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Precision Medicine

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Beyond One-Size-Fits-All:

The Revolution of Precision Medicine

by Pablo Zardoya-Laguardia

Picture a young girl with Type I diabetes. Her health depends on injecting insulin every day, and the dose and timing have to match exactly what she eats. An overdose can be life-threatening. Managing her blood sugar day in, day out is a harsh discipline to expect from a child, a constant worry for their parents. Only a few years ago, the only method available was pricking a finger, dabbing a drop of blood on a test strip and slipping that into a measuring device. But now she wears a small patch on her arm with a sensor linked to her smartphone. An app tells her the dose of insulin to use. Her parents can check how her blood sugar is and get alarms if the value goes off track. In the long term, she will be better protected against the cumulative effects of the disease.

Picture a woman in her forties with a diagnosis of bowel cancer. She could be facing chemotherapy, radiotherapy and surgery. She might be looking at using a colostomy bag for the rest of her life. But doctors test a biopsy of the cancer and find that the tumour cells are what they call "mismatch repair deficient". This is only the case in 10% of bowel cancers, but it means she can be treated with the monoclonal antibody drug dostarlimab. Six months later, she is cancer free.

Picture a man in his fifties who has had a mild stroke. He is recovering well, but the stroke was caused by a blood clot and now the challenge is to prevent any more blood clots forming where they can cause trouble. But blood thinning medication is tricky – too much, and there is a risk of uncontrolled bleeding. Not long ago, doctors had to rely on watch-and-wait tactics to see if the medicines and dosage were right. But now there are some gene tests that can help. For example, the drug warfarin is broken down by an enzyme in the liver, but some people don't have this enzyme, which means the drug reaches a higher concentration in the body and they have to be given a much lower dose. For the anti-platelet drug clopidogrel, it is the other way around: it is activated by a liver enzyme, which, again, some people don't have. Clopidogrel won't work for them and they need to take something else.

All of these cases, in different ways, are examples of what is called precision medicine (PM) – a growing trend that is changing the face of healthcare. PM tries to shift from "one-drug-fits-all" to "the right medicine, for the right patient, at the right dose, at the right time". This model is also referred to as personalized medicine, stratified medicine, or P4 medicine.

"Personalised medicine will give us more information about risks and options at every stage of our life."

Pablo Zardoya-Laguardia

Goals and development of precision medicine

Precision medicine aims to revolutionize healthcare by focusing on the patients' genetic and molecular profiles; by identifying more accurate and early indicators of health issues, enabling the detection and reversal of early stages of diseases, by enhancing effectiveness of treatment, and by avoiding side effects. Conventional medical practice relies heavily on clinical examinations backed up by just a few items of laboratory data, following differential diagnosis methods to categorize cases into quite broad groups. Per disease there are a small number of fairly standard treatments; this is the "one-size-fits-all" approach. Side effects may arise or the treatment may be ineffective for certain individuals, but these issues are dealt with reactively, if and as they arise. PM means greater use of biomarkers and companion diagnostics to have a more exact picture of what will work best before therapy begins.

The treatment response varies among individuals due to factors like genetics, ethnicity, and disease stage. And nowadays we have tests that can characterize these parameters in one shot. For example, genomics is a group of methods that characterize many of your genes at once or even sequence your whole genome (hence the name). And it has been joined by other technologies that give a snapshot of whole sets of molecules. 'Proteomics' gives a profile of which proteins are being expressed in your cells (hundreds of them). 'Transcriptomics' looks at messenger RNA, which shows which genes are being actively expressed at a point in time. 'Metabolomics' captures the status of your metabolism by measuring many small molecules. Epigenomics analyzes patters of modifications of DNA that do not change the sequence but are often important in shaping differences in gene expression between different cell types. Microbiomics studies the communities of microorganisms living in our gut.

In this way, PM arises out of a network of different disciplines, linking information between clinicians, laboratories, research enterprises, and clinical information systems. PM relies on correctly interpreting data, combining omics and clinical information (clinical phenotypes, family history, environmental and lifestyle contributors and genetic specific characteristics) to determine the best course of action for each patient group. As our understanding of diseases deepens through molecular biology, a more precise disease classification incorporating new molecular knowledge emerges. As PM generates information about which patients will be responders or non-responders to specific treatments, its potential applications grow.

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Applications of personalised medicine

Doctors can use patients' molecular and genetic profiles to help select the most effective drug or treatment for a particular disease. Genetic stratification already has a major role in cancer treatment and improves survival rates.

PM also improves prevention by identifying people who are at high risk for certain diseases. It can help doctors diagnose diseases earlier and more accurately, which ultimately can save lives. For instance, people who have a family history of breast cancer may be tested for the BRCA1 or BRCA2 gene mutations. PM can also help diagnosing a disease more quickly and accurately. This can aid doctors avoid prescribing drugs that are not effective for individual patients, which can reduce the risk of side effects. A good example for colorectal cancer is the blood test called the Cologuard that can be used to detect DNA changes associated with the disease. This test can be used to screen people who are at high risk, and it can help to diagnose the disease early enough, when it is more likely to be treatable.

