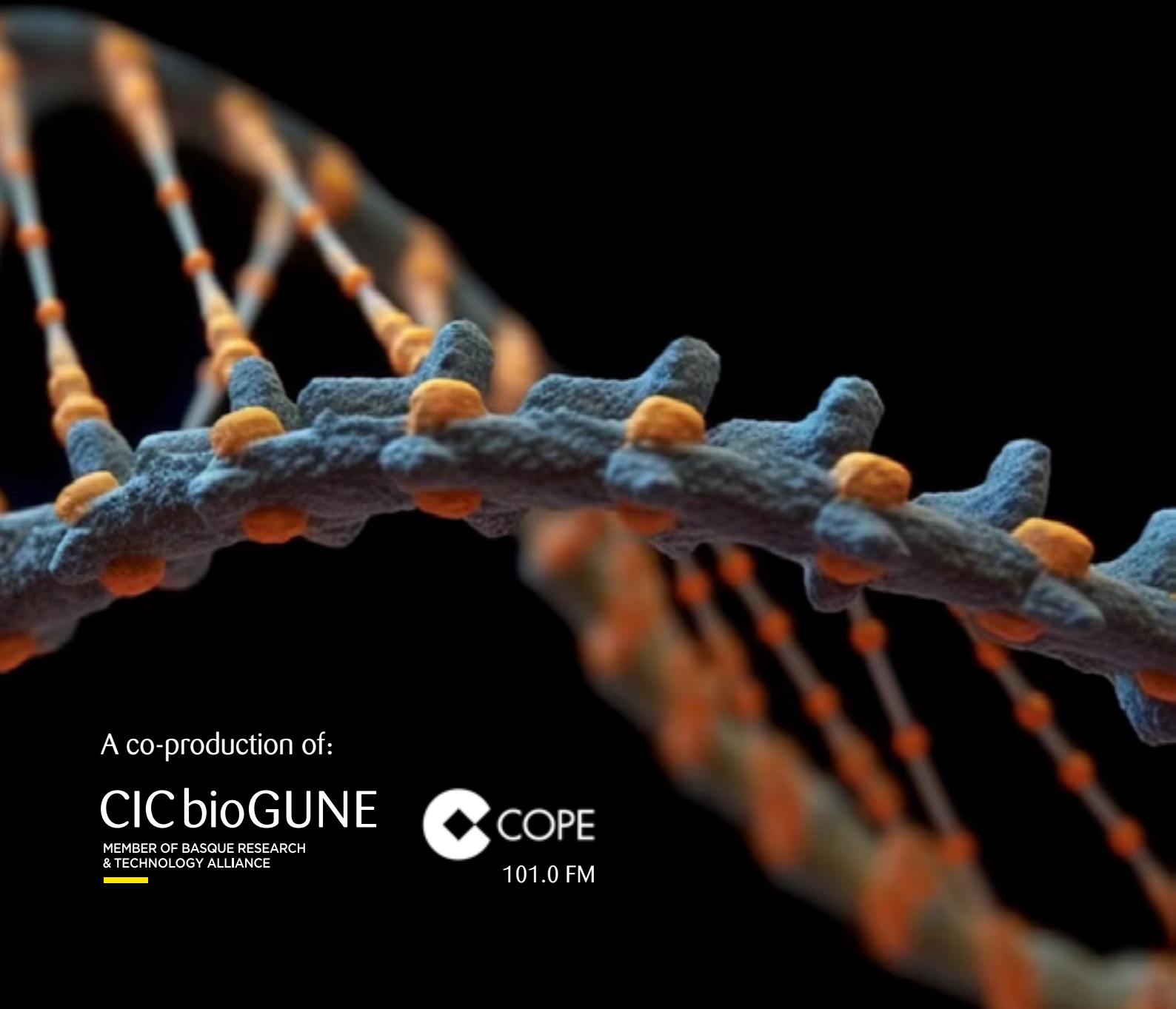
BioEnredados

Uniendo Ciencia y Vida

First Season - Volume 2



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Welcome to our podcast BioEnredados: Uniendo Ciencia y Vida!

We are your gateway to the cutting-edge research in biosciences that is taking place at the heart of CIC bioGUNE.

In each episode, we will immerse you in an exciting journey through the most innovative scientific and technological advances that are transforming our understanding of the biosciences, from basic chemistry to biology and medicine.

Our mission is clear: to bring you science in an accessible and exciting way. We aim to ignite your curiosity and nurture your interest in cutting-edge bioscientific research.

Are you ready?

BACK TO THE PAST

THE POWER OF GENE EDITING

Imagine a world where we could edit the fundamental building blocks of life as effortlessly as we revise a text document on our computers. What if correcting genetic errors could be as simple as fixing a typo? We journey into the fascinating and transformative realm of molecular biology to uncover a tool that is reshaping the future: CRISPR-Cas.

This groundbreaking genetic editing technology allows scientists to alter DNA with unparalleled precision, like fine-tuning the words in a digital manuscript. The implications of this technology are vast and profound, with the potential to correct genetic defects, treat incurable diseases, and even eradicate certain conditions before they manifest.

In recent years, CRISPR-Cas has emerged from the confines of the laboratory to become a beacon of hope for millions. Its approval for treating genetic diseases has sparked a wave of excitement and possibility, heralding a new era in medicine where the seemingly impossible becomes achievable. Diseases once deemed untreatable are now within the realm of potential cure, offering a glimmer of hope to individuals and families affected by genetic disorders.

