LONGEVITY WORLD FORUM


# FIRST CONGRESS IN EUROPE ABOUT GENOMICS AND PRECISION MEDICINE

Summary and conclusions #Longevity18

TALENTUM Cambridge Precision Medicine Genética Médica News

# Session 1: Genomics of longevity

## Ángela Nieto - Reactivation of embryonic programs during degeneration

Ángela Nieto began her presentation by stating that, although embryonic development has apparently little to do with ageing, several scientific studies have shown that during ageing, certain molecular programs related to such development are activated that should be silenced and may be harmful.

Ángela Nieto also spoke about epithelial-mesenchymal transition (EMT), a programme that makes it possible to convert epithelial cells into mesenchymal cells. This mechanism is important in different processes of the body such as, for example, morphogenesis. All the tissues are the result of at least one round of EMT, with the exception of nervous tissue. In adults, although this is normally silenced, it can be activated in specific situations, such as in tissue regeneration or wound healing. In addition, it becomes activated in different pathologies, such as cancer or fibrosis. Finally, it is also related to the acquisition of the characteristic properties of stem cells.

During embryonic development, certain types of cells must migrate from their position of origin to a specific destination, where they once again lose their ability to move, they differentiate themselves and they take on their final function. Ángela Nieto stated that something similar occurs in cancer, during metastasis, where certain tumour cells acquire the ability to migrate and spread through the body, invading new tissue and subsequently giving rise to a tumour. This separation of the tumour cells occurs in the early stages, often at the time of diagnosis. This situation makes it less likely that treatments will be developed that prevent such metastasis. In fact, according to the researcher, different evidence suggests that this strategy would be counter-productive.

Dr. Nieto poses, then, a pathological situation in which re-epithelialisation could be beneficial: fibrosis, a condition characterized by the formation of fibrous tissue in an organ in the body. Fibrosis is important in different conditions, not only in ageing. This condition emerges as a loss of homoeostatic balance of the epithelium of the organs. With age, damage accumulates in the organs. Some of this damage is repaired, but over time a progressive accumulation is produced that can lead to organ degeneration.

Ángela Nieto described different experiments that were carried out to demonstrate that EMT is required for renal fibrosis to appear. Thus, with the reactivation of a program specific to the development and partial de-differentiation of renal epithelial cells, renal fibrosis is induced. The environment created by the fibrosis and the inflammation is very

similar to that which occurs in cancer. In this case, the EMT is partial because the cells de-differentiate, but do not acquire any invasive capacity.

In genetic models it is possible to reverse the EMT induced by snail protein, as well as fibrosis to recover the morphology and function of the body. The results suggest that the EMT transition is a promising therapeutic target for fibrosis, a process associated with ageing and certain pathological conditions. The inhibition of this process in animal models of renal fibrosis recovers the morphology and function of the body.

## Federico Pallardó - Epigenetic factors related to longevity

Federico Pallardó introduced the subject of longevity and talked about how human life expectancy has increased in recent years. The researcher noted that ageing is not a disease, rather it is a physiological process; although it is true certain diseases do produce an accelerated ageing.

He also addressed epigenetic mechanisms, which affect gene expression without altering the DNA sequence, as elements of great importance for the functioning of the genome. These mechanisms, the researcher stated, are one of the molecular components involved in ageing.

Dr. Pallardó mentioned how some epigenetic profiles are modified with age and how there is a substantial difference between young children and the elderly. In addition, he described the changes in epigenetic mechanisms associated with ageing, as well as their molecular consequences, such as changes in access to hereditary material, incorrect gene expression, the reactivation of mobile elements of the genome, not to mention an increase in the instability of the genome, which is another of the molecular features of ageing.

Finally, Federico Pallardó presented a number of therapeutic strategies in research that may address epigenetic mechanisms to delay ageing.

