YEAR VII (XLIV) - n. 3 - **SEPTEMBER** 2021

Neuromed news

Quarterly medical and scientific magazine

The new biplane angiograph system

Innovative drugs against migraines

Smart monitoring at Neuromed

A look to rare disease

A voice to tell your story

NEUROMED
I.R.C.C.S.
ISTITUTO NEUROLOGICO MEDITERRANEO

AIUTA LA RICERCA

INSIEME CONTRO IL COVID-19

DONA ORA **www.neuromed.it**

SOSTIENI I NOSTRI PROGETTI DI RICERCA

L'attuale pandemia ha sconvolto letteralmente il mondo intero per la rapidità della sua diffusione, per gli effetti devastanti sulla salute e sulla vita di ogni popolazione, per l'eccezionalità dell'impegno richiesto a livello di prevenzione e di interventi terapeutici.
Migliaia di ricercatori sono impegnati in un'opera silenziosa e invisibile, l'unica da cui ci si possa aspettare la soluzione del problema.

Neuromed conduce da quarant'anni una lotta senza quartiere a patologie anche rovinose, combattendo su più fronti: quello della cura, ovviamente, ma – con lo stesso impegno – quello della ricerca e della prevenzione. Contro il **COVID-19** il nostro Istituto ha preparato e avviato un progetto molto coraggioso e impegnativo – la **BIOBANCA COVID-19** – con l'ambizione di studiare per ostacolare e impedire il ritorno di questa terribile malattia, ma – ancor più – di rendere possibile la necessaria prevenzione di altri flagelli dello stesso genere.

Si tratta di un piano straordinario, che ha bisogno di risorse straordinarie.

1. **BIOBANCA COVID-19**
2. **GLI SFINGOLIPIDI CONTRO IL CORONAVIRUS**
3. **TELERIABILITAZIONE REALTÀ VIRTUALE E TERAPIA A DISTANZA**
4. **VALVOLE 3D CHARLOTTE DA INNESTARE SU MASCHERE PER SNORKELING**

ANCHE UNA PICCOLA DONAZIONE PUÒ FARE LA DIFFERENZA

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Summary

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A people's research

The place of I.R.C.C.S. Neuromed among the best health and research institutions in neurodegenerative diseases, and more

Thanks to the trust of the many citizens who choose I.R.C.C.S. Neuromed for their "5 per mille" (a voluntary contribution in tax return), the Institute made important contributions to the fight against chronic and degenerative diseases, with particular attention to nervous system's ones.

In past years, in particular, the funds have been used to explore new avenues against pathologies with a dramatic impact, both for patients and for society. Here are some examples:

Regarding stroke, researchers and clinicians in the Department of Epidemiology and Prevention have been able to identify new risk assessment strategies. At the same time, Department of Neurology has been deepening innovative methods for the rehabilitation of affected patients.

The relationship between heart and brain is at the basis of the research conducted by the Department of Angio-cardio-neurology. Researchers, in this case, are focused on the relationship between hypertension and vascular cognitive decline.

The numerous aspects of multiple sclerosis have been investigated by the Department of Neurology as part of the "5 per mille" funding, from the action of lymphocytes, involved also in other neurodegenerative diseases to the role played by Epstein-Barr virus.

Thoroughly exploring, by innovative methods, the harmful effects of smoking on blood vessels. This is the goal of the research carried out by the Vascular Pathophysiology Laboratory as part of the "5 per mille" Neuromed program.

The Neurobiology and Movement Disorders Unit is committed to the experimental exploration of the relationship between epileptic seizures and specific neuron receptors in selected brain areas.

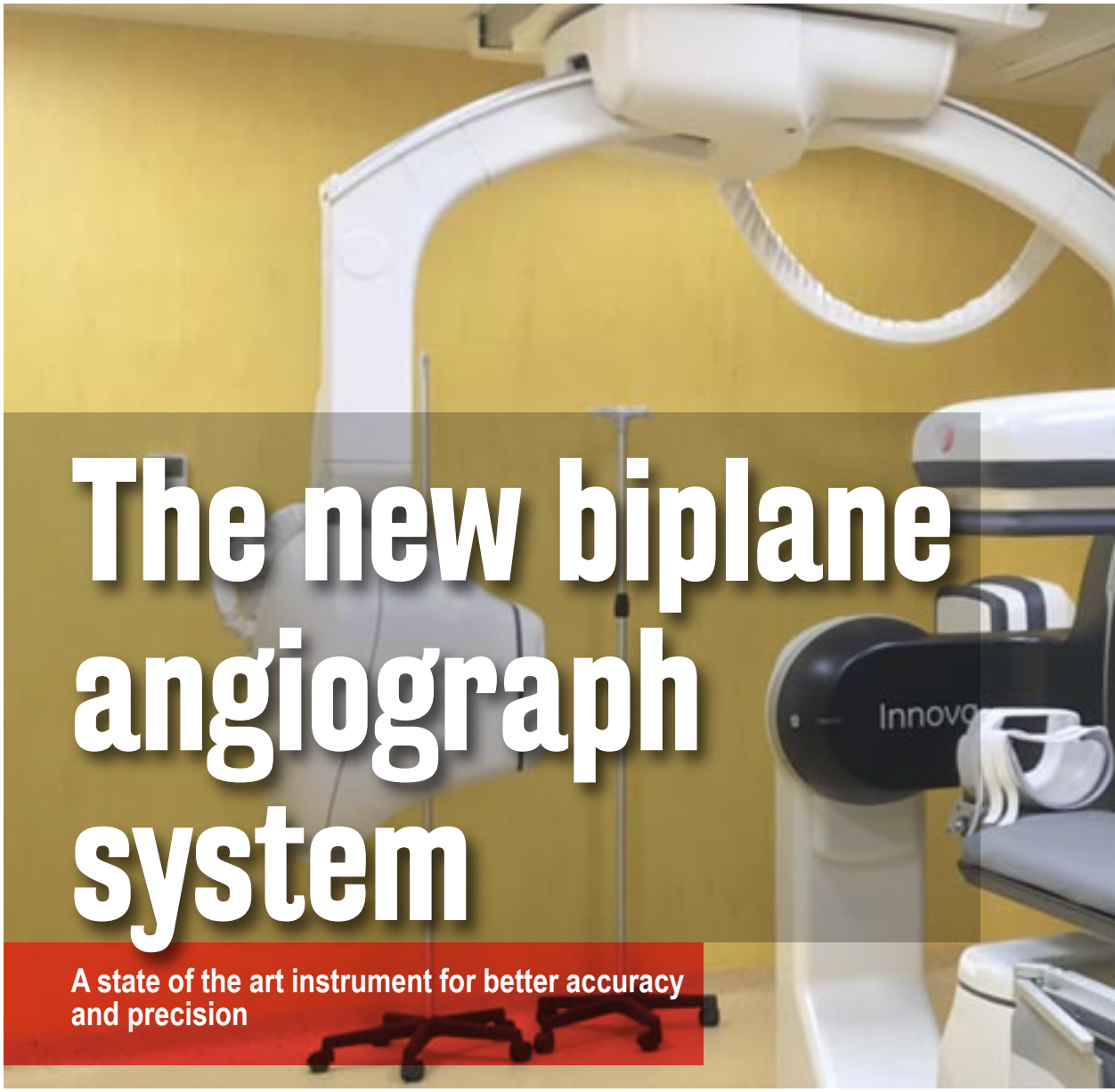
The "5 per mille" funds contributed to the research of the Neuropharmacology Unit in two very important fields: on the one hand, the role that particular receptors (mGLU) have in determining the onset and evolution of neurological and psychiatric pathologies, on the other hand, the role of stress and environmental factors in the development of a particular population of nerve cells, the interneurons.

Environmental pollution is becoming increasingly crucial to our health. It is here that Department of Epidemiology and Prevention, thanks to the "5 per mille" program, is carrying out research on atmospheric microparticulate.

All this, and much more, is the basis of researchers' and clinicians' daily work. At the basis of this commitment is the desire to offer the best treatments, tailored on the characteristics of the individual person, thanks to the so-called 'translational research' that goes from the laboratory to the patient's bed and vice versa.

YouTube

The importance of the 5x1000 contribution



The new biplane angiograph system

A state of the art instrument for better accuracy and precision

The new Biplane angiograph system at Neuromed is a new feature in the fundamental framework of a steady attention to technological innovation.
The latest generation device, replacing the previous angiograph already in use at the Pozzilli Institute, improves and innovates endovascular approach. Biplane technology, as with conventional angiography, uses a contrast medium in order to make vessels visible on X-rays, allowing endovascular and neurovascular surgery. But there is a big difference: three-dimensionality. The biplane technology, thanks to an advanced software, provides three-dimensional images of vessels. In this way it is possible to introduce catheters into the peripheral blood vessels, "navigating" them until they reach the site of the intervention, where surgeons and interventional radiologists can operate in a minimally invasive way, for example to remove a vascular occlusion or repair an aneurysm.

"This new equipment - says engineer **Fabio Sebastiano**, Managing director of Research and Operative Director at Neuromed – fits into our strong attitude toward continuous technological innovation. We wanted to renew the endovascular and interventional radiological instrumentation available for our patients. The three-dimensional environment offered by this angio-

graph has a strong integration with innovative software and mathematical algorithms. This allows us to push accuracy even further, accurately localizing the sites where an intervention is necessary, with a further reduction of the possibility of errors. Moreover, the new angiograph allows the execution of CT-like (computed tomography, ed) examinations directly in the angiography room. In this way, for example, a timely diagnosis of complications can be obtained. Overall, we are talking about a state-of-the-art technology, allowing us to enhance diagnostic and interventional activities, with particular reference to the treatment of cerebrovascular pathology, as well as vascular pathologies ".