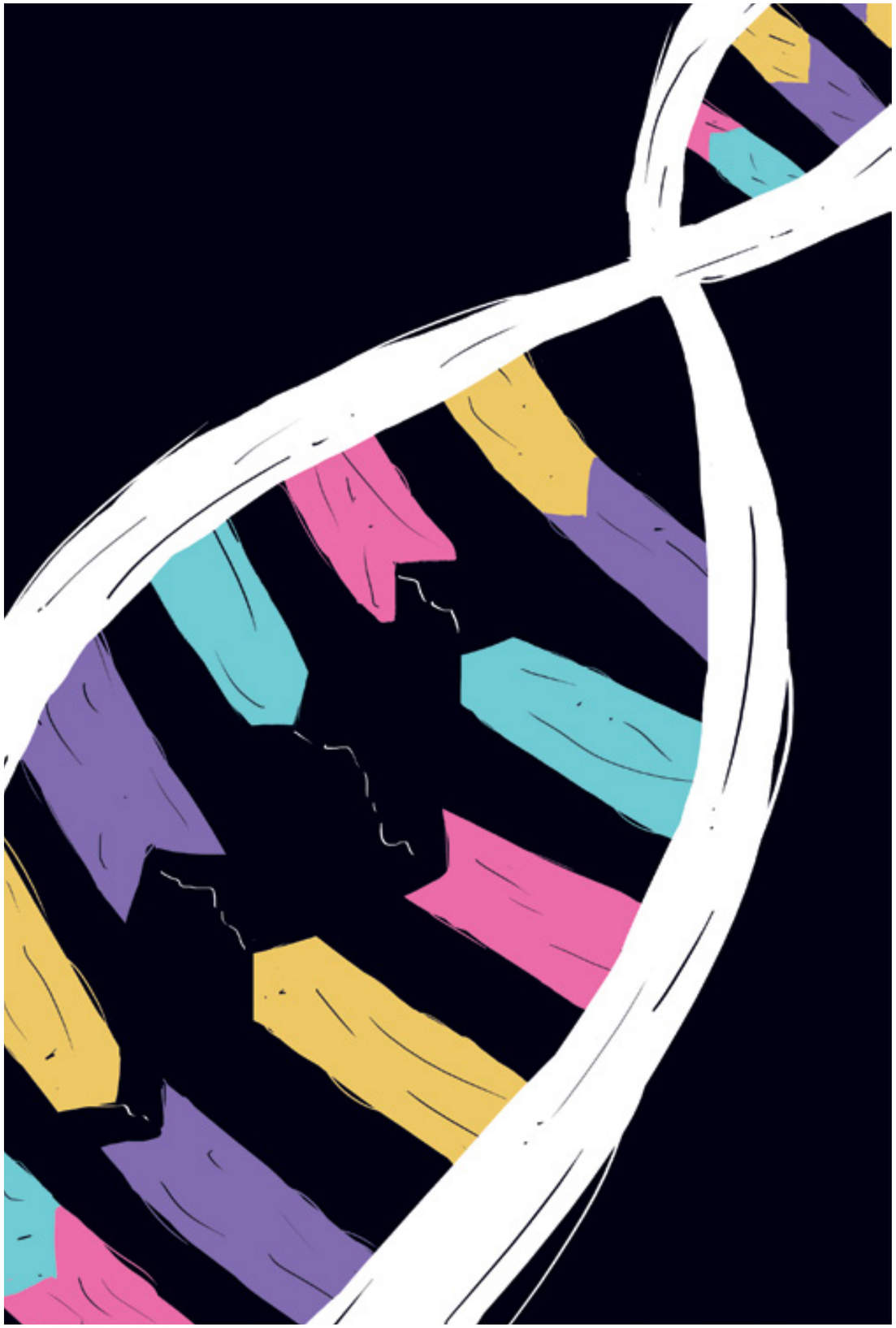
But how did we arrive at this revolutionary point? What is the science behind CRISPR-Cas, and how does it work? We will explore the origins and the mechanics of this extraordinary technology, shedding light on its current applications and future potential.

Our guide on this journey is **Ylenia Jabalera**, a postdoctoral researcher under the prestigious Juan de la Cierva program, who works in the Synthetic Biology Group at CIC bioGUNE. Ylenia's insights will take us through the historical roots of CRISPR-Cas, revealing how a discovery in bacterial defense mechanisms has evolved into one of the most powerful tools in genetic research and medicine.

Could you please elaborate on what the CRISPR-Cas genetic editing technique is and how it operates?

- It can be defined as a cut-and-paste or cut-and-rewrite tool at the molecular level. In nature, the CRISPR-Cas system serves as a bacterial adaptive immune system. Analogous to our antibodies, it memorizes genetic sequences of external invaders such as viruses. When the same virus invades again, this tool acts like molecular scissors guided by the system to cut the invader, preventing infection.

About a decade ago, scientists discovered they could apply this technology to genetic editing, sparking a scientific revolution. In fact, two researchers involved in this breakthrough were awarded the Nobel Prize in Chemistry in 2020, profoundly altering the field of molecular biology.



Right: Artistic interpretation by Ilargi Arakistain, student at Argi Arte. As part of the CIC bioART project.

Think of CRISPR-Cas as highly precise molecular scissors. To edit a gene, scientists design a guide RNA sequence that directs these molecular scissors to the exact location for cutting. Once they locate this region, the molecular scissors make a specific cut. Subsequently, cellular mechanisms take over, leading to different outcomes such as insertion, deletion, or rewriting of genetic material.