## Maria Blasco - Telomeres and Telomerase

Maria Blasco began her presentation by referring to the existence of major efforts on the part of the scientific community to understand the molecular mechanisms of ageing, due to its relationship with the appearance of diseases as we grow older.

The researcher pointed to the shortening of the telomeres, the terminal structures of chromosomes, as one of the molecular features of ageing. She also presented the role of the telomerase enzyme, which makes it possible to lengthen the telomeres during their development, when many cells divide in an active manner. In adults, however, it remains inactive in most tissues.

Alterations in the telomeres lead to a series of specific diseases, called telomeric syndromes. Specifically, Maria Blasco described different studies on mice that have no telomerase and present shorter telomeres, a premature loss of the regenerative capacity of the tissues, and develop diseases associated with ageing. In these animals it was observed that telomerase expression increased survival, that they presented increased survival in the face of cancer.

Dr. Blasco also described how the generation of mice with extra-large telomeres, induced epigenetically in stem cells, produces animals with greater resistance to cancer, as well as longer survival. In addition, these animals show a reduced metabolic ageing. Hence, it is concluded that the longer the telomeres, the slower the ageing process.

The researcher emphasized that ageing cannot be treated directly, but that you can treat diseases that arise as a result of ageing, and she presented several animal models of diseases associated with ageing (aplastic anaemia, pulmonary fibrosis) in which the treatment designed to lengthen the telomeres has shown an improvement in symptoms of the disease.

In the case of pulmonary fibrosis, the researcher posed a scenario in which the presence of short telomeres combined with various environmental factors, such as tobacco, radiation or pollution, gives rise to the accumulation of damage to the alveolar cells of the lung. Short telomeres alter the ability of stem cells to regenerate tissue and this ultimately gives rise to the appearance of fibrosis.

Blasco's laboratory has developed several mouse models of the disease in order to determine in detail the mechanisms by which the shortening of telomeres influences the pulmonary fibrosis. These models have made it possible to carry out preclinical studies that indicate that treatment with a gene therapy that induces telomerase expression improves the symptoms of the disease.

The preclinical studies show that telomere shortening is one of the initial steps in the development of the disease, and that by acting in the face of this process, it is possible to curb the appearance of different molecular events (inflammation, senescence, apoptosis), which ultimately lead to the onset of the disease.
Treatment with telomerase (an enzyme active in development, but not in most adult tissues, and active in cancer) raises the question of whether the activation of this enzyme may induce lung cancer. Maria Blasco showed from different studies that treatment with telomerase reduces the number of senescent cells in lung cancer, but does not induce cancer.

## Session 2: The role of diet, nutrition and physical exercise in the quality of life

## Mari Carmen Gómez - Physical exercise in the prevention and treatment of Alzheimer's Disease.

Mari Carmen Gómez introduced the subject of longevity in the human species and how societies are witnessing an ageing population. The researcher stated that the time has come for us to be able to age better.

The researcher distinguished between life expectancy and healthy life expectancy, understanding the latter as a process of development and maintenance of the functional capacity that allows for well-being in old age.

Dr. Gómez centred her presentation on Alzheimer's disease, whose major risk factor is increasing age. In particular, she went over the main molecular traits of Alzheimer's disease that lead to neuronal death, as well as some of the treatments currently available, highlighting the fact that they improve the symptoms of the disease, but only temporarily.

Mari Carmen Gómez stressed that dementia is not an inevitable consequence of ageing and that 35% of all cases can be preventable if action is taken on the following modifiable risk factors:

- In early age: receive education until one is 15 years of age, and continue learning throughout life.
- In middle age: treat hearing loss to prevent isolation, controlling blood pressure and weight to prevent obesity.
- In old age: socialise, prevent diabetes, do not smoke, seek treatment for depression early and stay active.

The researcher then presented physical activity within the context of ageing and showed results indicating that remaining active in advanced ages has positive results and decreases the risk of suffering certain ageing conditions. She also stressed that, although there are different interventions on ageing that can improve longevity, they do not usually increase healthy life expectancy.