Engineer Fabio Sebastiano

And the benefits are not limited to greater accuracy and speed, but they also extend to the patient's overall well-being. "The greater efficiency - continues Sebastiano - leads to a net reduction in procedure times, with less stress for the patient and, most of all, a substantial reduction in the amount of radiation he is subjected to". ■

A new piece for clinical and neurovascular research

The possibilities offered by the new biplane angiograph in the field of neurovascular intervention extend in three directions, reflecting the very soul of Neuromed: clinic, research and teaching

"Neurovascular interventional radiology - says Dr. **Salvatore Mangiafico**, Neuromed Neurovascular Intervention Consultant - is an important field because it offers minimally invasive solutions for a number of nervous system's vascular pathologies, such as aneurysms, arterial malformations, cerebral veins (so-called angiomas), cerebral dural fistulas, intracranial vascular stenosis and vascular malformations of the medulla. This new device is placed at the highest levels in the Italian landscape. It offers innovative diagnostic and, above all, therapeutic possibilities with a minimally invasive treatment that avoids surgery where possible. I want to underline how in interventional radiology practice we have a fruitful collaboration with neurosurgery. On this basis, Neuromed, with this new technological advancement, will increasingly represent a fundamental center in the treatment of neurovascular pathology".

Research will also benefit from the new biplane angiograph, as Mangiafico explains: "The advantage with a device like this is to have a different view of the brain, with the possibility of separating arterial and venous cerebral flows, but also of merging vascular angiography with nuclear magnetic resonance imaging. These are all

Doctor Salvatore Mangiafico

Doctor Marcello Bartolo

important elements not only for patient care, but also for the advancement of new clinical and diagnostic applications. The new angiograph is therefore an important link in the chain for neurovascular research that we are creating in Neuromed".

And finally training. "The concentration of technologies and experiences under development in Neuromed - says Dr. **Marcello Bartolo**, Director of the Diagnostic and Therapeutic Neuroradiology Unit - can be the starting point for complex training programs, not only for our staff, but also for other Italian structures. We are aiming at training young neuroradiologists who want to engage in interventional activity, both spinal and vascular. It is a project that we already started months ago but, due to the pandemic, we had to carry on as distance learning. We are very confident that in a short time we will return to train neuroradiologists here, in presence".

Commitment to innovation and advanced training are attracting patients too, as Bartolo underlines: "Neuromed is becoming an absolute reference point at national level for neurovascular and spinal diseases. Many difficult to treat patients come to us, and thanks to the advanced technologies and experience of our staff, they find here important answers". ■

Professor Francesco Pompeo

Evolution in vascular surgery

The new Neuromed biplane angiograph offers the possibility of pushing vascular surgery, a discipline that has seen profound transformations in recent years, even further. The availability of state-of-the-art devices, with high precision and high safety, translates into faster surgery, never losing sight of the patient's well-being.

"We must first of all consider - says Professor **Francesco Pompeo**, director of the Department of Vascular and Endovascular Surgery of Neuromed - that today the vascular surgeon has a very complex role: to understand different situations and to choose the best opportunity for the specific type of the pathology. He moves closer and closer to the concept of personalized medicine. In this context, the new biplane angiograph allows us a qualitative leap in terms of diagnostics and intervention capacity".

It is a field in which the constant acceleration of available technologies greatly enriched the weapons that can be deployed. "With endovascular procedures -

Doctor Enrico Cappello

continues Pompeo - technology fundamentally replaced the scalpel, transforming a catheter into a surgical instrument. We can enter the arteries, navigate our path through x-rays imaging, reach the site and treat the problem. Not only these technologies changed many patients' fate, but they changed our profession too. But we must always be 'complete' professionals: on the one hand we go further and further towards endovascular techniques, with their huge advantages, on the other hand we do not lose sight of traditional vascular surgery. And I would like to underline that here at Neuromed we choose also stem cells therapies, for example in diabetic foot. The combination of different techniques and approaches, together with clinical choices tailored on the patient, allows us to save many limbs that would otherwise undergo amputation".

Personalization is the key. "The approach is on the single patient - says Dr. **Enrico Cappello**, head of the Neuromed endovascular surgery - never generalizing and never performing standardized interventions. Thanks to the recent advances, also due to the strong commitment of industries in creating innovative devices, today we can treat more and more pathologies with approaches completely based on endovascular surgery, managing any complications in the same way. The benefits for the patient are enormous. Consider aortic aneurysms, for which very invasive surgery was necessary in the past, with a long recovery period, several days to walk again, and with significant post-operative pain. Today, thanks to endovascular surgery, this does not happen: the patient is in locoregional anesthesia, the prosthesis is introduced through a small cut in the groin and it is installed directly inside the artery. The patient gets up the day after surgery and can go home by the third or fourth day, without the need of intensive care. It also means a quick return to his job, to his normal life and to his/her family".

Generations confronting each other. "Alongside the many doctors 'born' with traditional vascular surgery - Pompeo specifies – then setting out for on new paths, there are now young people who find an already changed landscape".

"It is a completely different way of treating vascular pathologies - continues Cappello - It's like going from walking to driving a car. We are talking about a completely different way of living this discipline and probably, also for this reason, young people are very attracted to it. We have something that did not exist before, and young people are always attracted to crossing new borders".

YouTube

A heart for the mind

YouTube

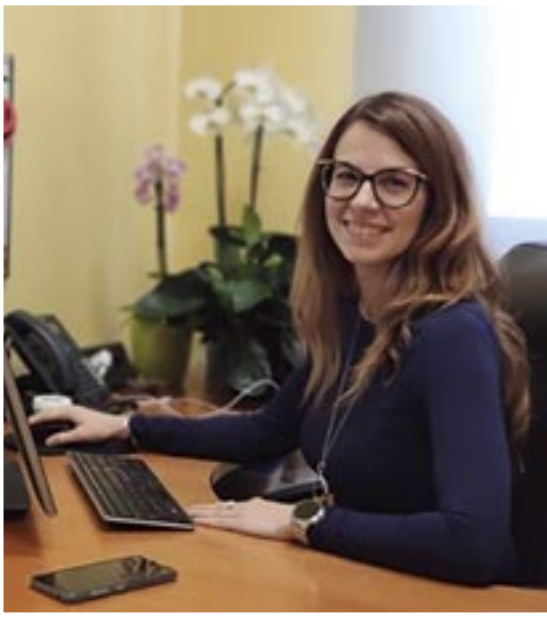
Cardiovascular system and brain health are increasingly linked. Hypertension and dementia at a crossroad

High cholesterol, high blood sugar levels, hypertension. These are all conditions making anyone worry about heart health, right away. Quite right, but the story does not end there: the brain is also at stake, and with it, the mind.

"Historically - says Professor **Daniela Carnevale**, Department of Molecular Medicine at Sapienza University of Rome and Department of Angiocardioneurology and Translational Medicine at Neuromed - clinical and basic research demonstrated that cardiovascular risk factors are the main factor behind acute brain events such as stroke. But what has been emerging more and more clearly in recent years is that the same factors can also have a strong impact on chronic neurodegenerative diseases. The study of this heart-brain connection arises first of all from the demonstration that arterial hypertension is the main risk factor for vascular dementia".

Recently, this scenario was expanded, even including pathologies, such as Alzheimer's, previously believed to be exclusively neurological. "If we study in details many forms of cognitive impairment - continues Carnevale - even through autopsy findings, we clearly see that there is a non-negligible vascular component. Our group, more than a decade ago, started studying this association between cardiovascular pathology and dementia. We want to better understand what happens in the brain, especially in cerebral vessels, when there is a dysregulation of cardiovascular homeostasis, as for example in the case of high blood pressure".

In order to perform these researches, Carnevale's laboratory at the Department of Angiocardioneurology and Translational Medicine



Professor Daniela Carnevale

developed experimental animal models of vascular dementia induced by arterial hypertension. This already led to the identification of molecular mechanisms that will potentially be future targets for innovative therapies. "At the same time - says the researcher - we are adding human research, thanks to our clinical department of Angiocardioneurology. In particular, we are conducting studies that combine the mere cardiological approach to a neurovascular analysis by magnetic resonance. Thanks to innovative imaging techniques, we aim at early detection of neurological damage in hypertensive patients. We then follow these patients over time, in search of new treatment options to counter the evolution of a pathology that, unfortunately, is becoming one of the major health problems at an international level"(1).

The "neuroimmune" system is proving to be decisive for many cardiovascular risk factors

Other studies by the same research group explore the opposite direction: communication between brain and heart. At the core is the role that the nervous system has in influencing blood pressure and, consequently, the health of vessels. "Not only the brain is a 'target organ' for hypertension - explains Carnevale - but it is also one of the main regulators of the cardiovascular system. The regulation takes place through two main modalities: the first one is a continuous exchange of information. Signals come from peripheral organs to the autonomic nervous system, which responds with impulses aimed to maintain a balance,

the so-called homeostasis. In addition to this, we were able to identify another way of communication and control: the immune system. The nervous system, in fact, controls the spleen, an organ that for decades was considered of little or no importance. Now we know that it is important for organizing appropriate immune responses, and the brain di-

1) Carnevale, L., Maffei, A., Landolfi, A., Grillea, G., Carnevale, D., & Lembo, G. (2020). Brain functional magnetic resonance imaging highlights altered connections and functional networks in patients with hypertension. Hypertension, 76(5), 1480-1490. DOI: https://doi.org/10.1161/HYPERTENSIONAHA.120.15296

2) Carnevale, D., Perrotta, M., Pallante, F., Fardella, V., Iacobucci, R., Fardella, S., ... & Lembo, G. (2016). A cholinergic-sympathetic pathway primes immunity in hypertension and mediates brain-to-spleen communication. Nature communications, 7(1), 1-13. DOI: https://doi.org/10.1038/ncomms13035

rectly controls which cells in the spleen are released into the bloodstream to reach peripheral organs (such as heart, vessels, kidneys) which, in turn, control cardiovascular functions. We call it the 'neuroimmune' system, and a growing evidence show us how it is crucial for many cardiovascular risk factors"(2).