Therefore, we can use this tool to correct mutations associated with various pathologies.

What are the main applications of this technique in medicine, and what are some current examples of its use?

- Essentially, the primary application is genetic editing.

In fact, 2023 has been a pivotal year for this technology. In the last quarter of 2023, all major drug regulatory agencies, including the European, British, and American agencies, approved a medication called Casgevy. This drug, developed by Vertex and CRISPR Therapeutic, is based on CRISPR-Cas technology. It has been specifically approved for treating certain cases of two rare diseases: sickle cell anemia and thalassemia.

In simple terms, this therapy involves extracting the patient's hematopoietic stem cells. These cells are then modified in the laboratory using CRISPR-Cas tools to correct the mutation responsible for the disease. The edited cells are carefully screened to ensure they have been properly modified. Once confirmed, these edited cells are reintroduced into the patient, replacing the defective cells with the corrected ones.

"Despite these challenges, ongoing research advancements suggest promising strides towards realizing the technology's full therapeutic potential in the near future."

You've provided us with a general overview of the technique and its applications online, but could you explain specifically how your research is contributing to the understanding and advancement of this technology?

- The CRISPR-Cas technology has immense potential in biology and medicine, but up to date, it is not perfect and faces several challenges. One of the primary issues is known as sequence recognition. Imagine these molecular scissors are highly precise and can make cuts, but to do so, they need to recognize a tag next to the sequence they are supposed to cut. Each scissor is specific to a particular tag. So, even if you can guide the molecular scissors to the target site, such as a mutation you want to correct, if the scissors do not find the tag, they will not be able to make the cut.

The current molecular scissors technology is limited by its need for specific tags to target mutations, restricting its application. To overcome this, our research group has turned to ancient times, resurrecting and characterizing ancestral scissors. These scissors are surprisingly flexible, recognizing multiple tags and thereby broadening the range of mutations that can be targeted. We are collaborating with the FUNDELA association to use these super-flexible ancestral scissors for treating Amyotrophic Lateral Sclerosis (ALS), focusing on mutations in the SOD1 gene. Our preliminary results show potential, as these ancestral scissors can reach mutations that current technologies cannot.

What can we expect from the future of CRISPR-Cas?

- This technology holds immense promise for correcting and potentially curing genetic diseases at their core.

Despite its undeniable potential, we lack complete control over CRISPR-Cas technology. Current therapies involve complex ex vivo processes where cells are extracted, modified, verified, and reintroduced into patients. However, achieving in situ therapy—directly editing genes within the body—requires overcoming significant hurdles related to safety, efficacy, and precise targeting. Key obstacles include developing efficient delivery systems that can target CRISPR-Cas exclusively to desired cells or tissues without off-target effects. Despite these challenges, ongoing research advancements suggest promising strides towards realizing the technology's full therapeutic potential in the near future.

Right, up: Ylenia Jabalera, below: podcast episode cover.

GLYCANS

THE SWEET SIDE OF INFECTIONS

In the vast and complex landscape of cellular biology, glycans play a crucial role as essential molecules that contribute significantly to the composition of our bodies. Representing approximately 90% of the molecules found within us, glycans are chains of sugars, technically known as molecules with glycosidic bonds. These include compounds like polysaccharides and carbohydrates.

Glycans are predominantly located on the surfaces of cells, where they serve not only as structural elements but also as essential facilitators of cellular communication. Beyond their role in cellular communication, glycans also act as pivotal gateways for microscopic invaders like viruses and bacteria. These pathogens exploit glycans as entry points to infiltrate our cells. Once inside, they can hijack cellular mechanisms to reproduce and spread, leading to various infections and diseases.

Understanding the way glycans function as access keys for these pathogens is crucial for developing innovative strategies to combat infections. The study of how glycans enable such invasions provides valuable insights that could lead to new preventive and therapeutic measures against many diseases.

Delving into the world of glycans leads us into the field of glycobiology, which focuses on the complex interactions between glycans and other molecules. But, what types of molecules do glycans interact with? How are these vital connections established and analyzed? What role do glycans play during the infection process when pathogens invade our bodies?