PM opens a promising frontier in healthcare, but as always, new possibilities and technologies bring new challenges, and the changes in progress now have many dimensions that need to be worked on.

A key aspect of PM is the discovery and development of biomarkers – diagnostic parameters or characteristics. As it turns out, it can be a long road from the initial discovery that some factor changes in a disease-related state, to having a biomarker developed and validated to the point where they can be used reliably in clinical practice. However, advances in molecular biology are giving us a deeper understanding of diseases and when we understand the role of a certain factor in a disease mechanism, this makes the route to a real clinical application more logical and shorter.

Another task is selecting the most relevant omics data types to obtain from tissue samples, due to cost and tissue availability constraints. Analysing just one omics subset can provide an incomplete and biased picture of the underlying biology. An attempt to solve this is the integrated personal omics profiling (iPOP) project, a longitudinal study using multi-omics data for health assessment and

prediction. Longitudinal studies by their nature take time, but they can show us the way to using such multidimensional data.

An efficient bioinformatics architecture is necessary to analyse, manage, and record all collected information. Medical records containing sensitive personal information are closely guarded and not openly available; data is often siloed in clinics or hospitals, limiting the velocity and volume of data needed for big data methods. The complexity of medical data requires processing to make it readily usable, and the technical infrastructure to handle and manage medical data is lacking compared to that available to large companies. A solution to this problem could be to use data warehouses, systems that take input data from many sources and convert it into common formats so that it can be accessed any analysed as a whole. Data warehouses also carry out quality control on input data to ensure that their contents are as clean and informative as possible.

Implementation of PM raises legal and ethical concerns. Cross-collaboration among health care professionals is crucial, and policies need to be harmonized and integrated into existing health systems. Considerations must include genetic counselling, because people faced with new kinds of information need guidance on risks and possible strategies for their health. Healthcare professionals need training to deal with the new kinds of communication and advice expected of them. And a common, ethically validated policy framework is needed, because for PM to be feasible, general trust among patients in what is being done with their data and in the recommendations they are being given is essential.

Data security and consent to data processing are also big issues that need careful handling, especially with regard to the pooling of data, and for example in using data and biobank samples for purposes that might not have been possible to predict when they were collected. Data regulation such as the GDPR is well intentioned, but it is important not to burden researchers and startups with regulatory processes beyond their capacity to fulfil. Regulation needs to be intelligent, responsible and adaptable and avoid box-ticking exercises that aren't really relevant to protecting patients' interests. Institutions have work to do on guidelines for genetic information, privacy and data security, and also on education and awareness of this technology.

> "Implementation of PM raises legal and ethical concerns."
>
> **Pablo Zardoya**

To enable big data science in genomics, standardization of sample collection is essential. While genomic material like DNA from blood and fresh tissues has been successfully standardized over the past two decades, other samples such as DNA from paraffin-embedded tissue, RNA, and proteins remain sensitive to tissue type and handling, making replication studies less reliable. So more standardization is needed for collection of these types of sample.

To make data collections useful, controlled vocabularies for data entries are needed. Annotations such as clinical and laboratory findings, sample characteristics etc., need to be standardized so that data can be analysed using machine learning and AI methods. This is an effort requiring a lot of communication and coordination across many institutions.

Present and future trends

In clinical settings, patient information like clinical phenotypes and family history is regularly recorded. Environmental and lifestyle data are typically collected through questionnaires, though they may be inaccurate. The increasing popularity of wearable devices such as fitness trackers, smartwatches but also genetic testing, are providing more practical and detailed data for PM purposes,.

High-throughput methods like next-generation sequencing allow the collection of genetic and "omics" data, making genomic data integration in healthcare more feasible and cost-effective. This abundance of data offers the potential for personalized healthcare and individualized treatment approaches. Consumers, patients, and healthcare providers are actively engaging with digital health technologies, while healthcare administrators and policymakers are exploring value-based care models that leverage integrated systems for large-scale data collection. The convergence of new technologies, including AI analytics, with biometric datasets from digital health devices is driving a cultural shift in healthcare towards a digital transformation. These advances hold the promise of improving outcomes, reducing costs, and enhancing the efficiency of healthcare delivery helping with some of the challenges proposed before.

PM is not changing the way all medicine is done overnight. Not yet; though it probably will bring sudden breakthroughs in some fields. And yet in the mid-term, it will bring profound changes: possibly the most profound may be that the idea that we are either sick, and need a doctor, or healthy, and don't need one, will dissolve. We will have much more information about risks and options at every stage of our life and, with advice, we will decide what is the best way for us, personally, to proceed.

In this new, emerging landscape, all of the companies and projects presented in this issue are working on their own parts of the puzzle.

Das Kinderwunsch Institut Schenk GmbH | by Gregor Weiss & Michael Schenk

Microbial influence on the fate of the oocyte

A recent study by "Das Kinderwunsch Institut Schenk GmbH" highlights the importance of precision medicine for the selection of oocytes in assisted reproductive technologies.