The brain communicates with electrical impulses. This is giving rise to a new field of research: bioelectronic medicine, with the possibility of electronically intervening on the nervous system. "We are developing - concludes the professor - techniques that will selectively modulate nerve impulses in order to control the immune response. One of the first objectives will be controlling neuroimmune response involved in hypertension, but it is clear that the prospects can be much broader and can extended to different pathologies. ■

3) Carnevale, L., Pallante, F., Perrotta, M., Iodice, D., Perrotta, S., Fardella, S., ... & Lembo, G. (2020). Celiac vagus nerve stimulation recapitulates angiotensin ii-induced splenic noradrenergic activation, driving egress of CD8 effector cells. Cell reports, 33(11), 108494. DOI: https://doi.org/10.1016/j.celrep.2020.108494

The importance of contacting a specialist center for the correct classification of the disease

Innovative drugs against migraines

A disease affecting a large number of Italians, often underestimated. New drugs are now expanding treatment options for the most severe cases

The word migraine is often used inappropriately to generally indicate a headache. But it is something much more specific and complex. "It's not a simple headache. - says Dr. **Anna Ambrosini**, Head of the Headache Medicine Unit of the I.R.C.C.S. Neuromed - With the word headache, or cephalea, we generally refer only to pain in the head. Migraine, on the other hand, is a very specific pathology in which head pain is of course present, but it is not the only symptom. We talk about a real neurological syndrome, often accompanied by other symptoms such as sensory hypersensitivity, photophobia, phonophobia, osmophobia, nausea or vomiting during the attack. In short, it is not just pain, and it should not be treated exclusively as such. Migraine needs a detailed specialist's evaluation".

Migraines can present in various forms, different both in the frequency and in the characteristics of the attacks. "It can have - continues Ambrosini - different temporal patterns. It can be an episodic form, in which the attacks last between four and 72 hours, but it can also recur several times a month, and in this case we are talking about a frequent episodic form. Finally, there is the chronic form, in which the patient suffers from this type of headache for more than fifteen days a month, with understandably very heavy effects on his/her quality of life. Even considering all these forms, however, we must remember that migraine is a form of primary headache,

not caused by other disorders of the head or cervical spine. And it shows a high inheritance rate: almost 90 percent of patients have first or second degree relatives with headaches. Since migraine, in the vast majority of cases, is not secondary to other pathologies, diagnosis can be achieved, if the criteria of the International Headache Society are respected, on a clinical basis, with a detailed anamnesis and a careful observation of the patient. No need for laboratory or radiological tests".

A time comes when contacting a specialized center becomes crucial, both for the correct classification and for the therapy. "Our patients usually do not have a light or easily manageable form. In the vast majority, we see complex cases, either with a high frequency of attacks or not responding to the symptomatic drugs commonly proposed by pharmacist or family doctor. At that point, more targeted treatments, developed over decades, enter the scene. As triptans, which have been around for almost thirty years. They are not painkillers, but have a specific action aiming to stop the migraine attack. With this category of drugs, combined with others and with the study of the most suitable methods of administration, we are able to successfully manage migraine attacks in most cases. However, if mi-

Doctor Anna Ambrosini

Doctor Armando Perrotta

graine crises are very frequent, preventive pharmacological treatment becomes necessary, and drugs borrowed from other pathologies are available: beta-blockers, antidepressants, antiepileptics, calcium antagonists".

For some patients, however, traditional approaches could be no longer sufficient. "We have - says Dr. **Armando Perrotta**, Headache Medicine Unit of Neuromed - a percentage of patients failing to receive benefits from standard treatments, or having side effects. About two years ago, a brand new class of drugs, albeit with a long history of research, appeared on the market. As is always the case in medicine, advances come from a better understanding of the underlying mechanisms of a disease. In the case of migraines, during the 1980s it was understood the role of a peptide (a small sequence of amino acids called CGRP, ed) in activating the system governing pain perception in the skull. So a key element in the triggering of the migraine attack was discovered. During the last ten years, technological progress made it possible to create specific molecules, monoclonal antibodies, specifically targeting CGRP and neutralizing its action. In short, these two scientific advances led to a completely new class of drugs".

YouTube

Results obtained with these new drugs, administered through subcutaneous injection, were decidedly encouraging: "Since they target a specific mechanism, they have minimal side effects, as shown during the experimental phase and then in our clinical experience. As for the benefits, the patients treated in our center have a very good response. In at least 50-60% of severe cases treated with monoclonal antibodies, we managed to halve the number of days with headaches".

YouTube

It must be highlighted that these new drugs are not a definitive solution to the problem. "They are an extra weapon - continues Perrotta - to manage the most serious cases. As the Italian Medicines Agency (AIFA) states, they are not intended for everyone, but just for that minority of patients who, despite a traditional therapy course, continue to have disabling migraines eight or more days a month. In other words, monoclonal antibodies therapy is reserved to specialized centers like ours, and it is used only after a careful evaluation of the actual patient's needs". ■

Smart monitoring at Neuromed

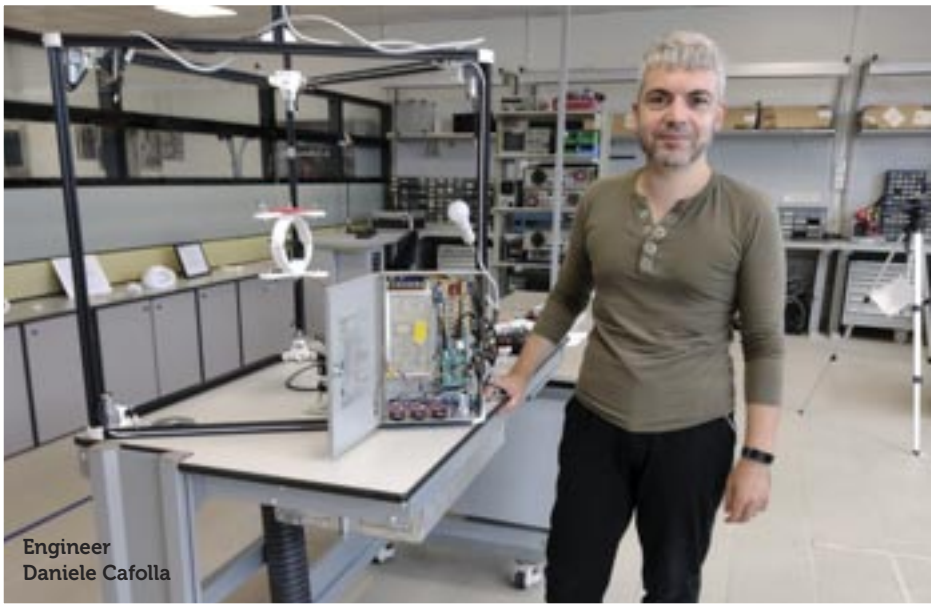
A new integrated system for monitoring temperature of refrigerators and environmental conditions in critical rooms

An anomaly in maintaining the temperature, for example in refrigerators, can mean the loss of years of sacrifices

Whether in a hospital setting or in a research center, monitoring environmental conditions of premises and equipment is crucial. This is the case, for example, of refrigerators containing biological samples, the basis of future scientific studies, but not only: entire rooms intended for specific applications need to be maintained in stable conditions. Neuromed has developed its own intelligent system, aimed to constantly monitoring the Center's environments in order to immediately call for intervention in the event of anomalies.

"Some conditions, as temperature and humidity - explains engineer **Monia Cambio**, of the Clinical Engineering Service at Neuromed Technology Park - are an extremely critical element, especially when it comes to environments intended for specific uses, such as rooms housing PET-CT for preclinical studies, or histological repositories, with their precious tissue collections, or even rooms for animals. Furthermore, there are refrigerators hosting cells or biological samples. An important part of our researchers' work is based on specific and appropriate environmental conditions. A failure in the cooling systems, or perhaps just a mere anomaly in maintaining the expected temperature, can mean the loss of years of sacrifices".

For a complex and articulated research center like Neuromed, keeping various rooms and refrigerators under control is essential, even in distant areas. And time is a crucial factor in responding to any problem. For this reason, a network of



Engineer
Daniele Cafolla

Engineer
Monia Cambio

sensors, integrated into a single control system, has been designed in order to provide laboratory and safety managers with a constant overview of the situation, even on their smartphone.

"The network - explains engineer **Daniele Cafolla**, head of Neuromed Biomechatronics Laboratory - is based on two types of devices: the sensors, installed in the environments to be monitored, and a 'mother' device in charge of checking the system to understand if everything is working properly or not. All control equipment devices "talk" continuously each other through the so-called 'man in the middle' system, as it is known in the "Internet of things" language. In this way we are not limited to receiving data, but we can immediately know if there are problems in the detection network itself. All the parameters of the desired environments, moreover, can be monitored by operators both via web interface or mobile phone ".

What kind of devices are you installing?

"The system is entirely modular, and this allows us to easily integrate it into different types of environments, regardless

of the number of sensors and their location. In refrigerators, the probe is inserted inside, while the control circuit can be applied to the outside by a magnet, avoiding any need for technical changes. Then we have environmental humidity and temperature sensors and, finally, devices able to detect power supply problems".

Something is going wrong in an environment. What happens next?

"A message is immediately sent to the smartphone of the person in charge of that environment, while the surveillance officers are being alerted on their computer by a change of colour in the affected area. In a few seconds everyone knows what kind of problem is occurring and which room or equipment is involved. Speed is everything: we are talking about environments and equipment for which an environmental anomaly can mean, within a few minutes, the loss of samples that are fundamental for research".