On the other hand, Mari Carmen Gómez commented on different interventions that do show potential in Alzheimer's Disease, highlighting certain controlled programs of dietary restriction and exercise among others. The researcher presented the following conclusions based on different studies with mice or persons:

- Exercise is an effective intervention to promote ageing and prevent neurodegeneration.
- We should start as soon as possible to maximize its beneficial effects, only prevention seems to be effective.
- It is advisable to exercise in a group, choosing an activity you enjoy and in a pleasant atmosphere.

## José Viña - Physical exercise as a drug for fragility and increased quality of life

José Viña began his presentation by stressing the need to have a multidisciplinary group of people to address the different aspects of ageing and Alzheimer's disease, and to promote healthy ageing. "Unless we change the paradigm, there is a limit to life expectancy," he said.
He also talked about the consequences of an ageing population: In his opinion, this situation will give rise to the onset of chronic diseases, a limitation of health resources, health inequalities, and economic inability to maintain the system.

Dr. Viña argued that the only way to treat different diseases that arise as a result of ageing is to intervene before the fragility associated with age appears, and he showed different evidence that exists whereby exercise should be considered to be a drug that can curb the frailty associated with ageing, even as a supplement to promote greater quality of life as we grow older.

The researcher also spoke of free radicals that result from the oxidation of oxygen, which are not only considered a source of damage, but also signals.
The researcher presented different theories related to longevity such as free radicals or oxidative stress, and he argued that the latter does not depend on age or ageing, but rather on fragility.

José Viña presented a scenario in which there is oxidative stress associated with or promoted by a healthy life, but that when fragility increases (as it does with age), it becomes something negative. Thus, in a pathological ageing, the role of oxidative stress acquires a negative result, while in healthy ageing it is not so harmful.

The researcher ended his presentation by talking about the development of a program to prevent ageing through exercise. This program offers various cognitive and physical improvements and reduces the number of visits to the doctor. "Growing old is not so bad if you look after yourself as you grow older," he concluded.

## Mercedes Aguirre - The importance of diet and nutrition for healthy longevity

Mercedes Aguirre began her talk by saying that ageing is a natural process, a progressive and inevitable physiological deterioration associated with age. She stressed diet as a very important factor for ageing, especially if one takes into account that we are continually exposed to it.

The expert introduced the concepts of nutrigenomics and nutrigenetics, i.e. how diet can influence gene expression and how certain variants of the genome may influence how nutrients are processed in each person. She also presented different longevity biomarkers.

Mercedes Aguirre also spoke about the importance of intestinal microbiota in nutrition. Although the basic microbiota is installed in the first few days after birth, diet plays an important role in its composition throughout life. In addition, intestinal microbiota can affect different body functions, including the brain. Patients suffering from different diseases have shown alterations in the intestinal microbiota. "If we want to have a healthy microbiota, it is vital that we make changes to our diet," he noted.

Mercedes Aguirre also spoke about the relationship between oxidative stress and ageing. The expert pointed out that the oxidative stress that is found in multiple diseases is one of the major contributors to non-healthy ageing. She argued that the use of antioxidants in one's diet may have a beneficial effect, but this requires knowledge of how to use them.

Finally, Dr. Aguirre spoke of inflammation as a response to damage in the cells and how this process, which is normally necessary, becomes a problem when it becomes chronic. More precisely, the inflammation associated with ageing is chronic, asymptomatic and systemic.

Mercedes Aguirre noted that diet may influence the inflammation and stated that a fatty diet and sugars encourage inflammation. The expert summarized her presentation saying that:

- A disorderly and highly processed diet cannot provide the necessary balance of nutrients.
- Each person has their own characteristics when it comes to processing food and taking advantage of nutrients. This changes according to the body and also with age.
- An anti-ageing diet should lower the consumption of animal protein and increase the intake of vegetable protein which is often accompanied by antioxidants.

