet.

Luigi Fontana 25:58

Is it only the diet? No, it is not only the diet, as I say in my book, diet is one of the components, exercise is very important. There are several mechanisms why exercise is acting on some of these longevity pathways, including the insulin pathway and cognitive training, relationships, even if you're super healthy and you eat a healthy diet, but you live in a very bad environment with a lot of anger, a lot of bad emotions, this is detrimental for health. We know that depression is often known to increase inflammation, they increase -- they have immune dysregulation effects. It's a combination of factors we have been studying diet, but there are other factors that are contributing to improve our health. Both our physical metabolic health, our emotional, creative, and intelligence health. Who cares to live long if you are a nasty, angry, selfish, greedy human being?

Marvin Yan 27:03

Now that we have mentioned that -- I was reading your book, and one of the things mentioned in regards to Okinawans was that mental health in terms of like, they're not getting old together, right? They have a community there. Because I think you mentioned loneliness is a huge factor, right? You might live a long time, but like you said, if you're just this mean person who's lonely, and just there's nothing good going on, that's terrible. It affects your health as well. This is a little bit of an aside, but are there any methods to help older people foster that same sense of community to help them improve their health together instead of just focusing individually?

Luigi Fontana 27:39

Well, look, that's not my field of expertise. I'm not an expert of a -- But, I've been living in many countries. I've been living again, in Italy, Germany, the UK, the US, and now, Australia for three years. I've been traveling for conferences or lectures all over the world. My understanding is that, of course, culture is very important. When you are born somewhere in a certain historical, cultural environment, you absorb what is there. The dogmas, the values, because you see what your parents are doing. As you learn how to speak Chinese or Japanese or Italian, you also absorb, what are the conventions, the dogmas, the habits and stuff like that and what I can see is that in Italy, in South Italy, as in Okinawa, families are very important. As you're born, the idea that your parents, your brothers, sisters, your cousins, and your extended family is very important. There is this respect, this willingness to live together, to support each other. It is very important. Instead of, for example, in this country of Australia, and when I was living in London, it is the opposite. They are very individualistic. For example, believe it or not, I've been calling my mom, even if I'm living in Australia or the

US every single day, for my entire life. We talk for half an hour and maybe when I'm eating dinner, stuff like that. When I was in London, and I told my colleagues that I was calling my mom every day, they said, "Are you crazy? I call my mom twice a year and sometimes if I tell her 'May I come home', she tells me, 'No, no, no, I have to play bridge you cannot come.'"

Luigi Fontana 29:37

And that's one of the reasons why in this country, in Australia, the number of people with mental disease is huge. In Australia, there is a Ministry of Health, and there is a Ministry of Mental Health. The number of people who are abusing alcohol and drugs is huge in this country. There is this obsession with getting drunk, with getting wasted. I think that one of the components of these mental, emotional issues, that is very common in these Anglo-Saxon countries, Northern European countries and less so, in India, South Europe, Asia, Japan, is -- even if Japan is getting worse because they are living in these pack towns with too many people but let's talk about the traditional Japanese that were living in a nicer environment in the countryside. It's that there is this very extroverted relationship with other people, caring for other people, and being supportive, instead of these societies that are very individualistic, very selfish, even within the family. You cannot count on your parents, you cannot -- you don't have this emotional bondage where when you have problems, and in life, we have problems, you cannot talk with your mom and father in a friendly way. You're alone, you are left alone, since you're a kid, you don't have any emotional support, you cannot count on someone you love, and they love you and you know that they love you. I think this has huge emotional consequences, and has huge emotional, and lifestyle consequences that go very well beyond the metabolic physical health.

Sufal Deb 31:33

Since we're on the topic of mental health, I just wanted to ask this very quickly. I know a lot of mental health issues like depression or anxiety, they cause you to not live life in a healthy lifestyle, whether that's having the motivation to get up and go exercise or get up and make yourself a healthy meal. How is it that these psychological stresses, how do they impact how we deal with our metabolism and our immune system?