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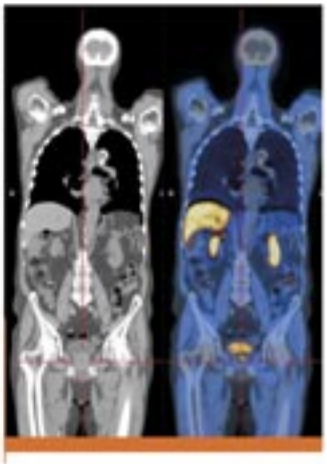
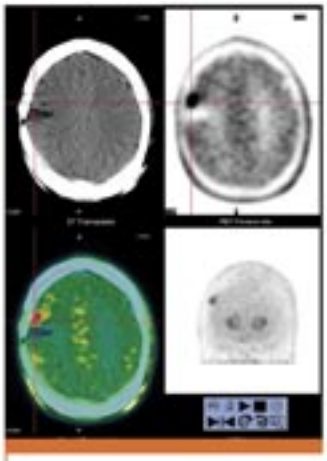
PET-TC

TECNOLOGIA D'AVANGUARDIA PER DIAGNOSI TEMPESTIVE ED ACCURATE

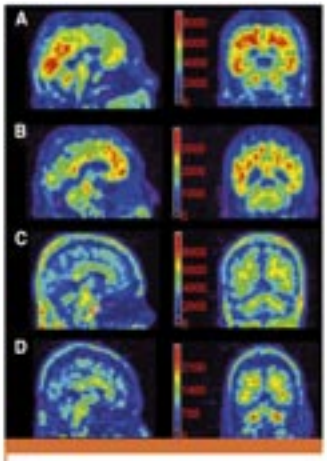
in campo oncologico e neurologico



^{18}F-COLINA PET/TC
indicata nella valutazione dei pazienti con carcinoma prostatico



^{18}F-DOPA PET/TC
indicata nella valutazione dei tumori cerebrali, neuroendocrini e sospetto per malattia di Parkinson



^{18}F-FLORBETABEN E ^{18}F-FLORBETAPIR
per pazienti con decadimento cognitivo e malattia di Alzheimer

^{18}F-FDG PET/TC
indicata nelle patologie neoplastiche per la ricerca del tumore primitivo e di eventuali metastasi, nella valutazione post terapeutica dei tumori e in campo neurologico

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In the fight against COVID-19, sport is a player

Physical activity is a valid tool against neurological and psychological consequences of isolation and inactivity during lockdowns, but also against long-term effects of the disease

Professor Francesco Fornai

"Even before the pandemic, we knew very well that sensory and motor deprivation can aggravate various pathologies, not only of the central nervous system but also of the cardiovascular system, and even in the oncology field". **Francesco Fornai**, Professor of Anatomy at the University of Pisa and Head of the Neurobiology Unit of Movement Disorders at Neuromed, highlights an underestimated aspect of the COVID-19 emergency: the negative effects due to the lockdowns established to curb the infection. Gyms closed, limited outdoor walks, zero social activities were all necessary, of course, but they can present now a heavy bill to public health.

In order to develop post-pandemic recovery strategies focused on the relationship between physical activity and health, Fornai was recruited to be part of the "Health in sport" technical table, set up by the Italian Ministry of Health. This structure, promoted by undersecretary Andrea Costa, is composed by relevant professionals in the field of research, medicine and sport, under the coordination of Pier Francesco Parra, university professor and medical director of the Italian Tennis national team.

"During the emergency - says Fornai - citizens experienced first of all a physical deprivation. It is not just a matter of reduction in real sports activities (going to the pool or gym, soccer with friends, for example), but we also observed a decrease in all those small activities related to daily life, even the simple walk to a bar for a coffee". In short, more citizens engaged in teleworking, distance learning or even just in the latest television series. Medicine has known for many years that the negative effects of sedentary life on cardiovascular system are severe. "We are not simply talking about those who already had cardiac, respiratory or musculoskeletal patholo-

Sport has the ability to create socialization and interaction, enriching the brain

gies - continues the head of the Neurobiology Unit of Movement Disorders - Obviously in this people we saw a worsening of their conditions. But there are also healthy people who in this year and a half developed a series of small diseases previously unknown to them, because they never experienced such a long period of physical and psychosocial inactivity. Let us remember that limiting physical activity means also taking away social activity. Sport can create socialization and interaction between people, so it can enrich the brain".

And the world is facing another problem: the long term neurological effects in COVID-19 patients. Here, too, a return to physical activity, social interactions and, in general, greater stimulation of the brain can come into play for rehabilitation. "Beyond - continues Fornai - the early neurological complications related to the infection in progress, such as cerebral stroke or epileptic seizures, which are events related to the severe inflammatory state in progress, we are observing more subtle and prolonged effects over time. In fact, alterations in the ability to concentrate are well described, as well as loss of attention and of clear thinking. We can see this phenomenon especially in professionals, people who were used to a very intense intellectual activity. In some cases, after the disease, they realize that their abilities are diminished, and this lasts months. An Italian research group identified the possible reason. According to the research, Sars-Cov-2 virus invades an area of the nervous system called reticular formation. It is here that the underlying brain rhythm is generated, guaranteeing awakening, state of alertness, ability to concentrate or ability to orient oneself in respect to new stimuli. Then, we must add anxiety, alterations of sleep-wake rhythm and sudden fits of drowsiness. The return to movement, to sharing spaces, to socializing, is a very valid help for these patients, which is why the establishment of this technical table by the Ministry, in my opinion, represents an important meeting point between doctors, researchers and sportsmen looking for the best solutions".

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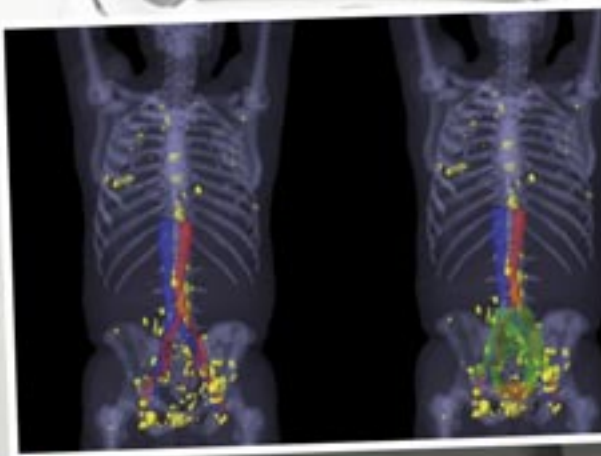

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Mitochondria: the helpful guest

YouTube

Born from an ancient alliance between different life forms, the power plants of our cells are at the center of new research related to important diseases

Professor Speranza Rubattu

It happened some two billion years ago. Somehow, thanks to a not yet fully understood process, a species of bacteria formed a symbiosis with eukaryotic cells. Now they are still there: the ancient bacteria become precious hosts, small organelles called mitochondria ("chloroplasts" in plant cells). Their job is to provide energy, and in school books everyone read their description as "power plants".

They are definitely exotic: they have their own DNA, independent from the hosting cell one, and we inherited them only from our mother. Without them, the cell would have no energy to live, and various pathological processes revolve around energy production. "Mitochondria - says Professor **Speranza Rubattu**, I.R.C.C.S. Neuromed and Sapienza University of Rome - have a fundamental role in preserving our vital functions and maintaining our health. In fact, any dysfunction in them creates a pathology. We are not just talking about spe-

cific mitochondrial diseases, inherited and already well described in medicine. Today we know that mitochondria are also implicated in more complex and widespread diseases, such as myocardial infarction, stroke, metabolic diseases and cancer. In short, any dysfunction of the mitochondrion causes damage to the entire cell which, in turn, lead to tissue and organ damage".

Are we talking about genetic aspects? Or environmental factors, perhaps linked to lifestyle?

"We still don't have a very clear idea about the specific role that mitochondria play in diseases such as heart attack, stroke, cancer or diabetes, to name a few. Certainly in all these pathologies we observe a form of mitochondrial dysfunction. This could be the primary cause (perhaps starting from an altered mitochondrial gene), or it could be the consequence of a disease caused by other factors. There are still many aspects waiting to be clarified in relation to this topic. What we currently know is that alteration of mitochondria functions, once it is established, contributes to the disease and worsens its manifestations".

Your laboratory is working on various substances, including natural ones, capable of improving the health of mitochondria.

"Over the last years we identified various mechanisms through which problems affecting the mitochondria can cause damage to organs, as can happen, for example, in the case of myocardial infarction and stroke. Having understood the importance of mitochondrial dysfunction as a contributing factor behind these pathologies allows us to develop therapeutic interventions as well. It is a very promising research field, and several data show

that some natural molecules are capable of correcting mitochondrial dysfunction, maybe even preventing them. At the same time, in collaboration with other research groups, we are working on the identification of new molecules with the same target. Our goal is to find new ways to develop prompt treatment of myocardial infarction and stroke".