She also believes that sugar is the main food poison in the 21st century, as it is responsible for numerous conditions. For this reason, she proposed eliminating fast sugars, without fibre, and increasing fibre intake through fruit, vegetables and whole grains. In addition, she recommended paying special attention to the labelling of products. "To age in a healthy manner, we need to eat in a healthy manner", she concluded.

## Round table: How to achieve healthy ageing

### Moderated by: Consuelo Borrás

### Participants: José Viña, Mari Carmen Gómez and Mercedes Aguirre

"It is very interesting to add years to life, but above all life to years". Consuelo Borrás used this phrase to begin the round table, addressing the anti-inflammatory diet in the first instance and highlighting the role of fatty acids in this diet.

Fatty acids are part of the cell membrane and the balance between their different fractions is important for the optimal functioning of the cells and their relationship with the environment. Mercedes Aguirre again defended a diet that balances the consumption of different fatty acids in line with the recommended proportions for improved cell functioning.

The table also mentioned fatty acids and how consuming different types of them can positively or negatively influence the body.

With regard to diet, it was also commented that it is important to maintain a balance and supplements or components that are considered beneficial within certain limits, which is why using or consuming them in excess can lead to other health problems. Thus, one of the conclusions of the round table was the need for balance in diet and nutrition.

On the other hand, the table addressed the topic of proteins in a diet. Mercedes Aguirre indicated that animal proteins contain all the essential amino acids, but plant proteins do not. Therefore, in the latter case, it is necessary to combine different vegetable products if we are to obtain all the essential amino acids. Dr. Aguirre pointed out that it is not that animal protein should not be consumed, rather that there is an overdose of it, which is usually accompanied by cholesterol and other factors that are the ones that are not really necessary or may have adverse effects.

The table also addressed the issue of sugars and sweeteners and the importance of the microbiota in ageing, as well as the benefits of melatonin as a supplement to delay ageing, something defended by José Viña.

The table was also asked to comment on protein deficiency in the elderly, a characteristic that affects 40% of the elderly in Europe. Protein supplementation was raised as a measure to combat protein deficiency, which together with physical exercise could be a highly successful way to prevent fragility and enhance the development of muscle mass and strength. In addition, it was commented that a diet rich in protein and low in carbohydrates can be protective in individuals with a high genetic risk of suffering Alzheimer's Disease.

Finally, the table identified certain shortcomings in the healthcare system, such as the need for more geriatricians, which explains why older people may not be well looked after. Viña stated that “the lack of geriatricians is a scandal". In the same way, he highlighted the lack of compulsory subjects in medicine on geriatrics, nutrition and education in exercise and sport.

# Session 3: P4 medicine in longevity: predictive, preventive, personalized, participatory

## Manuel Corpas - Interpretation of the clinical genome for risk prevention in chronic diseases

Manuel Corpas introduced population ageing as an important social and public health problem, and highlighted genetic testing as a tool that holds great potential for diagnosis and prevention. However, the researcher acknowledged that such testing also has certain limitations, such as the continuing evolution of knowledge, the fact that genetic risks are based on statistics, or that the existence of non-genetic factors also contribute to disease.

Dr. Corpas outlined the different types of technologies used to analyse hereditary material, as well as their advantages and disadvantages, and commented that, although to date whole genome analysis has primarily been conducted on people suffering from a disease, as the cost of sequencing has decreased and access to data has increased, whole genome sequencing is beginning to be seen as a tool to obtain a healthier life.
Manuel Corpas stated that, with regard to the analysis and interpretation of the results of sequencing, it is more difficult to analyse genomes in relation to healthy people who do not have any symptoms.

The researcher also stressed the communication between those who analyse the results, and the clinicians who treat the patients. The presentation of results to clinicians should be appropriate and adapted to facilitate their understanding in an unambiguous manner. This step is critical for clinical interpretation as too much information can be counter-productive, as it is easy to reach conclusions that have not been tested properly and there is the possibility that there may be conflicting sources and problems with uncertain or relative results.