Infertility is a public health issue with ever-increasing numbers of couples struggling to conceive. The causes of infertility have not yet been completely elucidated but are predominantly associated with age, lifestyle, and diseases like endometriosis. Assisted reproduction technologies (ART) aim to overcome this global phenomenon, however, finding new biomarkers to predict embryo quality and improve treatment outcome is a constant challenge in reproductive medicine research.

In the last couple of years, the microbiome of the female reproductive tract has become a promising target in ART treatment. Bacteria are found throughout the entire female reproductive system including follicular fluid (FF). FF is found inside the follicles and surrounds the oocyte during maturation in the ovary. This fluid contains a mixture of secreted products of granulosa and theca cells as well as serum components like hormones, fatty acids, sugars, and growth factors. Due to this special microenvironment, FF plays a pivotal role in follicular growth, oocyte quality and subsequent fertilization and early embryo development. In most studies in which FF has been pooled for analysis, further information on the fate of the respective oocyte or embryo development is not provided.

In order to overcome this gap in the data, the Kinderwunsch Institut Schenk GmbH developed a standard operating procedure to separately collect and store FF from each follicle after oocyte retrieval. In a recent study approach FF were analyzed for bacterial composition. Two FF per woman were analyzed and compared: one contained an oocyte that developed into a good quality embryo, the other an oocyte that failed fertilization. The study revealed an increased pathogenic bacterial load in follicles from oocytes that failed fertilization (70.8%) compared to those with good fertilization results (8.3%). The most prominent bacterial strains (*Atopobium vaginae, Ureaplasma spp.*) were mainly found in follicles of non-fertilized oocytes. The absence of pathogenic bacterial load in FF appeared to be the most significant predictor of successful oocyte fertilization and embryo development.

These results indicate that a separate collection of FF and subsequent microbiome analysis may be a promising method in fertility research to select the best suited oocytes for insemination. This study points to an individualized approach for patients trying to conceive and highlights the importance of precision medicine in ART treatment.

Gregor Weiss, head of research & development

VTU

Cell and Gene Therapies

Cell and gene therapies (CGTs), also referred to as "advanced therapy medicinal products" (ATMPs), correct or cure diseases by directly repairing genetic defects within the body or by introducing tissues or cells with a new function into the body (see Figure 1). The range of diseases amenable to such therapies include inherited genetic disorders such as sickle cell anemia, as well as disorders acquired during life that manifest in the genes, such as cancer. Development and manufacture of these medicines are novel and complex; thus, they are still intensely researched and have only begun to enter the commercial realm in the last ten years. However, they are remarkable for their potential to provide a permanent cure rather than temporarily treat or reduce symptoms.

Currently, there are 19 cell and gene therapy products commercially available in the European Union [EMA, 2023]. These products are produced by 15 different companies, highlighting the diverse nature of the field. Even for a single product, in most cases several companies are involved in the development, manufacturing, analytical testing and commercialization of the products.

Due to their novelty, the industrial players for new applications in the field are often startups which contribute significant scientific expertise. However, the commercial manufacturing aspects of those medicines are often overlooked at the early stages of development. The manufacturing process needs to be translated into an industrial manufacturing environment, and patient safety aspects become especially relevant as these medicines require sterile application. The therapies are mostly customized for the patient and still must undergo elaborate manufacturing. Input and output parameters need to be selected and categorized according to their importance (see Figure 2). All these aspects are combined into a control strategy to ensure that the production process meets the high quality requirements set by the health agencies and that the final product meets fixed specifications.

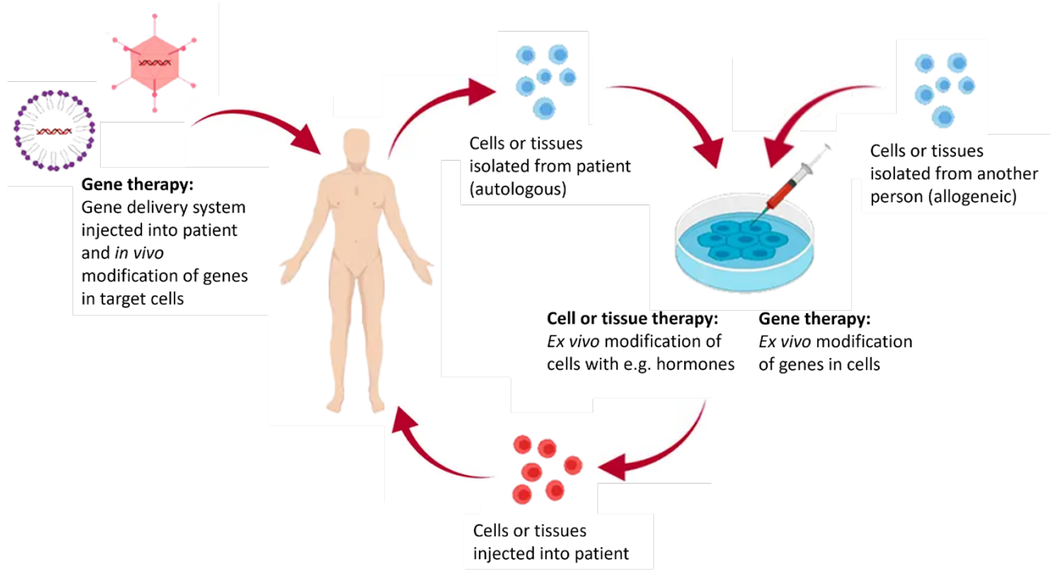

Figure 1: Cell and gene therapies.