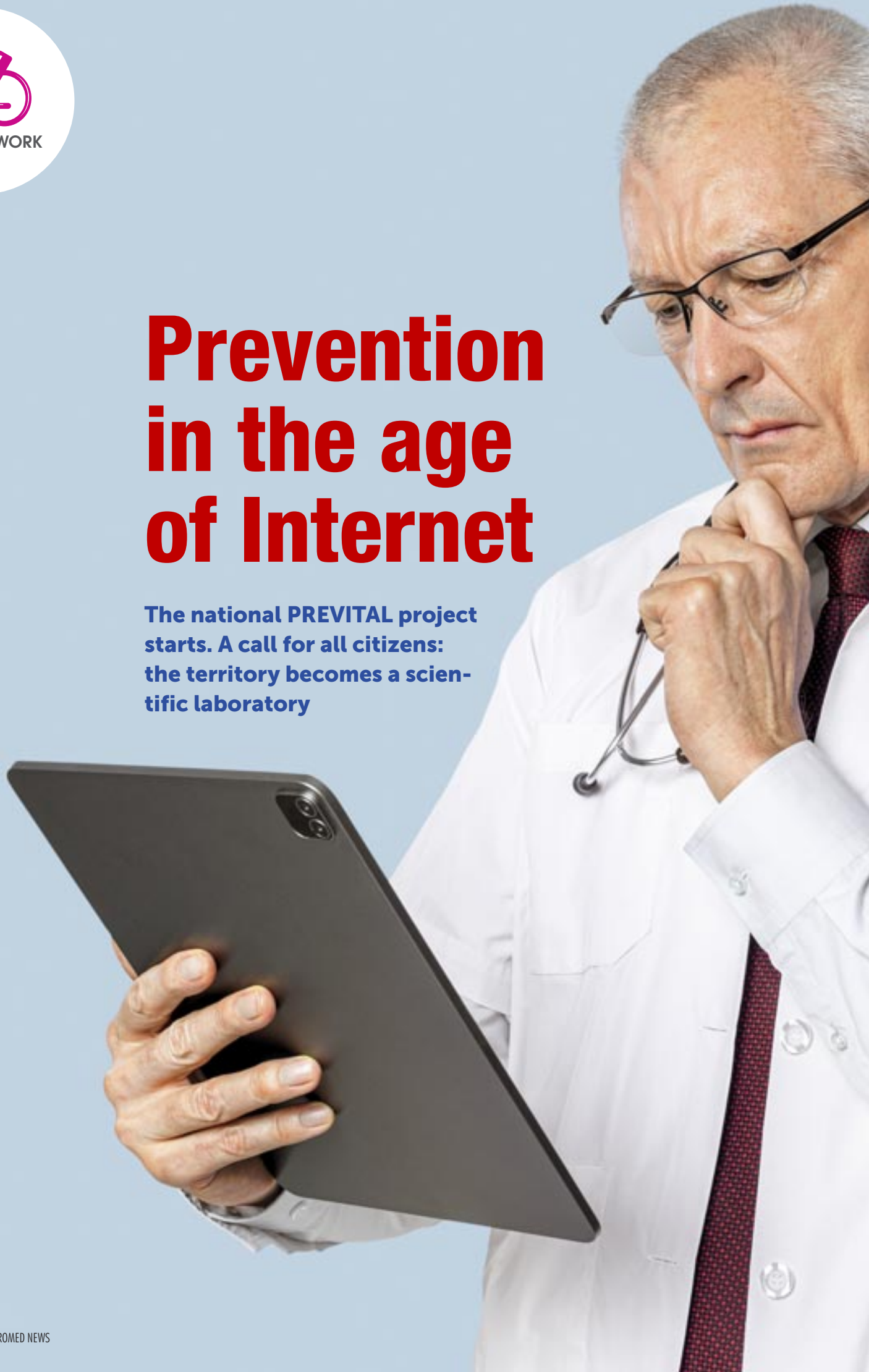
Is there a prevention that we can adopt in our daily life? Or, in other words, can we "ruin" our mitochondria with bad habits?

"All negative behaviors, both in nutrition and in lifestyle, damage the cells and their organs, and therefore the

mitochondria. This happens even more so in the case of a subject with a hereditary predisposition, perhaps due to a defective mitochondrial gene. This person will be much more sensitive to harmful environmental agents, such as cigarette smoke or an excess of salt in the diet. In our lab we developed a good experience in relation to mitochondrial genes mutations. We first characterized the pathological role of a mitochondrial gene in an animal model of spontaneous stroke, and we subsequently verified that a mutation of the same human gene brings to an increased risk of stroke and myocardial infarction. Take a subject with this genetic variant: maybe he/she is still healthy, but if he/she smokes or eats too much salt, he/she will develop a mitochondrial damage greater than subjects without the mutated mitochondrial gene. From this evidence we can draw an important message on the possibility to prevent cardiovascular diseases with an early genetic characterization. In any case, a healthy lifestyle still means avoiding damage to these precious components of our cells, for everyone".

Prevention in the age of Internet

The national PREVITAL project starts. A call for all citizens: the territory becomes a scientific laboratory



There is the calm family doctor who looks at his/her patient, whom he may have known for years. He takes a look at the latest clinical tests and then tries to suggest some changes, to quit smoking, eat better, do more physical activity. A scene that has become classic since the enormous value of prevention was understood. It is the weapon that, according to Eurostat / OECD, would make it possible to avoid more than half of the deaths in people under 75.

But the patient spends only a few minutes in the family doctor's office. An increasingly large part of his life is immersed in a digital world that can deeply influence his/her behavior, for better or for worse. This is the field Italian cardiovascular prevention wants to move in, and the PREVITAL Project (Primary cardiovascular prevention strategies in the Italian population) represents the spearhead for developing new communication and information strategies for citizens.

"PREVITAL - explains **Licia Iacoviello**, Director of the Department of Epidemiology and Prevention of Neuromed and Professor of Hygiene and Public Health at the University of Insubria in Varese - is a major project for the prevention of cardiovascular diseases, born under the auspices of Italian Ministry of Health with the collaboration of the IRCCS cardiovascular network. Neuromed will play a fundamental role in Southern Italy, thanks to its Clinical Research Network, extended from Lazio to Puglia".

PREVITAL's objectives are ambitious, and they will need the cooperation of citizens. "Basically - continues Iacoviello - the aim is to exploit new technologies, from telemedicine to the simple use of mobile phones. The question is: can we use these sys-

YouTube

tems, this Internet in which we all live by now, to improve the health of Italians?"

Mobile phones or tablets are with us in every moment of our life. Can they also become partners in our health? Can they guide us towards a prevention that is "tailored" to the single person? The answer is not obvious. We are not talking about one of those generic training apps that anyone can download and install on the pone: PREVITAL aims at an integration between general practitioners, scientific knowledge and the new frontier of personalized medicine. But, as it happens for all innovations in science, it is necessary to test whether this approach can work effectively, on the field. "We will study these technologies - says the Head of the Department of Epidemiology and Prevention - exactly as we do with a new drug. Citizens who choose to participate in the project will be first of all assessed to know their risk situation from a cardiovascular point of view. Then they will be divided into two groups: one will be followed according to traditional criteria, with prevention advices of GPs and, in general, the involvement of local health services. The other group will receive the same attention (it must be noted that the role of family doctors will always be essential) but they will also have an app to download on their mobile phone. The software, designed by experts from Health Ministry and participating centers, will follow articipants step by step. And they will "train" it by providing information on their health and lifestyle habits. In other word, the software will learn, so to be able to design a personalized prevention path, consisting of recommendations, advice and warnings. After a year, we will re-evaluate the cardiovascular risk situation of all participants in order to find out if the ones with 'electronic tutoring' have reduced their risk compared to those who have continued to use only traditional clinical approach".

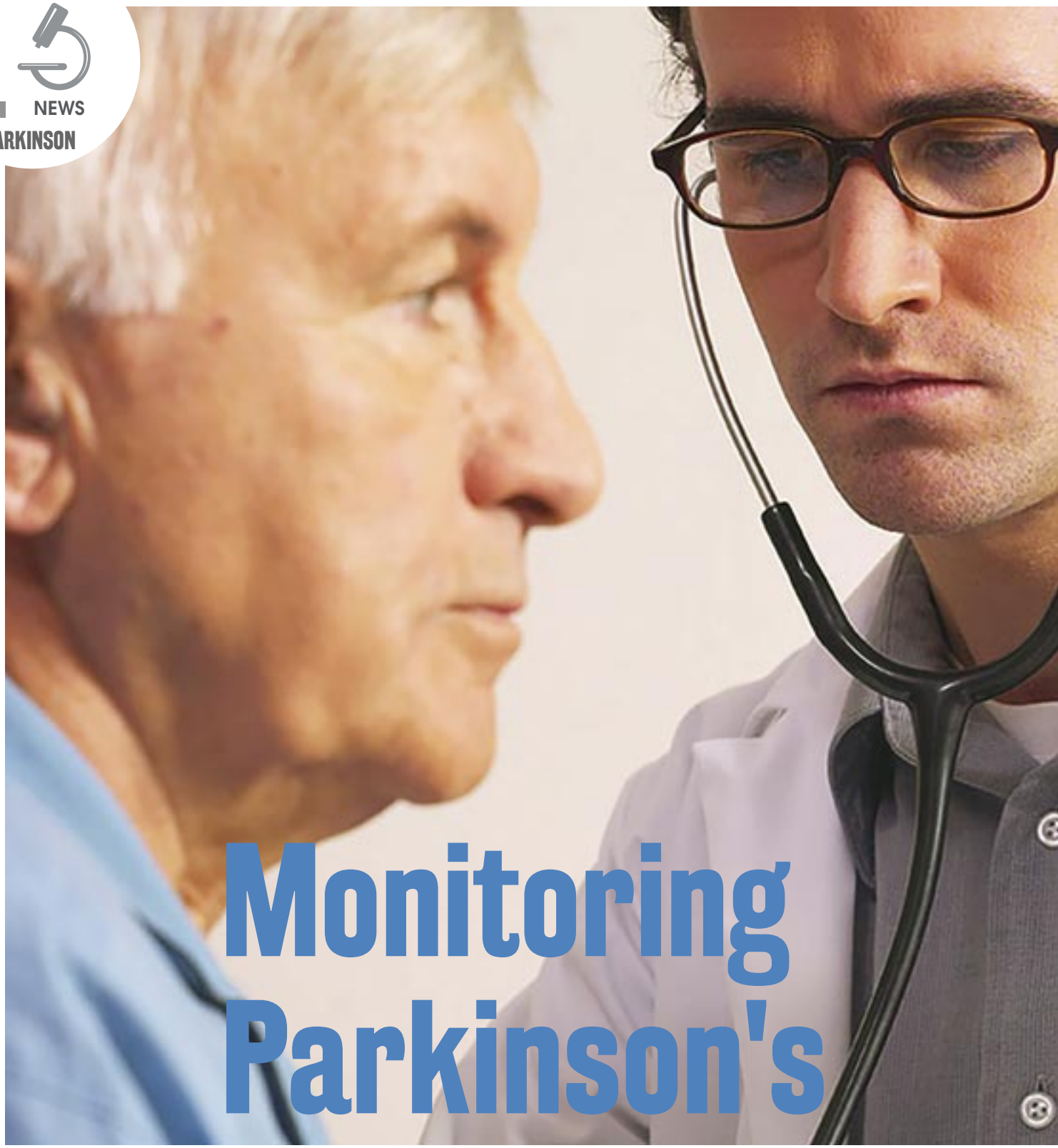
COVID-19 has taught us that there is no more powerful weapon than prevention

The project is ambitious: Neuromed Clinical Research Network aims to involve ten thousand citizens. "All the clinics of the network will invite citizens from their territory to participate in PREVITAL. People will be asked to sign an informed consent, essential for participating in the study. Then they will fill out some questionnaires on their general health, on past and current diseases and on other elements related to cardiovascular risk, such as ¬¬smoking¬, nutrition, physical activity, stress, sleep and so on. A medical examination will evaluate blood pressure, weight and height, while a blood sample will be drawn in order to evaluate various biological parameters that are at the basis of cardiovascular risk (glycaemia, triglyceridemia, hdl). After this first contact, participants will start

to receive two different kind of messages, depending on the group they belong. After a year, everyone will be called back to fill in again the same questionnaires and to collect a new blood sample. That will be the moment in which we will understand if the new method has improved their health".