On the other hand, Manuel Corpas presented the concept of the risk of developing a disease, especially in the context of direct-to-consumer testing, where results are often presented as proportions of risk. These tests are carried out as isolated events and are not integrated with medical or clinical information, which prevents the results from being contextualized. In addition, these tests do not allow the consumer to have adequate informed consent and to know the consequences of taking the test. Finally, the interpretation of results is left to the user, thereby losing the value of genetic counselling conducted by a trained professional.

The researcher pointed out that there has never been such an acute need for easier ways to interpret genetic reports: reports must be more consistent and clearer if we are to translate clinical genomics to medical practice.

## Jorge Cortell - Integrating data into the work flow of precision medicine: from image to genomics and including…

Jorge Cortell introduced precision medicine as something that is not new, given that this concept was already known centuries ago. He stressed that precision or personalised medicine should be something practical, and suggested that the major challenge was to combine clinical and genomic data, and their integration in the individual patient.

The entrepreneur spoke about his personal case and how he had been faced with a common problem in the medical field: the existence of different computer systems for different medical imaging techniques that do not interact with each other. Jorge Cortell told us how he used engineering strategies to optimize and streamline the acquisition and integration of medical data. In fact, his team applied communication theory techniques to data integration, breaking down the challenge into parts, solving each one of them and uniting them again to test whether or not the complete system worked.

His company, Kateron Systems, developed a software that helps healthcare institutions to effectively manage medical imaging data and genomic data in order to improve patient care. In this regard, Jorge Cortell recognized that the major challenges are:

- The ease of use of the data flow.
- When using the tool, the ease with which data can be entered and displayed in an integrated manner.

Jorge Cortell concluded his presentation by stating that “science is important, the clinic is important, but the approach of an engineer to solve problems is also necessary in the healthcare field”.

# Round table: Personal health information data clouds

### Moderated by: María Chatzou

### Participants: Manuel Corpas, Jorge Cortell and Pablo Marín

Maria Chatzou wondered what is needed to achieve true precision medicine. Emphasis was placed on clinical judgement supported by the integration of information in a way that is designed to provide context to clinical, genetic and imaging results. In addition, she stressed that genomic data require judgement, not only when it comes to interpreting the data, but also when it comes to knowing what to ask the data.

The members of the round table discussed the challenges of integrating data into something that can be useful. The following aspects stand out:

- Ignorance and inability to adapt the system: systems evolve and we must be prepared to accept that what you have at any given time may not be perfect.

- The background noise that can be obtained from patients, especially in the case of longevity, where one starts with people who are poly-medicated or who may have their own reactions to drugs, for example.
- Creating appropriate analysis models and being able to integrate different data into them.
- Knowing what to ask the data.
- Data security, where technological, legal, and attitude issues enter into play.
- Knowing how to translate the diversity of people to integration and data management software.
- Adapting to the latest data technologies and technological advances that are going to change precision medicine.

Maria Chatzou concluded the round table with a summary of the topics that had been covered, stating that "if you want to translate precision medicine to a given reality, you need to integrate data and to recognise the challenges you are facing, such as how to model the data and display an open and appropriate attitude".

## Arancha Galán – Vitrification of oocytes to prevent infertility

Arancha Galán argued that there is a widespread perception that we are going to remain young forever, and that we're going to have the chance to have children at any age. However, the ability to have children decreases with age, that is to say, conception and fertility. In addition, as age increases, many pregnancies that do actually begin end up having complications that compromise the viability of the foetus.

Arancha Galán explained the different mechanisms used to preserve female fertility, and emphasized that many of the advances have been made possible by efforts to preserve the ovarian tissue of patients with breast cancer, which paved the way to preserving embryos or eggs for future pregnancies.