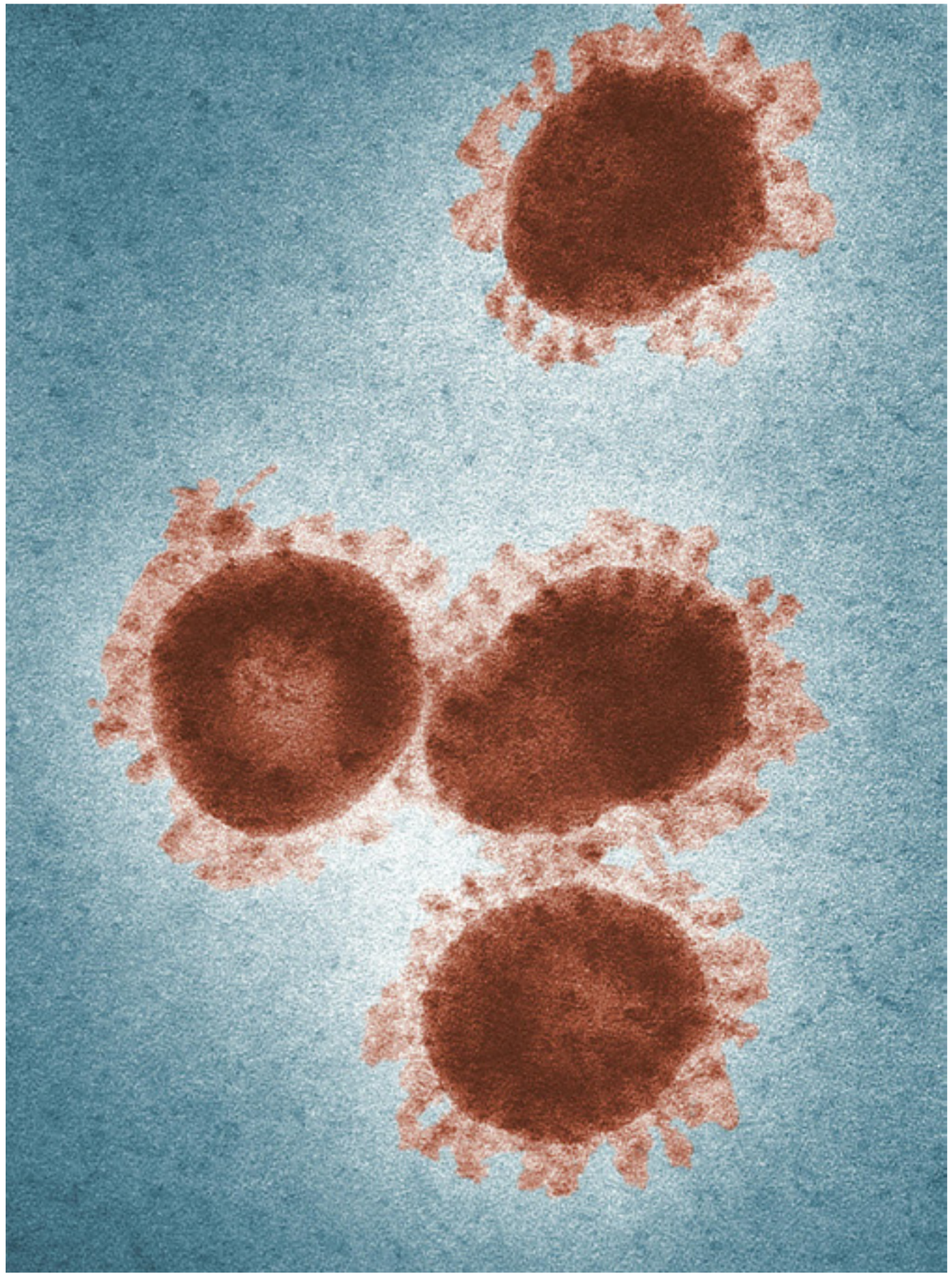
We seek answers to these fundamental questions with **Luca Unione**, Associate Principal Investigator in the Chemical Glycobiology Group at CIC bioGUNE. Luca's work explores the significant roles glycans play in health and disease.

Let's now discover what glycobiology is exactly, and for that, Luca, the first question is: what exactly are glycans and what role do they play?

- When we talk about glycans we are referring to molecules, biological molecules that naturally occur in our body, and essentially we are talking about sugars.

These are the same molecules that constitute the sugar we add to coffee or tea in the morning. They simply form a diverse family containing various members, very similar to each other but different, consisting of small molecules that assemble to form highly complex structures. And what role do they play? Well, all our cells are covered by a layer of sugars, as you mentioned earlier, and there, on the cell surface, they play two fundamental roles.

The first is a structural and stability role, providing stability, structure, and presentation to the larger molecules they are attached to, such as proteins or lipids (fats).



Right: CDC, taken from Pexels image bank.

On the other hand, they play a crucial role as intermediaries for communication between cells and between cells and pathogens.

How can glycans interact with various molecules in the cellular environment? And what methods are used to study these complex connections?

- When we say they interact, it's because both other cells and pathogens have a series of proteins called glycan-binding proteins. These proteins recognize and bind to glycans on our cells, allowing cells to approach, communicate, and exchange signals. When the other entity is not a cell but a pathogen, these proteins facilitate not only binding but also fusion between these two entities, promoting colonization and infection.

To study these mechanisms, we now have various spectroscopic techniques that allow us to see the atomic details of this interaction between these molecules.

With the context you've provided so far, Luca, could you explain more specifically how your research is contributing to advancing our understanding of this field of chemistry?

- Well, in this context where glycans are pivotal in virus infections, our research endeavors to unravel the precise mechanisms: which specific glycans facilitate the infection process and the exact proteins that orchestrate these interactions. Understanding these dynamics is crucial as it holds the key to potentially inhibiting viral infections, such as influenza, and other similar pathogens.

The significance of this research cannot be overstated. Viral infections, particularly those like influenza that have persisted for centuries, continue to pose significant challenges to public health worldwide.

"We now know that glycans also play a crucial role in infection processes. If we can define specific glycans, we can also develop vaccines that are more effective against infection."

By pinpointing the glycans and proteins involved, we aim to develop strategies that could disrupt the infection process at its core. This could lead to advancements in antiviral therapies and vaccines, offering new hope in the ongoing battle against infectious diseases.

What do you think could be the future applications of this knowledge and how could they impact our understanding and treatment of infectious diseases?

- There are more common viruses like the flu, for example, which remains a virus with high mortality in people with underlying conditions. But there are also recent viruses that have alarmed us, like coronavirus. Thanks to this type of research, we now know that glycans also play a crucial role in infection processes such as that of the coronavirus, enabling a structural change in the spike protein of the virus, which facilitates binding.