It is important to underline that Neuromed's participation in PREVITAL does not come out of nowhere. Behind it, in fact, the Department of Epidemiology and Prevention has the experience of one of the largest epidemiological studies ever carried out in Europe: the Moli-sani, as Iacoviello explains: "That study, which of course still continues, is strongly connected with this new initiative. Much of the information collected in Moli-sani has been used to design PREVITAL, the questionnaires for example, but not only: the algorithm that will evaluate cardiovascular risk of the people participating in PREVITAL comes from Moli-sani scientific results".

There is a final question: why should a person, perhaps still in good health, participate in PREVITAL? "Because, as COVID-19 has unfortunately taught us, there is no more powerful weapon than prevention. But let's also keep in mind another aspect: our goal is not just to recruit individual citizens. Actually, the study will involve entire communities: we will talk with the Mayors, with local administrators, we will meet citizens in their towns and villages. As already happened for Moli-sani, PREVITAL brings science to the territory ". ■



Monitoring Parkinson's

It could be an indicator of disease progression, allowing doctors to accurately follow patients

Patients with moderate or advanced Parkinson's disease have a lower level of caffeine in their saliva than healthy people. The results of a research conducted by a group led by Professor **Alfredo Berardelli**, I.R.C.C.S. Neuromed and Sapienza University of Rome, could pave the way for a rapid and non-invasive method to monitor disease

Leodori, G., De Bartolo, M. I., Belvisi, D., Ciogli, A., Fabbrini, A., Costanzo, M., ... & Berardelli, A. (2021). Salivary caffeine in Parkinson's disease. Scientific reports, 11(1), 1-9.

DOI: https://doi.org/10.1038/s41598-021-89168-6

progression. The study, published in Scientific Reports, delves into a little known field that is drawing increasing attention in recent years. "It is known that caffeine intake reduces the risk of developing Parkinson's disease. - explains **Giorgio Leodori**, I.R.C.C.S. Neuromed and Sapienza University of Rome, first author of the scientific work - In our research we studied 86 patients who were at different stages of the disease and we compared them with a control group of 83 healthy subjects of the same age. Both in patients with Parkinson's disease and in control subjects, we evaluated the level of absorption of caffeine, its metabolism and finally the quantity of caffeine present in saliva".

Results showed that caffeine absorption and metabolism were similar in patients and control subjects. In contrast, the level of caffeine in saliva was lower in patients with moderate or advanced Parkinson's disease than in the control group. "We still do not know clearly - says Leodori - what may be the causes of the difference in concentration of caffeine between patients and controls, given that we have observed no alterations in absorption or metabolism. Further studies will be needed to clarify this aspect. However, what emerges from our work is that the measurement of caffeine in saliva can be a valid tool to more precisely staging Parkinson's disease and to follow its progression. We could have a potential 'biomarker', useful for clinicians. But, beyond that, our findings suggest that caffeine may play a role in the progression of Parkinson's disease. Understanding the mechanisms linking caffeine and Parkinson could lead to new knowledge on the genesis and development of a pathology that takes a heavy toll on patients' quality of life as well as on National Health Service".

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Parkinson's genetic

After genome sequencing of 500 Parkinson's disease patients, researchers identified twenty-six genes, sixteen of which have been associated for the first time with the disease

A collaboration between I.R.C.C.S. Neuromed and "Adriano Buzzati Traverso" Institute of Genetics and Biophysics of the National Research Council of Naples (Cnr-Igb) highlighted how some rare genetic variants, if present simultaneously, can play an important role in significantly increasing the risk of getting Parkinson's disease.

The study, published in the journal Molecular Neurodegeneration, examined the genetic data of two types of patients: those belonging to families in which Parkinson's disease is recurrent and those in which the disease appeared as "sporadic" cases. In addition, the authors deepened the research by examining, both on human tissues and animal models, gene expression (the transcription of genetic information into functional proteins). Five of the genes studied were found to be particularly expressed in Substantia Nigra dopaminergic neurons, whose degeneration is the main cause of Parkinson's disease.

This is the largest genetic study carried out on Italian Parkinson's patients by using the latest generation sequencing methods. "We were able to identify - says **Alessandro Gialluisi**, researcher at the Department of Epidemiology and Prevention, first author of the work - variants related to the risk of Parkinson's in twenty-six genes, sixteen of which had not previously been associated with the disease. And we were also able to find that most of these genes are involved in important pathways determining the functionality of dopaminergic system, whose degeneration leads to the disease".

A crucial finding of the study is that the examined variants may have some sort of cumulative effect. "The simultaneous presence of two or more of these

rare variants - explains **Teresa Esposito**, researcher at the Institute of Genetics and Biophysics Buzzati-Traverso of the CNR and head of the CNR Laboratory at Neuromed, latest author of the study - proved to be associated with a higher risk of developing Parkinson's in 20% of patients. We can think of it as a growing 'load' of mutations which, in the future, could lead us to precisely assess the risk of disease by identifying the number of harmful variants present in the DNA".

"These results - comments Professor **Antonio Simeone**, Director of the Institute of Genetics and Biophysics 'A Buzzati-Traverso' - appear promising in the effort to improve molecular diagnostic techniques aimed at an early identification of people at risk. Further studies will be needed, on the one hand to increase the number of diagnosis, on the other hand to understand and develop potential therapeutic approaches, based on pharmacological and regenerative medicine developments. What we can think of, for the nearer future, is a genetic test that takes into account the burden of harmful variants present in an individual's genome. This could lead to start population screening, improving early diagnosis of a disease that develops over time, and in which symptoms occur only when patients have already lost 50% of dopaminergic neurons". ■

Alessandro Gialluisi, Mafalda Giovanna Reccia, Nicola Modugno, Teresa Nutile, Alessia Lombardi, Luca Giovanni Di Giovannantonio, Sara Pietracupa, Daniela Ruggiero, Simona Scala, Stefano Gambardella, International Parkinson's Disease Genomics Consortium (IPDGC), Licia Iacoviello, Fernando Gianfrancesco, Dario Acampora, Maurizio D'Esposito, Antonio Simeone, Marina Ciullo and Teresa Esposito. Identification of sixteen novel candidate genes for late onset Parkinson's disease. Molecular Neurodegeneration.

DOI: doi.org/10.1186/s13024-021-00455-2
https://molecularneurodegeneration.biomedcentral.com/articles/10.1186/s13024-021-00455-2

YouTube

An alliance between doctors, caregivers and patients

Once again this year, a day dedicated to physical activity for Parkinson patients, on the banks of Castel San Vincenzo lake

There is the lab, but there is also a research that can involve the people. Yes, because Parkinson's is a disease to fight on several fronts. Among them, the psychological and physical part, the ones that take patients to the sea, in the mountains, on the shores of a lake in a canoe.

Initiatives aimed at spreading the right knowledge of Parkinson's disease continue. In September, Swim for Parkinson, in collaboration with LIMPE, promoted the 'Crossing on the Strait of Messina'. People with Parkinson's, doctors, caregivers, swam together with the Swim for Parkinson relay. A three-kilometer challenge aimed at promoting a positive message. Even with a neurological disease you can win, thanks to physical and group activity. A test not only physical but of courage and resilience.

The initiative, promoted by the Parkinzone association in order to engage Parkinson's patients in activities on the lake, is back this summer. On the shores of the Castel San Vincenzo lake, in the province of Isernia, a full Sunday has been dedicated to outdoor sports in a suggestive and healthy place. This year, the initiative was accompanied by "Put your face in ParK", a social campaign to raise awareness on Parkinson's disease through a photo project. A tour throughout Italy will bring a photographic set to patients, caregivers, doctors and operators, to face the disease with pride. The initiative touched Molise region, achieving excellent results in terms of public sharing. The collected funds will be used to create books, video, panels. The idea started with the commitment of Valeria Chiara Bastoncelli and Vittorio Andretta (aka Vic Parky), a 45-year-old librarian and a former photographer, supported by neurologists specializing in Parkinson's disease such as Dr. **Nicola Modugno**, Consultant at the Center for study and treatment of Parkinson's disease, IRCCS Neuromed, and of the University of L'Aquila, Professor Alessandro Tessitore, Head of the Parkinson's Disease and Movement Disease Center of the first polyclinic, University of Campania Luigi Vanvitelli, Francesca Morgante, St George's, University of London, and the associations ParkinZone Onlus of Rome and Parkinson Parthenope of Naples.