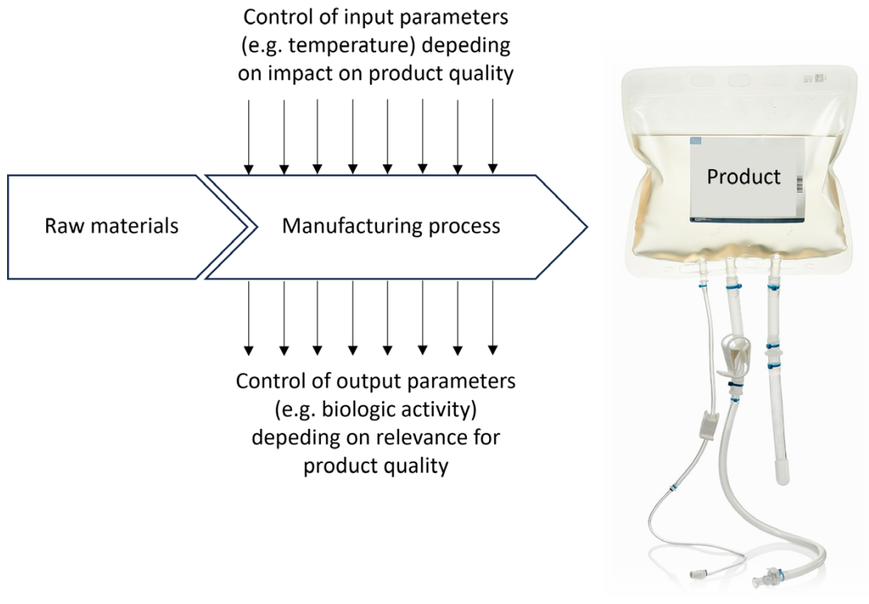

Figure 2: Control of the manufacturing process.

A consulting partner such as VTU can help translate the manufacturing process into the GMP manufacturing environment and generate all the relevant CMC (Chemistry, Manufacturing, and Controls) (chemistry manufacturing and controls) information required to submit the product for clinical studies and eventual commercialization.

There is a particularly high diversity in the products and manufacturing processes as cell and gene therapies are not yet well established nor streamlined. This results in major differences between manufacturing processes of different products compared to well-established types of medicines such as antibodies. Consequently, fulfilling regulatory expectations is more challenging, as it is less standardized and not many best practices are available from already launched cell and gene therapy products.

A study conducted in March 2022 found 583 clinical trials being conducted in the USA and EU [Wilkins et al., 2023]. Even if only a small fraction of these potential therapies reach the market, this would multiply the number of therapies available. A few licensed products are being evaluated for new indications (i.e. another disease), but most are new products. Most clinical trials analyzed were in the early stages (phase I/II), where the establishment of an integrated control strategy is highly recommended.

Austrian presence in the field

Cell and gene therapy development is dominated by the USA, where most developers are situated, and 70% (8.1 bn USD) of the capital investments were made in 2023. The second-largest area active in cell and gene therapies is Asia-Pacific, followed by Europe [ARM, 2024].

There are a few active companies involved in the development of cell and gene therapies in Austria. The most established cell and gene therapy company in

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Austria is Takeda, which has its global site for process development and manufacture of cell and gene therapies in Orth an der Donau. There, they cover all steps from the gene delivery system to the final product, including quality control. Takeda's cell therapy product Alofisel was discovered by the Belgian startup TiGenix NV and co-developed prior to the acquisition of the company by Takeda in 2018.

invIOs, situated in the Vienna Biocenter, is developing the cell therapy platform "EPiC" as well as two cell therapy products. This platform is a closed manufacturing system intended to enable *ex vivo* treatment and genetic modification of autologous immune cells in delocalized sites. To date, for commercial products, the *ex vivo* treatment and genetic modification of cells are conducted in specialized centers. Conducting the *ex vivo* treatment and genetic modification closer to the patient without complex logistics enables shorter times until the cells can be reinserted back into the patient. The platform is used by invIOs for two cell therapy products against solid tumors. One of them completed phase 1 in 2023, and the other will start clinical trials this year.

Another relevant company is Allcyte, a spin-out of the CeMM in Vienna, which was taken over by Exscientia from Oxford in 2021. Their innovative approach is to grow actual cancer cells *ex vivo* and test drug candidates directly on them using AI image recognition.