Therefore, by understanding how this mechanism takes place, we can develop potential drugs that can prevent this binding and thus protect ourselves. Some of these molecules are medications, small molecules, and to do this we need to identify accessible regions of the virus proteins, which we can then target with these small molecules.

On the other hand, this research also plays a crucial role in vaccine development. When pharmaceutical companies develop vaccines against infections, they enable our bodies to produce a harmless viral protein—not the entire virus—activating our immune system so it can recognize and fight the virus when encountered.

Glycans play a critical role in shaping the protein's structure. Identifying specific glycans could enhance vaccine efficacy against infections and detailed examination of how the virus attaches to and colonizes cells is essential for anticipating and preparing for future pandemics. Just remember that for the flu virus, throughout the last century, we have experienced four pandemics, and we know that sooner or later another one will come.

The virus constantly mutates, so the only way we have to predict the arrival of a new pandemic and be prepared to face them is to study in detail those mechanisms of attachment and colonization of the virus to our cells, and to develop potential medications.

Right, up: Luca Unione, below: podcast episode cover.

BETWEEN AIR AND HEALTH:

THE VITAL ROLE OF OXYGEN

Oxygen, that essential yet imperceptible gas that surrounds us, is vital to our existence from the moment of our birth. Every cell in our body depends on it to carry out its most basic functions. However, have you ever wondered what happens when we lack this vital element? How does our body react to oxygen deficiency? In environments where oxygen concentration is low, such as in high altitudes or situations where access to sufficient oxygen is limited, our bodies face a critical challenge known as hypoxia.

Hypoxia occurs when cells do not receive adequate oxygen to function properly. This can have significant consequences for our health, as oxygen is crucial for cellular energy production and maintaining vital bodily processes. How does our body adapt to these adverse conditions? What mechanisms does it activate to ensure survival and function?

Moreover, understanding the connection between oxygen deficiency and the development of serious diseases such as cancer, cardiovascular and respiratory diseases, and anemia is crucial. How does hypoxia influence these contexts? What role does it play in the progression of these diseases, and what research is being conducted to better understand this relationship?

To delve into these questions, we are joined by **Edurne Berra**, Associate Principal Investigator in the Signaling and Metabolism of Cancer Cells Group at CIC bioGUNE. Through her expertise and insights, we will explore how studying hypoxia can offer new perspectives for human health and the development of innovative medical treatments.

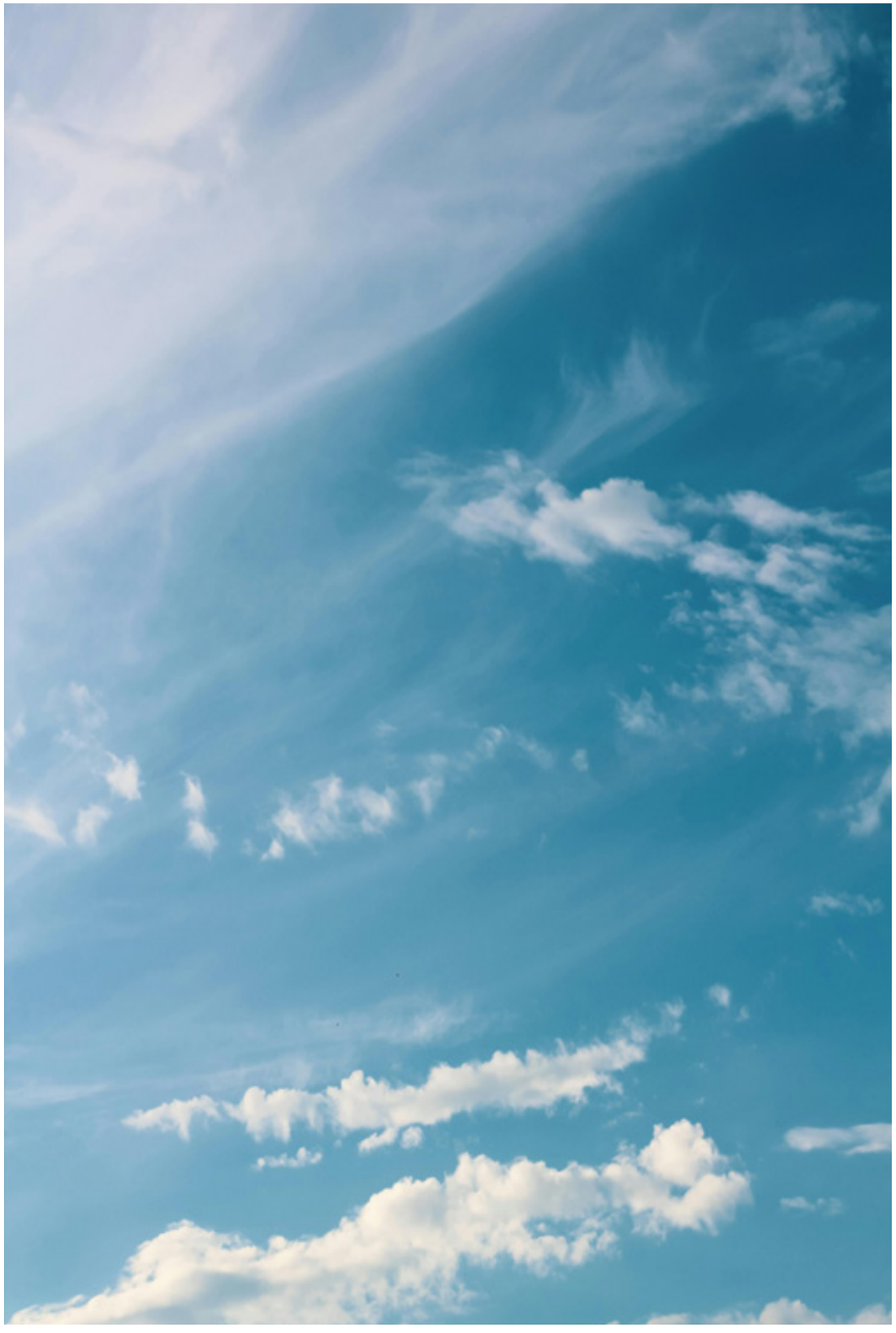
What is the role of oxygen in our body and how does it affect our health?