Luigi Fontana 31:53

Okay, well, this is a vague question, again, I'm not an expert. I've been reading a lot about it but our understanding of how mental health and emotional health is impacting our metabolic health, inflammation, immune system, is very rudimentary. There are a number of new studies, but they are very, very, very limited. I'm a doctor, and I'm teaching at a university to medical students. Unfortunately, as I told you, I've been teaching and working in Europe, in the US, now in Australia, and everywhere. Unfortunately, the focus is on treating diseases, not preventing diseases. You go through medical school, with almost zero teaching about how lifestyles are mechanistically important for preventing diseases. There is no mention of emotional health and as you said, the consequences. If you are emotionally unwell, how can you take care of yourself? If you're wasted mentally, then of course the only way you can cope with your life is to drink or take drugs or become obsessed with something. It can be video games, it can be anything. Then, instead of using your energy, to invest, to stay healthier, enjoy life, enjoy your friends, your family, invest in your energy in creating something,

painting, writing, poetry, music, you waste your time in front of a whiskey or a bottle of wine or a beer or cocaine or whatever. Facebook, by watching for hours what other people post, is a problem, it is a big problem. But I think our society is not ready yet, to understand what people do, and education is super important. Going back to the analogy right now, all the medical systems are concentrated -- most of the medical system is concentrated in treating diseases, not preventing them. Let me make an analogy.

Luigi Fontana 34:10

Let's say you buy a new car, now you go to one of these shops and say you buy a new Ferrari, or a new Mercedes. Let's suppose that the guy who sells the car doesn't give you any instructions on how to take care of the car. He doesn't tell you that every 5000 or 10,000 kilometers, you have to change your oil. He doesn't tell you that you have to change your tires. that you have to change your -- you have to change your brake pads. Nothing. You start to drive this car happily and the car is working beautifully because it's new. But you'd have to be a genius to understand that if you don't do anything, probably around 20 to 25,000 km, your car is going to die. Because the oil is gone, and the engine is going to be destroyed, or because your tires are bald and there is some rain and you're going to lose control, you're going to have all your brakes -- brake pads or whatever. You know what I mean. Instead of -- if you take good care of your car, your Mercedes can easily last 300,000 kilometers instead of 30,000 kilometers. That's exactly what's happening in our society, people have no clue about what they have to do to keep their body healthy. There is no education. You go through primary, secondary, University, and there is nothing. They teach us everything about coding, math, algebra, calculus, poets, grammar, but nothing about what I'm telling my book. What are the mechanisms driving aging, how to exercise, different types of exercise, different types of nutrition, calories and mindfulness act on many metabolic molecular and other pathways. Nothing. Do you think it's normal in society? The most important education is first of all, how can you stay healthy? How can you improve your emotional health? How can you improve your intuitive creative health? Is it a key subject that should be taught in primary, secondary, and tertiary school? So, some of my colleagues and some people I know say, "Ahh, yes, well people, they will never change their lifestyle. I like my food." What does it mean, I like my food? You are Indian, from what I can see, isn't it?

Sufal Deb 36:52

I'm Bengali. Yeah.

Luigi Fontana 36:53

Yeah, so what you like, is not what I like, because you were born, where your mom was preparing, the Daal, very spicy, with certain spices that are very friendly to you, and you love them.

Sufal Deb 37:11

My palate is different.

Luigi Fontana 37:13

Yeah. If you're born in England, or if you're born in Japan, the type of food is completely different. The taste is

not something that you are born with because there is even an emotional linkage with your infancy, your mother, your parents, your traditions. I think that probably there is no education. It's like, if you say to my kid, do you prefer to play on your games, your PlayStation, or do you prefer to go to school? You know the answer. If you let him free, he is probably going to go to school twice a week, and then he's going to stay in front of the TV all day long. Instead, what we do is force them to go to school, they have to go to school step by step, eventually, they become engineers, doctors, lawyers. This is because step by step, day by day, in 15-18 years of education, they build that knowledge that allows them to design an airplane, to design an iPhone, do you know what I mean? But if you let them play all day long, what is going to happen? Nothing, they're going to become ignorant. They're going to stay ignorant. It's the same concept. I think if people were slowly educated about health, how to eat healthy, how to exercise, use their mindfulness and other stuff, to become better human beings, healthier human beings, then this is going to become part of our -- is going to become like second nature.

Marvin Yan 39:00

I know we don't want to keep you too long today. That seems like -- the overall message of today's podcast seems very clear, but because what you're talking about is a larger societal problem, right? We've normalized unhealthiness, almost in a sense, but for someone who wants to take control of their life today, whether it be diet or exercise, is there a recommended way to get them into this healthy habit and for them to stick to it for the rest of their life?