Cell and gene therapies had several first-of-its-kind moments in 2023. The first gene editing product (Casgevy) was approved, and for the first time, six cell and gene therapy products were approved in the USA within one year (four of them are expected to be approved in the EU in 2024). Thinking about 2024, the sights are set even higher. The first approval for a solid tumor therapy and the first immunological mass-produced therapy (allogeneic CAR-T-cell) are expected to be approved. Furthermore, up to 17 cell and gene therapy programs are in a state where approval is likely in 2024 [ARM, 2024]. With this wind in the sails, the revolution of medicine continues for the sake of patients worldwide.

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Cornelia Haas and Birgit Krenn work for VTU Engineering as consultants for manufacturing science and technology transfers of cell and gene therapies and other biologics in Europe.

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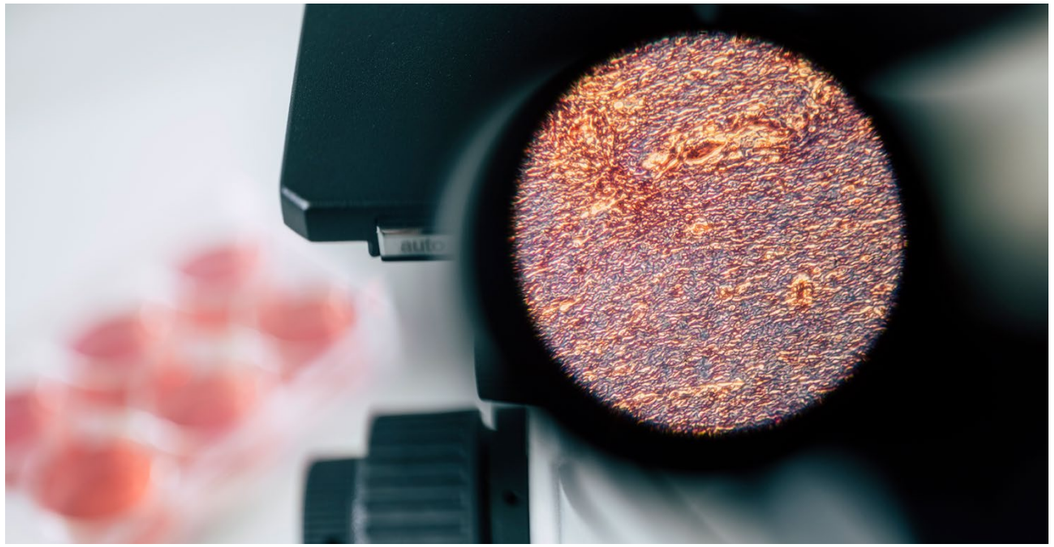

Personalized Approaches in Wound Care

Why are chronic wounds difficult to treat?
Chronic wounds, characterized by a strongly delayed healing process, represent a significant challenge in modern healthcare. The pathogenesis of chronic wounds involves a complex interplay of various factors such as impaired cellular responses, inflammation, and compromised tissue regeneration. Traditional wound care approaches often provide only limited success. Thus, the one-size-fits-all approach to wound care may not be optimal for chronic wounds due to their heterogeneous nature.

How could personalized approaches help to improve chronic wound treatment?
Personalized wound treatment involves tailoring interventions based on the patient's unique physiological and molecular profile. Advances in biomarker identification, genetic testing, and imaging techniques enable clinicians to gain insights into individual variations that influence wound healing. Personalized wound care strategies may encompass targeted drug therapies, customized dressing materials, and lifestyle modifications to address specific patient needs.

Why and how to bring personalized medicine and skin-on-chip technology together?
Skin-on-chip technology is an innovative platform that replicates the microenvironment of human skin, allowing for the simulation of physiological and pathological conditions. In the context of wound healing, skin-on-chip devices mimic the intricate interactions between different cell types, extracellular matrix components, and signaling molecules within a controlled microfluidic system. These systems provide a more accurate representation of in vivo conditions compared to traditional cell culture models. Skin-on-chip models offer a unique opportunity to study the dynamics of wound healing in a personalized manner. By incorporating patient-specific cells into the chip, researchers can observe how individual variations in cellular responses impact wound closure, tissue regeneration, and inflammatory processes. This personalized approach enables the identification of targeted therapeutic interventions that are more likely to succeed in specific patient populations.

The Division of Plastic, Aesthetic and Reconstructive Surgery of the Medical University of Graz and JOANNEUM RESEARCH with the institutes COREMED, MATERIALS and HEALTH are joining forces to develop suitable skin-on-chip approaches to study processes and factors involved in wound healing progression. These chips will be used to evaluate innovative treatment options intended to improve wound healing in the future.

CBmed GmbH | by Barbara Prietl

CBmed in the ATTRACT Project: Pioneering Precision Medicine for Glioblastoma Treatment

Glioblastomas, the most common malignant brain tumors in adults, present a significant clinical challenge due to their poor prognosis and resistance to conventional treatments. In response to this critical issue, the "Personalized targeted glioblastoma therapies by ex vivo drug screening: Advanced brain tumor therapy clinical trial," or ATTRACT, spearheaded by an interdisciplinary consortium led by the Medical University of Vienna, has emerged as a revolutionary initiative to redefine the future of glioblastoma treatment. CBmed, a key contributor to this project, is proud to be at the forefront of developing precision medicine solutions for this challenging disease.