- As mentioned, oxygen is vital for each and every one of the billions of cells that make up our organs and tissues. We could say we are oxygen addicts. Oxygen is our energy source, which makes it incredibly important—it's like gasoline for a car.

We need oxygen to survive, but it's crucial that we have the right amount—not too much, not too little. Excess oxygen isn't beneficial, and as you pointed out, oxygen deficiency, or hypoxia, is even more dangerous. The good news is that our bodies are capable of reacting, adapting, and restoring necessary and appropriate oxygen levels.

Unfortunately, our body's response and adaptation aren't always as precise as we need them to be. Sometimes, our response is insufficient, while in other cases, it's excessive. In these instances, yes, hypoxia does affect our health.

Conditions such as anemia, stroke (like a stroke), heart attacks, and sleep apnea are all associated with inadequate adaptation to oxygen levels. On the other hand, some conditions, like cancer, for example, actually benefit from hypoxia.



Right: Taken from Pexels image bank.

What scientific advancements have been achieved in understanding these regulatory mechanisms of the diseases and what are their potential effects?

- Over the past 25 years, significant strides have been made in this field, achievements we can be proud of. Specifically, three major breakthroughs stand out. Firstly, scientists have identified the conductor, the mastermind orchestrating our adaptation to oxygen deprivation.

This conductor is HIF, the Hypoxia-Inducible Factor, a protein that oversees a highly intricate program with a dual purpose: when oxygen is scarce, it aims to increase its supply while simultaneously reducing its consumption. HIF plays a pivotal role in this process. Secondly, oxygen sensors have been pinpointed.

These sensors act as vigilant guardians, triggering alarms when oxygen levels are insufficient. They communicate this crucial information through intermediaries to the conductor, HIF, thereby initiating the necessary responses.

Thirdly, Von Hippel-Lindau (VHL) protein has been discovered. This protein serves as an intermediary or actor in this intricate biochemical scenario. When VHL malfunctions, it can lead to conditions such as the Von Hippel-Lindau syndrome.

The scientists responsible for these groundbreaking discoveries were awarded the Nobel Prize in Physiology and Medicine in 2019, underscoring the significance of their findings. However, much remains to be uncovered in this fascinating field.

"Understanding the regulation point by different pathologies is crucial, as it can act differently in various cases. Indeed, we have two potential avenues for manipulating hypoxia."

Now that we have this comprehensive overview of the research unfolding in this field, specifically, Edurne, could you please elaborate on what your research focuses on and how it is contributing to the advancement of this field?

- Our research can be summarized into three main areas. Firstly, we aim to unravel the remaining mysteries regarding the mechanisms of adaptation to hypoxia, which is our fundamental pillar of investigation.

Secondly, we investigate the role of hypoxia in a specific type of cancer, precisely prostate cancer, as we have mentioned before how cancer cells exploit and benefit from hypoxia.

Thirdly, we collaborate with two patient associations focused on Von Hippel-Lindau (VHL) syndrome: the Spanish VHL Alliance and the Basque Country Sendabide Patient Association.

Understanding the regulation point by different pathologies is crucial, as it can act differently in various cases, as mentioned earlier. Indeed, we have two potential avenues for manipulating hypoxia.

What do you think could be the future applications of this knowledge, or what prospects do you foresee in this field?

- First and foremost, I wouldn't want to raise false hopes, but it's true and important to acknowledge that there are medications available on the market today for treating anemia.

These medications target the oxygen sensors, the guardians we discussed earlier. Additionally, in the United States, a medication has been approved. Here in Europe, it is currently only used in clinical trials, but this medication targets the conductor we mentioned earlier, HIF, and is used to treat certain types of tumors.

I like to think that one day we will be able to improve the diagnosis and, above all, the quality of life of prostate cancer patients and those suffering from VHL syndrome thanks to our research and gene therapy project. However, let's remain humble and recognize that for now, it's essential to continue researching.

Right, up: Edurne Berra, below: podcast episode cover.

FROM NATURE TO VALUE:

THE POWER OF ENZYMES

Enzymes stand as indispensable agents driving numerous essential biochemical processes. These specialized proteins transcend their role as mere catalysts; they are the cornerstone of biochemical transformations that support the fundamental essence of life.

Enzymes operate with remarkable precision and efficiency, accelerating chemical reactions that would otherwise occur at impractically slow rates. They enable us to break down nutrients for energy, replicate genetic material, and repair cellular damage, all with exquisite specificity and control.