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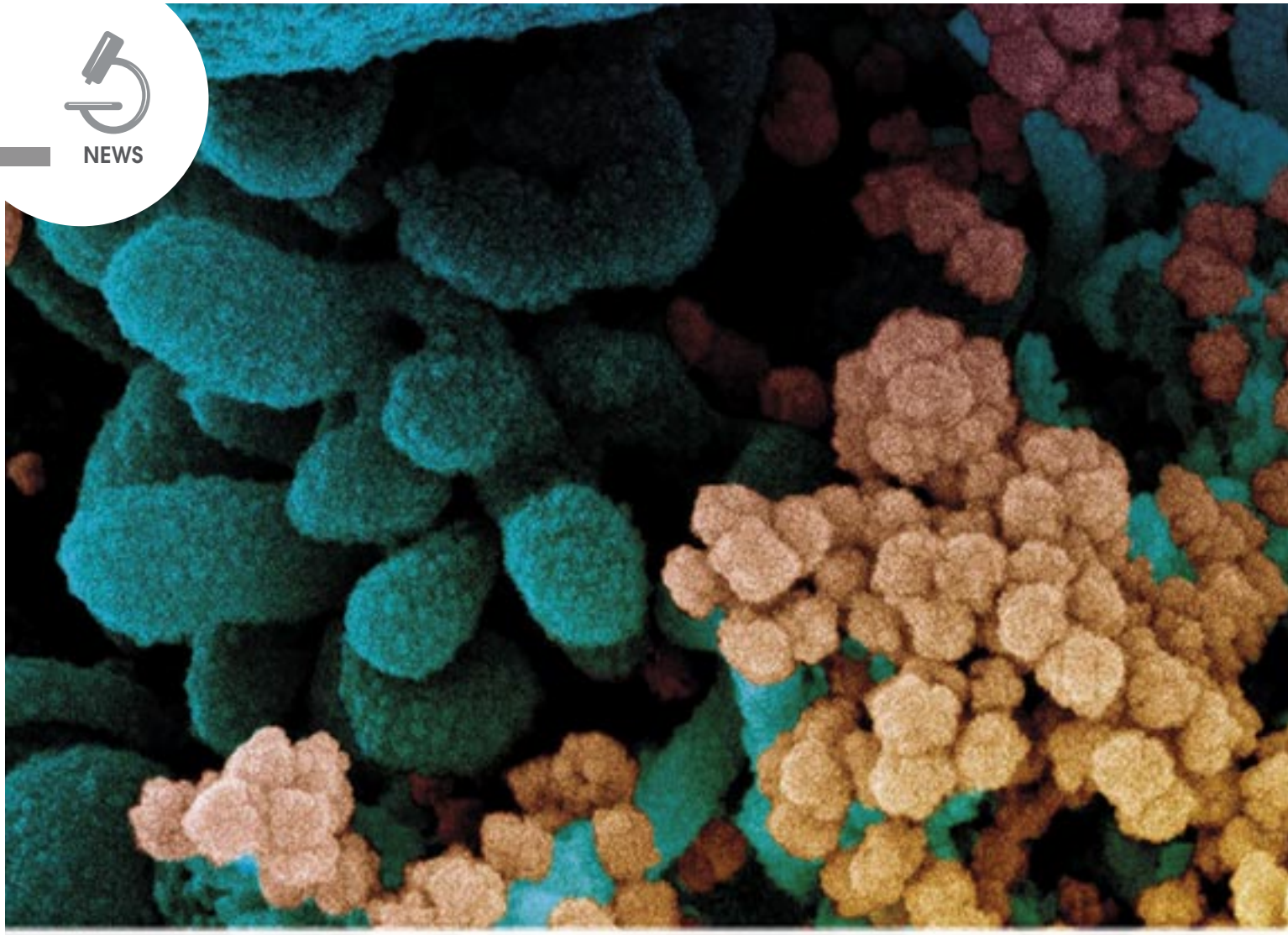


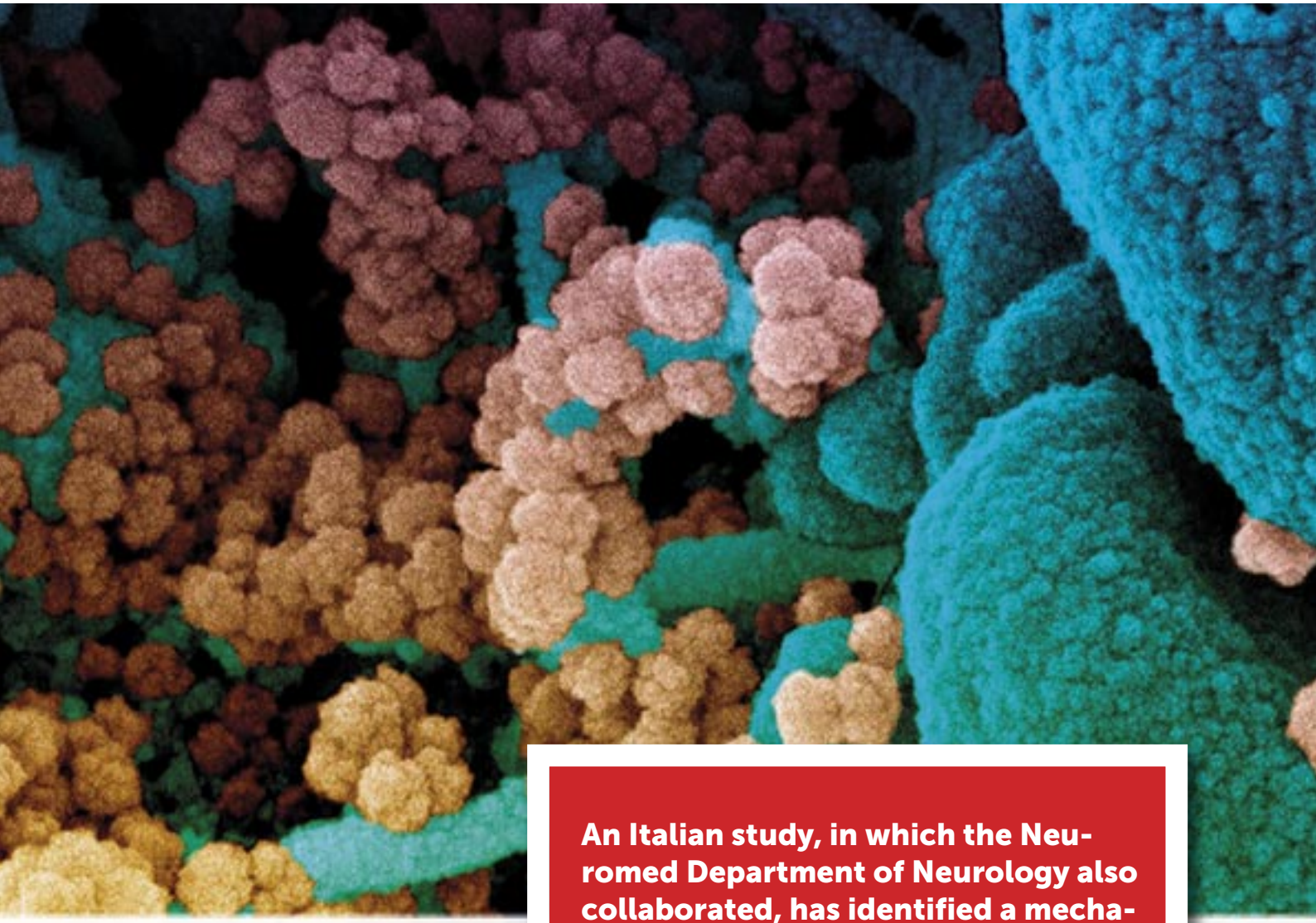
Multiple sclerosis

A potential method to reactivate immune cells involved in inflammation control

Regulatory T lymphocytes (Treg) play a fundamental role in modulating the response of the immune system, controlling that it reacts effectively against external agents without attacking our body's cells and leading to auto-immunity.

Due to their role as "sentinels", a reduction in the number or a dysfunction of Treg cells are strongly implicated in various autoimmune diseases, including multiple sclerosis. A new research, led by the Federico II University of Naples in collaboration of I.R.C.C.S. Multimedica of Milan, National Research Council (IEOS-CNR) of Naples and I.R.C.C.S. Neuromed, highlights a crucial element for the life and functioning of regulatory T lymphocytes. The study was published in the journal Immunity.

"This study - says Professor **Diego Centonze**, head of the Neurology Unit of Neuromed - show that the efficiency of Treg cells strongly depends on the production of a protein called SLC7A11, which is severely limited in multiple sclerosis". SLC7A11, located in



An Italian study, in which the Neuromed Department of Neurology also collaborated, has identified a mechanism that causes the dysfunction of regulatory T cells

the cell membrane, acts as a "transport channel" for two amino acids, allowing the entrance of cystine and the exit of glutamate, an important process for the control of free radicals and, therefore, of oxidative stress at cellular level.

"We saw - continues Centonze - that production of SLC7A11 can be restored in regulatory T lymphocytes if the body is subjected to caloric restriction. This reduces the excessive metabolic work of the cells themselves, typical in overweight or obesity, two conditions well known for aggravating the course of multiple sclerosis. But an important observation that emerged from the study is that a drug already widely used against this disease, dimethyl fumarate, seems to 'mimic' the state of caloric restriction, obtaining the same results".

These observations could be lead to the development of new therapies and new approaches to multiple sclerosis, aiming at restoring the role of Treg cells in patients, reactivating their ability to "tame" the immune system. ■

Claudio Procaccini, Silvia Garavelli, Fortunata Carbone, Dario Di Silvestre, Claudia La Rocca, Dario Greco, Alessandra Colamatteo, Maria Teresa Lepore, Claudia Russo, Giusy De Rosa, Deriggio Faicchia, Francesco Prattichizzo, Sarah Grossi, Paola Campomenosi, Fabio Buttari, Pierluigi Mauri, Antonio Uccelli, Marco Salvetti, Vincenzo Brescia Morra, Danila Vella, Mario Galgani, Maria Mottola, Bruno Zuccarelli, Roberta Lanzillo, Giorgia Teresa Maniscalco, Diego Centonze, Paola de Candia, Giuseppe Matarese, Signals of pseudo-starvation unveil the amino acid transporter SLC7A11 as key determinant in the control of Treg cell proliferative potential, Immunity, 2021,

https://doi.org/10.1016/j.immuni.2021.04.014.