Barbara Prietl, Scientific Lead Precision Medicine Technologies

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The ATTRACT project, funded through the Ludwig Boltzmann Society's "Clinical Research Groups 2022/23" call for proposals, brings together expertise from the Medical University of Vienna, the Medical University of Graz, the Medical University of Innsbruck, the Karl Landsteiner University / St. Pölten University Hospital, the Johannes Kepler University / Kepler University Hospital, the Danube Private University, and the Austrian Institute of Technology (AIT).

Recognizing the intrinsic resistance of glioblastomas to conventional therapies, ATTRACT aims to develop individualized therapeutic approaches based on tumor biology. In approximately 60-70% of cases, the promoter of the O6-methylguanine methyltransferase (MGMT) gene is unmethylated, leading to heightened chemoresistance and poor outcomes. CBmed's role in this initiative is pivotal, introducing an innovative ex vivo drug screening platform to analyze the response of patient-derived tumor cells (PDCs) to selected therapeutic agents. This approach paves the way for precision medicine tailored to the unique biology of each patient's tumor, representing a significant departure from traditional treatments.

The clinical efficacy of CBmed's ex vivo drug screening platform will be rigorously assessed through a prospective, multicenter, randomized phase 2 study, enrolling 240 adults newly diagnosed with glioblastoma. Supported by key organizations such as the Austrian Cancer Aid, the GPMed (Austrian Society for Pharmaceutical Medicine), and the Clinical Coordination Center of the Medical University of Vienna, ATTRACT is positioned to significantly enhance treatment options for glioblastoma patients.

About CBmed:

CBmed is a leading research center at the forefront of precision medicine, uniquely positioned at the interface of clinical and biomedical research. With a commitment to advancing translational research, CBmed integrates world-class infrastructure and global collaborations to pioneer individualized solutions, reshaping therapeutic approaches beyond traditional one-size-fits-all models. For more information about CBmed, please visit www.cbmed.at.

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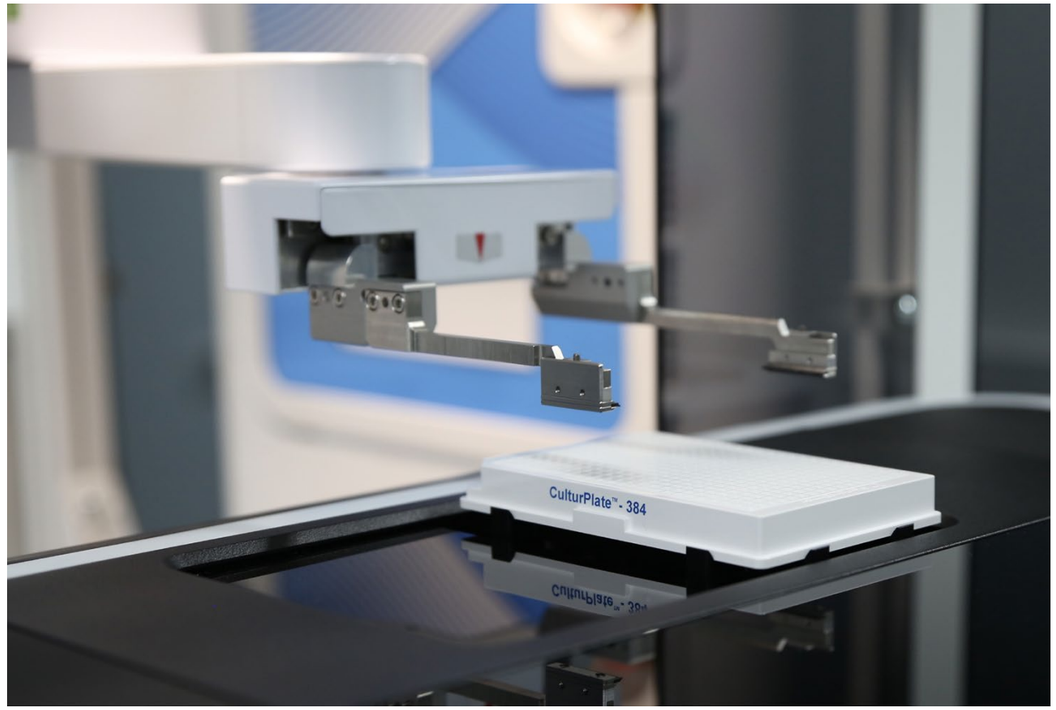

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The project also benefits from the guidance of a distinguished international Advisory Board consisting of experts in the field of oncology, including Michael Weller (University Hospital Zurich), Priscilla Brastianos (Massachusetts General Hospital), Annette Kopp-Schneider (German Cancer Research Center), Markus Zeitlinger (Medical University of Vienna), D.H. Nam (Samsung Medical Center, Seoul), and Helen Bulbeck (Chairwoman of the patient organization Braintrust, UK).