Finally, Arancha Galán introduced egg vitrification as a high performance method to preserve eggs and embryos efficiently, so they can be used later in reproduction. She presented preliminary studies that show how children born with embryos obtained with vitrified eggs do not present more perinatal problems than those born with recently extracted eggs.

## Ana Sabater - Gene drugs and personalised treatment

Sabater began her presentation by stating that as we grow older, we take more drugs to treat the different conditions that appear with age, and by emphasising that pharmacogenetics can help make drug prescriptions safer. "In the United States, some 100,000 people die each year as a result of adverse responses to drugs. A significant proportion of these deaths could be avoided by using genetics to adapt the treatment", the researcher pointed out.

She also spoke about what happens in our organism when we take a drug and how small changes in our genes may affect the absorption, transport, metabolism, elimination or distribution of drugs in the body.
“No two of us are alike, we do not have the same genes. Therefore, we should receive different doses of the same drug”, Sabater said, recalling that food and lifestyle also interact with medication.

Ana Sabater went on to present a scenario in which, when a physician prescribes a drug, he or she should take the patient’s metabolism into account: whether you take other drugs that might interact with it, their lifestyle, what they eat and possible interactions with supplements, as well as the possible presence of inductors of inhibitors at the enzyme level and, finally, the patient’s genetic composition.

Dr. Sabater continued her presentation with different examples of the use of software destined to determine the most appropriate drug and dose for patients according to their genetic composition and their eating habits. For example, the consumption of supplements or foods that contain inhibitors or inducers. She clarified that it is impossible to remember or memorize all the interactions between drugs or between the different factors that can intervene in how effective a drug is on a person. In this sense, the design of software that compiles and processes information and calculates the most appropriate treatment for each person can be very useful.

Ana Sabater also stressed how important it is to correctly mark pharmacogenetic information on drug labels and noted that, although doctors think that they are prescribing drugs safely, they need to take into account the fact that their patients may be taking other drugs or supplements and they must also consider their genetic composition.

She concluded that “as the population ages, they need to take more and more drugs, whose effectiveness depends not only on the interactions between them, but also on the person’s habits and their genetic composition. For this reason, we need to integrate all the information and develop tools to do so”.

## Round table: What role do laboratories, pharmacies, clinics and hospitals play in the overall development of precision medicine?

### Moderated by: Gonçal Lloveras
### Participants: Juan Sabater, Elisa Tarazona and Ángela Pérez

The round table addressed the reality faced by professionals in clinical practice and in laboratories or pharmacies when it comes to managing how genetic information can

help in healthcare. It was noted that in Spain alone, adverse reactions to properly prescribed drugs cause between 15,000 and 20,000 deaths each year.

Participants raised the need to change doctors' knowledge and to introduce the teaching of how to use genetics in clinical practice. The lack of genetic knowledge in clinical professionals was highlighted, and it was commented that, in many cases, the doctor does not actually know what to do with genetic information or how to use it.

The participants also commented on the need for both parties, clinicians and genetic professionals, to work in synergy to not only facilitate genetic testing whenever necessary, but also the clinical interpretation of the results obtained and their relevance for patients.

## Session 4: Technologies and biomarkers in longevity

### Tom Stubbs - Epigenetics and environmental factors in ageing

Tom Stubbs began talking about the need for biomarkers for ageing or longevity, and proposed DNA methylation, one of the most well-known epigenetic mechanisms, as a biomarker. The researcher and entrepreneur pointed out that epigenetic markers can be used not only to estimate chronological age but also biological age, which in the final analysis tells us how well we are ageing.

Tom Stubbs introduced a mouse model to use epigenetic measures and to develop interventions, something that is not possible in humans. The mouse model indicates that as we grow older, methylation increases in regions of the genome related to development-related processes. This model also makes it possible to predict the chronological age of the animals with a rate of error similar to that of humans, so it seems appropriate to develop biological interventions in which to study possible treatments or strategies to influence longevity.