A look at rare diseases

The importance of collaboration between health institutions, GPs and families, at the basis of a meeting promoted by the Neuromed Foundation

When disabling aspects are taken into consideration, Rare Diseases are pathologies with a very heterogeneous behavior. The lack of specific health policies for these conditions, together with a lack of knowledge, often bring to delays in diagnoses and difficulties in accessing care, sometimes with inadequate treatments, with an almost inevitable loss of trust in the health system. The essential condition for improving rare diseases strategies is to recognize their existence and to increase knowledge among professionals and population. Correct identification of a rare disease must be accompanied by the dissemination of precise information, through inventories and repertories responding to the needs of health professionals and people affected. It is with this concept in mind that the Neuromed Foundation promoted, together with the Abruzzo Association of People with Rare Diseases, the meeting "A look at rare diseases" in Pozzilli. Through a dialogue between the main stakeholders involved (Patient Associations, Clinics and Health Authorities), the scope was to analyze the key aspects revolving around the care of patients with rare diseases, from diagnosis to home assistance. Particular attention was devoted to epidemiology, regulatory aspects, health costs and sustainability problems, as well as the new frontiers of diagnostic innovation. "Collaboration between health institutions, clinics and associations is essential to help people with rare diseases. - says **Mario Pietracupa**, President of the Neuromed Foundation - Often these families have no reference points and we have the duty to understand what is the best way to give them concrete hope. In this perspective, the commitment of scientific research is essential because through study and monitoring of these pathologies we can find possible solution ". ■

Among the topics covered during the meeting, dermatology aroused considerable interest. Rare diseases are, in fact, linked to different branches of medicine, from neurology to ophthalmology, from dermatology to genetics. It is with this in mind that the Neuromed Institute promotes a network of specialists who can correctly address the diagnosis and the patient's path, together with the family.

"Rare diseases, especially neuro-cutaneous ones, often begin with visible skin manifestations - says Dr. Riccardo Acri, coordinator of scientific research in dermatology at Neuromed - We must think of the skin as a real communication organ. Therefore, dermatology must be included into these studies, allowing us to make an early diagnosis, such as in the case of spots characterizing neurofibromatosis in the first months of life. Moreover, often neurological manifestations are accompanied by skin tumors, which in many cases allow us a fairly correct diagnostic approach, naturally to be confirmed with a genetic test. Here in the Institute we work in synergy with geneticists and ophthalmologists. Knowing the skin symptoms allows us to make a quick diagnosis and to prevent complications. Regarding autosomal dominant diseases, causing serious damage during their progression, we believe in gene therapy. For us, even helping just one person is a goal that helps us in the study and support, including psychological one, of affected patients and their families. It is therefore important to convey the importance of research funding.

A voice to tell your story

A cornerstone of human evolution, a complex mechanism, with its wonders and its pathologies

Doctor Antonella Gatta

YouTube

"When we hear someone talking or singing, we think only of vocal cords. But what we are hearing, in reality, is the sound of an entire body, of complex structures emerged from the evolutionary process".

In the words of Dr. **Antonella Gatta**, speech therapist of the I.R.C.C.S. Neuromed and Director of the Degree Course in Speech Therapy at the Tor Vergata University of Rome, there is the long path leading the human species to a communication system as sophisticated and flexible as the voice. Of course, all animals exploit sounds in some way, even insects do (think crickets and cicadas). But in humans there was a huge leap in quality, which practically laid the foundations for a culture and a civilization.

"One of the most important differences between us and hominids - says Gatta - lies in the types of sound we can produce. In the course of evolution, a fundamental step took place: homo erectus, which achieves an upright position and a bipedal structure. This caused the 'descent' of the larynx and the creation of a big space above it, the 'oropharynx', present only in humans. With this structure, and with its wide resonance capacities, comes the possibility of articulating much more complex sounds: no longer simple groans, but also guttural sounds".

Emotion has no voice

It is a feeling experienced by everyone at one time or another, celebrated in films, songs and novels. Faced with a strong emotion, the throat is blocked, sometimes to the point of not being able to speak anymore. "We must always keep in mind - explains Dr. Gatta - that the first role of the larynx is to protect the airways. For this reason, when facing a danger the vocal cords tighten and the voice becomes a secondary task that is set aside for the moment, the so-called 'lump in the throat'. And it can also happen when one feels a strong emotion, not necessarily fear: the larynx is simply reacting to a very intense stress, which could very well be just meeting a loved one. This phenomenon, among other things, is further evidence of how the modulation of the voice is a secondary function of the larynx, born after its main purpose of protecting breathing".

So, while we often think of the voice as the product of the vocal cords alone, in reality behind a chat between friends, a great speech, a great song, there is an entire sound system. "We can imagine - explains the speech therapist - an organ pipe: first of all the air is pushed up by exhalation, then in the larynx we find two thin muscles, the vocal cords (curiously many think that they are seven, like the note), pressuring the air in the oropharynx, where we find all the following necessary parts for language articulation. And let us not forget the resonance function performed by the nasal cavities and the bronchial tree. The whole thing will give rise to the 'color' of our voice, different from person to person".

This complex sound equipment that emerged in the course of evolution laid the foundations for a subsequent step: the birth of language. "A time came when humans wanted to tell about themselves, as they did with paintings on the rocks of caves. Gradually, therefore, all those sounds acquired meaning, semantics. No longer only the primordial need to emit sounds in order to obtain a

Breathe, eat, talk: all in one box

Vocal cords are just one of the characteristics making the larynx a fundamental structure for life. Inside this organ there is also the separation between the digestive and respiratory tracts. "When we eat - explains Dr. Gatta – we need to swallow, and it is a very complex mechanism, governed by impulses from specific areas of the brain, leading to the closure of vocal cords and the lowering of epiglottis. This way the breathing tube stays safe and everything we eat ends up in the esophagus. It is a real safety system trimmed with extreme precision, and we can say that, from an evolutionary point of view, this is its original purpose. The voice came later, almost as an accessory function".

But the accuracy of this system can get jammed due to neurological pathologies. Dysphagia, a potentially very dangerous condition, may cause food ending up in the airways, leading to asphyxiation or pneumonia. "In some neurodegenerative diseases - explains the speech therapist - or even following neurosurgical interventions for brain tumors, the stimuli coming from the brain can become inadequate so the swallowing mechanism is altered. For this reason, dysphagia can give us very early indications about the existence of a neurological disease. In these cases, the speech therapist works closely with neurologists and other specialists both in the diagnosis phase and in the management of the problem".

result (like the child with the mother), but the need to continue the species, also culturally. The voice thus becomes the fundamental pivot of communication. At the beginning there are only onomatopoeias, sounds that reflect everyday life, then comes the lexicon, a true conventional code of sounds and meanings that emerge in a specific tribe and is specific to one territory".

A voice from the past

Articulating a complex language, with distinct vowels and consonants, is considered an exclusively human characteristic. Nevertheless, new research suggests that our "cousins," the Neanderthals, could produce the same sounds, and perhaps they had even a language.

Neanderthals are a hominid species that went extinct about 40,000 years ago. We Homo sapiens were already around, coming from Africa, and for several thousand years the two species not only co-existed, but probably had various cultural exchanges, and not only cultural if we consider that each of us has a 2% of DNA coming from the Neanderthals.

Of course, muscles and vocal cords, made of soft tissue and cartilage, have not been preserved for all this time, and so only bones remain of this ancient population. But just one bone, the hyoid, located in the throat, is at the center of a fascinating hypothesis: studying the only hyoid bone of certain Neanderthal origin ever found, researchers speculated that the structure of the Neanderthal larynx could have been very similar to ours, allowing the articulation of a real language.

The complexity of the whole system, however, can face pathologies, both related to the phonatory system and of neurological origin. “The most frequent dysfunctions affecting the larynx - explains Gatta - are due to an excessive or incorrect use of the voice (functional dysphonia) or to the formation of polyps or nodules (organic dysphonia). In both cases, 're-education' is very important: the speech therapist guides the patient towards a more efficient use of the voice, for example by teaching him to better modulate his breathing while he speaks. Even when surgery is necessary, such as in the case of cysts or polyps, this training is essential, both before and after surgery".

A much more complex case is when a stroke damages the language brain centers. “In these cases, the rehabilitation by the speech therapist must be prompt, almost immediate. It starts with an assessment of the deficit, to understand how to address the intervention. Then a very delicate job begins: it is necessary to reorganize the neurons connecting the 'meaning' with the 'signifier'. In other words, a patient who suffered from a stroke in the speech centers may know very well what he/she means, yet he/she cannot express him/herself, or maybe he/she uses wrong words without even realizing they are incorrect. In short, a connection has been lost, and our job is to guide the patient, help him/her recognize his/her communicative ineffectiveness and re-establish the connections. Let us keep in mind that the brain will always try to compensate for damage, but in the case of language it could perform this task in a pathological way. The patient will try to speak, because this instinct is very strong, but he/she will not choose the right words. We must prevent this from becoming a permanent situation. Much of the speech therapist's work, in these cases, consists in motivating him/her to silence and listening, in order to ensure a new orientation in a world of damaged language. Only after this phase the therapist starts functional recovery. We work with concrete ideas, but also with abstract concepts, and we have to be sure that the patient is able to express them. In this process, there is not only medicine, but linguistics and philosophy too". ■

Orlando Paciello

Animals as sentinels of the environment

Monitoring animals' health, especially for tumors, could be an innovative method for promptly discovering contaminants in a territory. We talked with Orlando Paciello, professor of Veterinary pathological anatomy at the University of Naples Federico II and scientific director of the Campania Animal Cancer Registry.

"Animals and humans share environment and lifestyle, but also negative factors, such as pollutants. Therefore monitoring animal health, especially for oncological pathologies, allows us to collect information that could be extremely useful for human health. The Animal Cancer Registry is an ideal tool for epidemiological surveillance of the environment. Thanks to the register, we can quickly be alerted about a higher incidence of specific pathologies, something that deserves immediate attention".

In short, animals as sentinels.

"We must be aware that animals have very fast latency. In other words, the time from exposure to a carcinogen to the onset of the disease is much shorter than in humans. For this reason, animals can be an efficient early warning system about potential environmental issues. So, if in a given territory we see the emerging of a 'cluster' of pathologies, then we can suspect a serious pollution problem".

It is a reversal of perspective. Territories usually are placed under surveillance when we learn that dangerous substances have been dumped there. Will starting from animal health make it possible to discover still unknown polluted areas?

"Yes, this is the approach we propose. We know that some diseases, especially oncological ones, are strongly related to contaminant exposure, so a higher incidence of a specific disease in animals is an alarm signal for the area they live in. At that point, we must investigate on the factors behind the anomaly, so we start looking for environmental problems, and maybe we find substances we did not know were present in that place".

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