Beyond advancing treatment options, ATTRACT aims to establish a unique biobank housing patient-derived tumor cells, comprehensive clinical data, and tumor tissue samples. Researchers will apply genetic, epigenetic, and metabolic analyses, coupled with AI-driven data integration, to identify new cross-platform biomarkers, offering deep insights into the biology of glioblastoma and laying the foundation for innovative treatment methods.

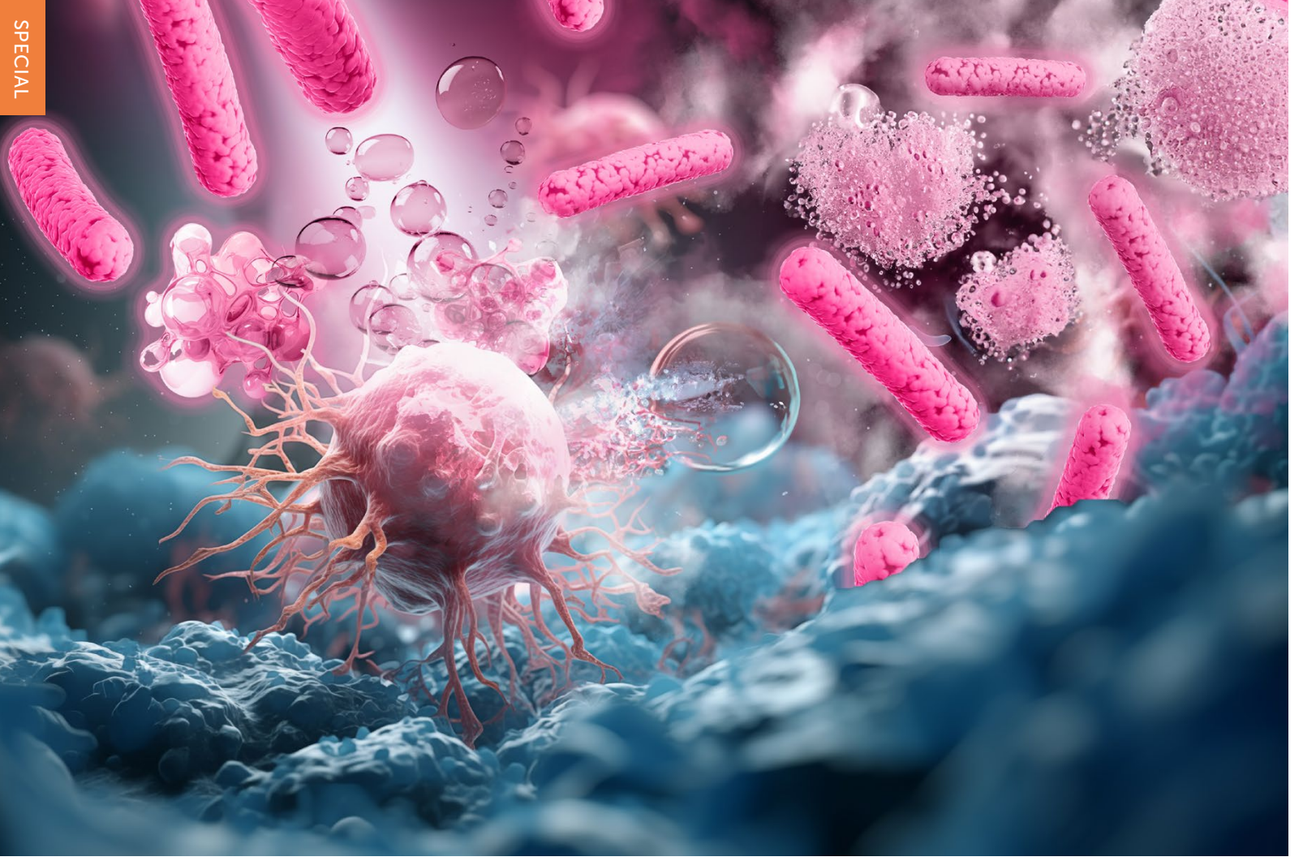
CBmed's participation in the ATTRACT project reflects a commitment to pushing the boundaries of glioblastoma therapy. By combining cutting-edge technology with a collaborative, interdisciplinary approach, this transformative initiative is poised to revolutionize glioblastoma treatment and bring hope to patients and their families worldwide.

Find out more about the ATTRACT Project:

https://www.meduniwien.ac.at/web/ueber-uns/news/2023/news-im-september-2023/forschungsgruppen-der-meduni-wien-erhalten-umfangreiche-grants-der-ludwig-boltzmann-gesellschaft/

Learn more about the selected projects and LBG funding program:

https://lbg.ac.at/news/innovationen-in-der-forschung-neue-klinische-forschungsgruppen-praesentiert/



Institut AllergoSan | by Stephanie Kolleritsch

Indication-specific Probiotics: Tailoring the Fight against Cancer

Despite tremendous scientific progress, cancer remains one of the leading causes of death worldwide and is a persistent major health concern in our society. A negatively altered microbiome is considered a crucial factor in both the development and treatment of malignant tumors. Targeted microbiome modulation using specially developed probiotics not only improves a patient's immunological health and reduces chemotherapy-associated side effects but also positively influences the response to oncological treatment.