The researcher introduced the concept of epigenetic age in order to make predictions about life expectancy or ageing, and he mentioned his latest developments in methylome analysis, presenting new methodologies that make it possible to analyse methylome and genome in individual cells. In his presentation, Tom Stubbs introduced methylation as a biomarker of great importance for health due to its characteristics: it is dynamic, it is affected by external and internal factors, it is incorporated into the memory, it integrates a genomic base, it is stable and epigenetic signatures are specific.

Tom Stubbs concluded by stating that the field of epigenetics is just starting, but that it has great potential for health and the prevention of chronic diseases. In addition, he pointed out that, as many chronic diseases have systemic effects, analysing biomarkers (such as methylation) in peripheral tissues can provide a vision of what is happening.

## Aubrey de Gray - Biotechnology of rejuvenation: making ageing so healthy that we will call stop calling it ageing

Aubrey de Gray began his presentation by posing the serious economic problem of increased longevity in human populations. The gerontologist pointed out that with age, multiple pathologies appear that also exacerbate each other; he also referred to ageing as a scenario in two parts. In part one, he highlighted the production of damage as a result of the body's metabolism. However, the body has tolerance to endure a limited amount of such damage. Even so, the second part occurs when you exceed the damage that the body can tolerate, which is when pathologies appear.

For Aubrey de Gray, the problem of ageing in medicine is that they have tried to use the same strategies as in other aspects of medicine. The researcher pointed out that we cannot approach ageing as if it were an infection. The pathology of age is caused by an accumulation of damage. As far as he is concerned, age is not a biological process, rather a physical one.

Aubrey de Gray differentiated between geriatrics, as a discipline aimed at the study of advanced age, when the accumulation of damage is already leading to pathologies, and gerontology, as the study of the mechanisms of ageing, which could act at an early age to prevent the accumulation of damage from becoming pathological. In addition, he added an important factor: maintenance as an essential tool to make the body function for a longer period of time, regardless of age.

The gerontologist outlined seven fundamental types of damages that occur in the cells and proposed different approaches in order to achieve their maintenance and hence to avoid pathological ageing. The different approaches are currently in different stages of research. “We need more philanthropic support in basic research”, he said. “We aren't working on longevity, we are working on medicine. The important thing is not to get sick. However, we know that this medicine may well increase longevity”, he claimed.

Aubrey de Gray concluded his presentation with rather more social issues, putting forward some of the different ethical considerations that arise from people not getting sick and living longer, such as overpopulation, inequality of access, the emergence of immortal dictators or the saturation of pensions.

## Attila Csordas - AgeCurve, proteomics and extension/elongation of life expectancy: from free climbing to assisted ascent

Attila Csordas, CEO of the company AgeCurve Limited, threw an interesting question at the audience: Is it correct to use a single biomarker to measure ageing? Each organ, although it is always related to the other organs, has its own gene expression which is therefore different from other adjacent organs. That is why the idea of using a single biological marker to detect the state of ageing of absolutely all the components of our body is totally wrong.

In order to avoid the mistakes that one might expect from an analysis of a single bookmark, AgeCurve is selling a proteomic analysis based on samples of saliva that aims to detect different symptoms of ageing in different tissues. The biomarkers that are used are human-specific to prevent contamination of the sample by micro-organisms that live in the oral cavity.

In the first instance, AgeCurve measures different protein markers to detect *inflammaging*, a systemic inflammation that occurs in older individuals. To analyse this symptom of ageing, the calgranulin and interleukin 36 alpha proteins are isolated and quantified. Then they measure the state of cellular senescence using the protein MMP-9 as a molecular marker. Other symptoms of ageing that they also measure are the metabolic changes and genetic instability; to do this they quantify the GAPDH and pyruvate kinase proteins in the first case, and the age-related histones in the second.

According to Csordas, the AgeCurve platform will allow many professionals to have an aid in the detection and proteomic quantification of ageing in different age-related factors. In his own words, AgeCurve will make it possible to “switch from free climbing to assisted ascent”.