Luigi Fontana 39:22

Yes, as I said there are a number of interventions. There is not -- another problem with our current society, people look for a magic fix. Give me something, give me one thing. One day is the paleo diet, one day is the 5:2 diet, the other day is going to be the ketogenic diet, and then this and that. But, in reality, it's like if you asked me "Can you give me an easy way to become a doctor? Just give me a booklet, give me a maximum of 50 pages that explains to me how to become a good doctor. Can you give me a 50 page book on how to become an engineer?" Are you crazy? Are you kidding me? So that's another problem. We are living in a society where people want some magic fix. There are unfortunately a lot of people out there that are selling, "Don't worry, we're going to find a pill for you and the pill is going to mimic calorie restriction. Are you going to do mini exercise and stuff like that? Don't worry, keep doing your crazy life. Then we're going to give you something." No, no, I'm sorry. It doesn't work like that. Because even if, in principle, as we said, if we can find some drugs, they're going to maybe have a calorie restriction. I don't believe in that. I figure that maybe some drugs can potentiate the effects of a healthy lifestyle, but they cannot substitute a healthy lifestyle. But what about emotional health? As we said before, what about spirituality, you want to create a pill. Who wants to live a dull, selfish, lonely life and live maybe 90 years, 100 years as a selfish, greedy, lonely person? What's the point? That's life? I don't believe so. At least that's my point of view.

Luigi Fontana 41:21

Life is just a beautiful journey, where we can explore ourselves, we can explore the world, make friends, encounter people, see beautiful stuff, create something, music, art, poetry. We can do a lot of fantastic stuff, live our lives. If we are healthier physically, metabolically, psychologically, spiritually, we are going to be in a

better place to enjoy the journey than just living immortally a boring, selfish, greedy, environmental, destructive life. I tried to summarize these concepts in my book, as I said, it's called *The Path to Longevity*, where I tried to describe what I think. It's my point of view, I understand I don't know everything, but I've been working in this field for the last 30 years. If I put together my MD and specialization, and my research, it's almost 34 years that I've been working in this field and not only scientifically but as a human being, I'm interested in the whole idea of health. Not only metabolic health, but also again I said, emotional, spiritual, creative health, environmental health, a lot of people don't understand. Let's assume that there's going to be a drug for each disease. Where are all the metabolites of these drugs, and where are they going to end up? So, do they realize that when they take a chemical agent and antidepressant, they pee and poop, these metabolites, and they end up in their river, in their fish? There are experiments showing that you can find metabolites of antidepressants, anti-inflammatory, and chemotherapy agents in the fish they're eating, in the food they're eating. If billions of people are taking medications, we are destroying this environment in 50, 70 years. We have destroyed this environment, we are destroying forests, we are polluting the oceans, and we are destroying the topsoil. Just because we are greedy. Can you imagine all 7 billion people eating meat three times a week? What is that going to do for the planet?

Sufal Deb 43:53

Absolutely. If someone's a student or somebody who's very excited to get involved in this field, what can they do to get involved in the field that you're an expert in? How do they start?

Luigi Fontana 44:03

Look, probably they have to start like how I did. First of all to understand what they love, what they are really interested in. When I was a 27-year-old resident in internal medicine, I said, "Look, I cannot do this job for the rest of my life, what are my interests?" I spent time trying to understand what I was really interested in and then I started to search for who is working in this field. Who is the best? Who is the guy who is really doing advanced science in this field? I started to search, and I found -- it took probably six months, eight months to find out that John Holloszy existed. I sent emails around saying who is working in this field? Then, Richard Weindruch, one of the top calorie restriction guys in mice, told me "Look, I'm working on mice and monkeys. If you want to work on humans, there is my friend John Holloszy. Write to him." I wrote to him, and I went there and then because I had a passion to understand this one, I started to do my research, I started to think because John Hall taught me to think independently. The good thing about having a good mentor is that he allows you to think independently, to start to process, to not believe in dogmas, but to challenge what people think is the truth and challenge the truth and come up with your own ideas, test your ideas and progress.

Marvin Yan 45:40

Okay, well, we won't keep you any further, Luigi, since I know you've discussed a lot today. Right, for any of you guys listening, Dr. Fontana, Luigi's book will be in the description below, *The Path to Longevity*. I think you had the quote in there about reaching 100 as if you're the health of a 40-year-old, definitely read that. Once again Luigi, thank you for coming on the podcast. This is *I'm a Mortal*, your source for all things immortal, and we really appreciate you coming on to take the time to speak with us.

Luigi Fontana 46:05

You're welcome. Thank you for having me.

Sufal Deb 46:07

Thank you for coming on.