Beyond their fundamental roles within organisms, enzymes are increasingly recognized for their pivotal contributions across diverse industries and environmental contexts. From agricultural practices to the emerging fields of bioplastics and biofuels, enzymes catalyze transformations that hold profound implications for sustainable development.

By converting agricultural residues into biofuels or transforming non-biodegradable plastics into eco-friendly alternatives, enzymes offer innovative solutions to pressing global challenges such as resource depletion and environmental pollution.

To delve deeper into the workings of enzymes, we will be joined by Dr. **Raúl Pérez Jiménez**, Principal Investigator at the Synthetic Biology Group at CIC bioGUNE. With his expertise, we will delve into how these intricate biochemical machines are shaping not just our understanding of biology, but also paving the way towards a more sustainable and resilient future for humanity.

What are enzymes and what is their primary function in these biological processes?

- Enzymes are proteins. The simpler name is proteins, but their more complex designation is biological macromolecules that serve two main purposes. The first is to accelerate chemical reactions within biological systems that would otherwise occur at time intervals incompatible with biological processes.

Additionally, they directly enable processes that wouldn't happen without their intervention, making them crucial for life's chemistry.

How are new enzymes with enhanced capabilities for specific applications being discovered and developed?

- In biotechnology, enzymes are prized for their remarkable specificity in catalyzing chemical reactions efficiently. When adapted outside their natural biological environments, they require modifications to function optimally, addressing challenges like temperature and pH variations. Techniques from rational design to evolutionary methods are employed to tailor enzymes for diverse industrial and biomedical applications, including biofuel production

Right: Taken from Pexels image bank.

including biofuel production and environmental sustainability efforts.

Enzymes' ability to facilitate complex reactions efficiently, while remaining environmentally friendly, underscores their immense value across industries. Their adaptation through advanced techniques ensures they can operate effectively beyond their natural biological settings, supporting innovation is crucial for sustainable development.

However, this is far from trivial because an enzyme is like a word composed of many letters. There are 20 different amino acids that can combine in complex ways. So, they are very complex "words" that cannot be modified in any way.

Each amino acid has a function and specific characteristics. Therefore, techniques ranging from informatics to evolutionary-based approaches must be applied to make applied to make very specific modifications and successfully adapt the enzyme.

What are the advantages of using enzymes for processing biomaterials compared to other methods used today? And what are the unused residues that can be utilized?

- Well, the advantages are twofold.

On one hand, as I mentioned earlier, enzymes are extremely specific and efficient. They can target a biological process with great efficiency, accelerating the reaction significantly. On the other hand, they are environmentally friendly because they do not cause pollution.

In other words, they are biological macromolecules that, unlike other metallic catalysts or solvent-based methods involving organic solvents, have virtually no pollution capacity. So, we are killing two birds with one stone. On one hand, we make processes much more efficient and selective, and on the other hand, we do not pollute.

So, enzymes are extremely interesting from a biological point of view. There are enzymes for almost any biological material. Depending on what you want to modify, you would look for a specific enzyme. But there is considerable interest in utilizing biological waste materials, such as biomass from forest residues, for example, which contain a significant amount of cellulose, lignin, and hemicellulose. These are very interesting materials for industrial use. Additionally, there are other polymers, for instance, crustaceans have a very interesting polymer called chitin, which also has a range of emerging applications. All these polymers can be chemically modified, but this often introduces factors that are not entirely environmentally advisable.

Therefore, using enzymes offers a significant advantage, not only because they are highly selective as I mentioned, but also because we could modify these components very specifically and without harming the environment.

"Using enzymes offers a significant advantage, not only because they are highly selective, but also because we could modify them specifically and without harming the environment."

What do you think are the future prospects in enzyme research and their applications in biological processes?

- Increasingly, biological processes are being integrated into industry. Unlike a few years ago, we now have in-depth knowledge and databases with millions of enzymes offering diverse solutions.

Over the past decade, advances in genomics and proteomics have provided a vast library of enzymes, enabling the modification of numerous industrial processes that use biomass and other biological components. The capabilities for enzyme modification have significantly improved due to bioinformatics and artificial intelligence, allowing for more precise predictions and adaptations.

In the near future, we will likely have enzymes to modify almost any industrial process imaginable, expanding their use in daily life and various industrial applications.

Right, up: Raúl Pérez-Jiménez, below: podcast episode cover.

THE SCIENCE OF:

BREAST CANCER

Breast cancer is a disease that has captured the attention worldwide due to its high incidence and the serious implications it has on the health of millions of people. Although commonly associated with women, this type of cancer also affects men, albeit to a lesser extent. It has become one of the most significant challenges in modern medicine and is one of the leading causes of mortality among women worldwide.

The incidence of breast cancer varies significantly between different regions and countries. However, in recent decades, an increase in incidence has been observed in developing countries, possibly due to lifestyle changes and environmental factors.

Breast cancer is characterized by the uncontrolled growth of cells in the breast tissue, leading to the formation of malignant tumors. This type of cancer can manifest in various forms and at different stages of life, presenting a wide variety of symptoms and development patterns. Factors such as genetics, lifestyle, and exposure to certain substances can influence the risk of developing the disease.

Despite significant advances in breast cancer research and treatment, many aspects of this disease remain a mystery. Early detection methods, such as mammography, have improved survival rates, but significant challenges remain, including variability in treatment responses and the emergence of resistance to conventional therapies.

But, what is currently known about breast cancer? Why do some cases develop resistance to therapies? And how could artificial intelligence revolutionize the detection, diagnosis, and treatment of breast cancer?