## Lisette Otero - Variables associated to telomeres, age and cancer

Over the last few years, various studies have linked telomere length to ageing. We now know that the length of the telomeres is variable in individuals of the same age and that it is not the only influential factor in ageing. Different factors related to lifestyle, such as food, influence the rate of telomere shortening.

In recent decades the quality of life has improved tremendously. This results in individuals who live longer, but are also more prone to suffer age-related diseases such as neurodegenerative diseases or cancer. Lissette Otero, the CMO and Laboratory Director of Life Length explained that “Cancer may be the result of cells surviving ageing thanks to telomerase reactivation". That is to say: it is possible that in some cases, senescent cells can ignore certain mutations in genes associated with telomerase activity, reactivating the function of this protein, giving rise to cancer cells.

Lissette Otero presented the telomere analysis test which uses fluorescent probes to determine telomere length. This technology makes it possible to use telomeres as biomarkers that can be related to different diseases such as pulmonary fibrosis or certain cancers. According to studies carried out by the Life Length laboratory, patients with pulmonary fibrosis had shorter than average telomeres, while those with leukaemia were larger than average.

As discussed in this presentation, Life Length, in addition to offering telomere measurement and diagnosis services, is also undertaking different projects related to ageing, oncology, fertility and cardiovascular risk. Currently the most noteworthy

project is Oncocheck, a grouping of six studies that seek to assess the clinical utility of telomerase in cancer and to attain a single telomeric biomarker that makes it possible to diagnose the patient.

The promising Oncocheck project consists on the one hand of a rigorous study of lung cancer prevention that seeks to provide an early diagnosis for this type of cancer. On the other hand, the project includes research on chronic lymphocytic leukaemia that aims to provide patients with a precise and reliable prognosis so that they can choose the best possible treatment. Other studies that are part and parcel of Oncocheck focus on the response of immunotherapies in different cases of solid tumours and prostate cancer.

### Ángel Alberich - medical imaging and artificial intelligence in longevity

All too often, the diagnosis of certain diseases is not entirely accurate. Professionals rely on their perception to draw the appropriate conclusions from a test. However, this can mean that they overlook subtle changes in the tests that could be decisive for the diagnosis of the patient.

In his talk, Ángel Alberich, CEO of Quibim, presented imaging biomarkers, a technology that allows you to base diagnoses on algorithms developed in an artificial intelligence.

The team at Quibim proposes the quantitative analysis of imaging biomarkers in routine medical care as a way to put an end to the inaccuracy of medical diagnosis based solely on perception. As Dr. Alberich himself commented, “what we have here is a model of health control that seeks to convert a clinical necessity into something real."

Researchers at Quibim have based their technique of quantitative analysis of imaging biomarkers on different studies. Among these investigations we find different initiatives that seek to provide the patient with a medical diagnosis before the symptoms of the disease begin to manifest themselves. These studies prove that molecular imaging analysis can be a great partner in improving the prevention of a large number of diseases and, therefore, in improving human longevity.

## MAJOR OVERALL CONCLUSIONS

- We are an increasingly elderly society and this represents a challenge: it is time to take into account all the factors that influence this fact.
- #Longevity18 has allowed us to understand the mechanisms that affect ageing and to develop biomarkers to develop strategies to delay it, as well as improve how we treat age-related pathologies.

- The ingredients in any recipe for healthy ageing are taking responsibility for one's own diet, physical exercise, adapted to each person's situation, and maintaining social relationships alive.
- We need to focus our attention on the development of the medicine P4 and the importance of genomic information in order to respond to drugs, and also on the applications of technology and artificial intelligence in medicine.
- The future is integrative and multidisciplinary medicine.
- It has been detected that medical professionals need to assimilate all the information that genetics and genomics generate. The scientific community is an ally in transferring this "tsunami of knowledge" for the benefit of the patients.