Disrupted gut microbiome as a trigger for cancer development

As is the case for many other diseases, studies have highlighted the significant impact of the intestinal microbiome on tumor development. Pathological dysbiosis promotes the colonisation of pathogenic bacteria which can negatively influence the immune response and trigger cancer progression. In contrast, specific probiotic bacteria, especially Lactobacilli and Bifidobacteria, show tumor-inhibiting effects, such as enhancing the apoptosis of tumor cells and protecting against oxidative stress. Ongoing research at the University Hospital of Zurich, in cooperation with Institut AllergoSan, explores the beneficial effects of the specially formulated multispecies probiotic OMNi-BiOTiC® 10 AAD on the gut microbiome, the immune system, and the reduction of tumor growth in colon carcinoma patients.

Targeted strengthening of the microbiome during cancer therapy

As commonly known, cancer treatment such as chemotherapy or radiotherapy can severely damage microbiome diversity, exacerbate inflammation, and destroy the intestinal barrier function. The resulting gastrointestinal symptoms can negatively influence patients and may even prevent them from continuing treatment. For optimal support, the use of OMNi-BiOTiC® 10 AAD has proven particularly effective in improving the negative side effects caused by cancer treatment. This probiotic has been in clinical use for years, especially in the field of oncology. As demonstrated in numerous scientific studies, the specific combination of probiotic bacterial strains inhibits the growth of pathogens, and reduces toxin production to zero, thereby significantly improving the patient's quality of life.

In recent years, there has been an increase in the use of immunotherapy with checkpoint inhibitors. While these newly developed agents offer promising perspectives, many patients do not respond to treatment. Studies have shown that a high diversity of the gut microbiome is crucial for the effectiveness of such treatment approaches. Further valuable insights are expected from a clinical study that will be conducted at the Technical University of Munich, in collaboration with Institut AllergoSan, analyzing the positive effects of specific probiotic intervention on the efficacy of immunotherapy with checkpoint inhibitors in breast cancer patients.

Future perspectives

The improved understanding of the microbiome's role in tumors offers a promising approach for both the identification of new biomarkers to predict treatment success and for the development of personalized therapeutic strategies. The use of indication-specific probiotics for microbiome modulation in oncology remains a research hotspot and is currently being investigated in large-scale clinical studies. Ultimately, this could potentially even become one of the key factors in tumor prevention.

"The improved understanding of the microbiome's role in tumors offers a promising approach for both the identification of new biomarkers to predict treatment success and for the development of personalized therapeutic strategies."

Stephanie Kolleritsch

Stephanie Kolleritsch, Research Department

SPECIAL

acib

Gentle alternative to antibiotics protects the skin

It nourishes, detoxifies and protects our body - the skin. A balanced skin flora is crucial for it to be able to fulfill its functions. "Healthy skin is characterized by a diverse ecosystem consisting of microbes that form a kind of protective shield - the microbiome. If it is disturbed, harmful bacteria can cause skin diseases such as atopic dermatitis, rosacea and acne. Many skin diseases are currently treated with antibiotics. This results in multi-resistant germs against which new antibiotics must be found that not only kill the 'bad' bacteria, but also the 'good' ones that ensure a stable skin microbiome," explains acib researcher Margit Winkler.

The Austrian Centre of Industrial Biotechnology (acib) and the Tyrolean (Austria) company Sanubiom have therefore developed a gentler form of treatment for skin diseases: "As tiny viruses, bacteriophages can specifically combat excessively present harmful bacteria such as Staphylococcus aureus by curbing their spread and restoring the natural balance of the skin flora. The rest of the microbiome is not affected," explains Christian Unterlechner from Sanubiom.

Complex phage search

The acib contributed its expertise to the complex phage search. The researchers took samples from spittoons in dental surgeries or wastewater from sewage treatment plants and carried out swabs. The samples were processed and combined with harmful bacteria that had previously been cultivated on agar plates. "If a plaque forms, i.e. a transparent dot appears, a phage has been found that lyses the bacteria, i.e. destroys them," explains acib researcher Daniel Luschnig. The researchers make use of this lysis in phage production. Winkler: "The phages specifically attack the bacteria by docking onto the surface of the host bacterium. The bacterium is transformed by the phages into a "phage factory" by using the bacterium's natural reproduction machinery. The bacterium then dies and produces a large number of bacteriophage duplicates," says Winkler. After a purification step, the phages can be used for skin care products, among other things.

Phage products for humans and animals

Sanubiom's products use phage technology to combat neurodermatitis, rosacea and acne. They also contain active probiotics to promote the balance of skin flora. The gentle antibiotic alternative is also used in veterinary medicine. Unterlechner: "Phages could be used wherever antibiotics were used in the past. The technology could also be used in the food or medical sector - provided the necessary approvals are granted."

www.acib.at