To delve into these questions, we are fortunate to have **Maria dM Vivanco**, Principal Investigator in the Cancer Heterogeneity Group at CIC bioGUNE. With her expertise and knowledge in the field, she will help us better understand these challenges and the advances that are changing the landscape of breast cancer treatment.

What is the present status of breast cancer incidence, and what is the impact of this disease?

- We can start with some figures because the incidence of breast cancer is still increasing today.

We know, for example, that worldwide, 2.3 million new cases were detected in just one year. In Europe, there were more than half a million cases, specifically 604,000. And if we consider Spain alone, there are more than 35,000 cases each year. In Euskadi, to give all the numbers, there are 637 cases annually.

These are numbers, but perhaps more interesting is realizing that today, breast cancer remains the most common cancer among women globally, and it also has the highest mortality rate.

Right: Anna Shvets, taken from Pexels image bank.

Nearly 96,000 women in Europe die from breast cancer annually.

Despite a slight decrease in mortality, incidence continues to increase. Most cases are diagnosed between the ages of 45 and 69, which is why screenings typically occur within this age range.

In Osakidetza, mammography is done every two years for women aged 50 to 69. However, 21% of cases detected before age 50 are not covered by these screenings. This impacts women significantly, not only in terms of health but also personally, psychologically, socially, and within their families.

In previous episodes, we introduced the concept of heterogeneity in a tumor. Could you explain what this concept entails and what its implications are?

- There are different types of heterogeneity and complexity.

There are differences between patients, as tumors in one patient may not be the same as in another, requiring different treatments and resulting in different prognoses. Additionally, there is heterogeneity even within the same patient.

For example, in a patient with metastasis, sequencing studies have shown that the original tumor in the breast is not the same as the one that appears in the lung, bone, or brain, due to mutations and changes. Another surprising finding in recent years is intratumoral heterogeneity, meaning that tumors are not homogeneous masses but contain diverse cells that behave differently.

Some of these are cancer stem cells, which have essential properties, especially self-renewal and differentiation. These cells are responsible for initiating the tumor and for resistance to therapy, making them a focus of our laboratory.

We've mentioned many figures before, but not survival rates. Although incidence is increasing, approximately 30% of cases see tumor recurrence. Forty years ago, only 40% of women survived, but today, 84% survive for five years. However, considering the incidence and the long-term outlook, the 84% five-year survival rate is still not sufficient.

"We know that not all molecules effective in the laboratory are FDA-approved. So, models that better mimic human microenvironments are crucial."

Building on your previous comments, the next question naturally follows: What role does research, especially the work done by your group, play in the fight against this disease?

- We focus on studying resistance. When a patient is diagnosed with a tumor, the doctor, along with their team of experts, prescribes a suitable treatment based on the tumor's characteristics. However, even if two women with similar tumors receive the same treatment, one might be cured while the other develops resistance. This occurs because, despite clinical similarities, tumors can differ at the molecular level.

To address this, we work on identifying biomarkers, proteins, or molecules that help distinguish tumors at higher risk of developing resistance. For example, we've found that elevated levels of the protein SOX2 are associated with increased risk. Now, we're seeking inhibitors to reduce the expression or activity of this protein.

Additionally, we study the tumor microenvironment, as obesity in postmenopausal patients is linked to a higher risk of breast cancer and therapy resistance. We aim to understand how the environment influences these risks. We also investigate healthy breast tissue to compare and better understand the changes occurring in tumors.

We've talked about what you are currently doing, but what are the future expectations in the fight against this disease?

- One of the most exciting transitions we're enthusiastic about is moving towards 3D studies that consider the microenvironment and co-cultures. It's not just about studying or focusing on what happens with one type of cell, but understanding how it interacts with others within the tumor, aiming to replicate the complexity and heterogeneity observed clinically, and to do so as accurately as possible in the lab.

We know that not all molecules effective in the lab are FDA-approved. So, models that better mimic human microenvironments are crucial.

Right, up: Maria dM Vivanco, below: podcast episode cover.

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EXCELENCIA SEVERO OCHOA

EUSKO JAURLARITZA GOBIERNO VASCO

Established in 2004 under the auspices of the Basque Government, CIC bioGUNE is dedicated to advancing biomedical science. Its interdisciplinary team of over two hundred scientists and technicians delves into the molecular foundations and mechanisms of diseases, aiming to innovate in diagnostic methods and foster the advancement of innovative therapies.

Recognized as a Severo Ochoa Center of Excellence, CIC bioGUNE leads cutting-edge research at the intersection of Biology, Chemistry, and Mathematics, focusing on Cancer, Rare Diseases, Infectious Diseases, and Metabolic Disorders. Our infrastructure includes advanced technological platforms that support scientific discovery and collaboration, positioning us among Europe's foremost research institutes.

We are committed to bridging the gap between complex scientific research and public understanding through diverse outreach activities. By translating our research into accessible language and engaging the community in scientific advancements, we emphasize the importance of investing in research for societal progress and well-being. These efforts not only strengthen our connection with stakeholders but also promote broader appreciation and engagement with science for the benefit of society.

Transcriptions, editing and layout:

These podcast episodes have been transcribed, translated, edited, and formatted for this magazine by **Jana Sendra Viscarro**.

"Cutting-edge science advancing at the frontier between Chemistry, Structural, Molecular and Cellular Biology, aiming to develop a more Precise Medicine for the future"

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