European Innovation Council

Workshop on Health & Biotech Challenges with Member States representatives

On 22 September 2022, Iordanis Arzimanoglou, the EIC Programme Manager (PM) for Health and Biotechnology, organised a workshop to present past, current and potential future EIC challenges under his umbrella to invited representatives from European Union Member States and European Union Associated States. The virtual workshop was moderated by Keith Sequeira who opened the discussion by explaining the novelty of the role of Programme Managers as EIC's in-house experts, who working in their respective area of specialisation and support the European R&D&I ecosystem.

Programme Manager Arzimanoglou followed up by introducing his past and ongoing challenges, namely the 2021 EIC Pathfinder challenge *Emerging technologies in cell and gene therapy*, and the 2022 EIC Transition challenge *RNA-based therapies and diagnostics for complex or rare genetic diseases*. These challenges, as well as the proposed future challenges, are purposely narrowly-defined to avoid overlaps with other European Commission funding mechanisms and to foster innovation in a very niche area of research, with the idea of championing this area before branching out.

In the second part of his presentation, PM Arzimanoglou opened the discussion by elaborating the key objectives, scope, rationale and underpinning evidence of his proposed 2023 EIC Accelerator challenge *New biomarker-guided treatment in the era of precision oncology*. He emphasised that through research on biomarkers, oncologist could understand the reaction of human bodies to different kind of cancer treatment better which then could affect the applied treatment method. Furthermore, he gave examples from already successfully operating European start-ups in this domain.

PM Arzimanoglou closed his presentation by giving an insight into four challenges that he envisions for the upcoming years. These include a 2024 EIC Pathfinder challenge on *Disease modelling in space* (jointly with the PM for Space, Stela Tkatchova), a 2024 EIC Accelerator challenge on *Monoclonal antibodies-based therapeutics for new variants of emerging viruses*, a 2024 or later EIC Accelerator challenge on *Gene therapy clinical trials phase 1/2a* and a 2024 or later EIC Transition or Accelerator challenge on *Industrial biotechnology: scaling up synthetic biology-based applications*.

Each presentation block was followed by an interactive part in which representatives from European Union Member States and European Union Associated States gave their input and raised their questions. The representatives were interested in hearing more about the role of the Programme Managers and the subtleties between the EIC funding schemes, especially with regards to Accelerator and its approach to target SMEs and start-ups that already are on the market. Some Member State representatives challenged the business potential

of biomarkers, others agreed with PM Arzimanoglou to not only limit the research on molecular biomarkers but to also focus on digital and mechanical biomarkers. Furthermore, they agreed with the PM on the statement that licensing remains a crucial topic in the field. For the upcoming challenges, the Member State representatives expressed their strong interest in following-up and providing input. Keith Sequeira then closed the workshop by announcing the publication of the EIC Work Programme after its adoption and the EIC Emerging Technologies report in early 2023.

For any question to Programme Manager Arzimanoglou, please reach out to EISMEA-D.02@ec.europa.eu.

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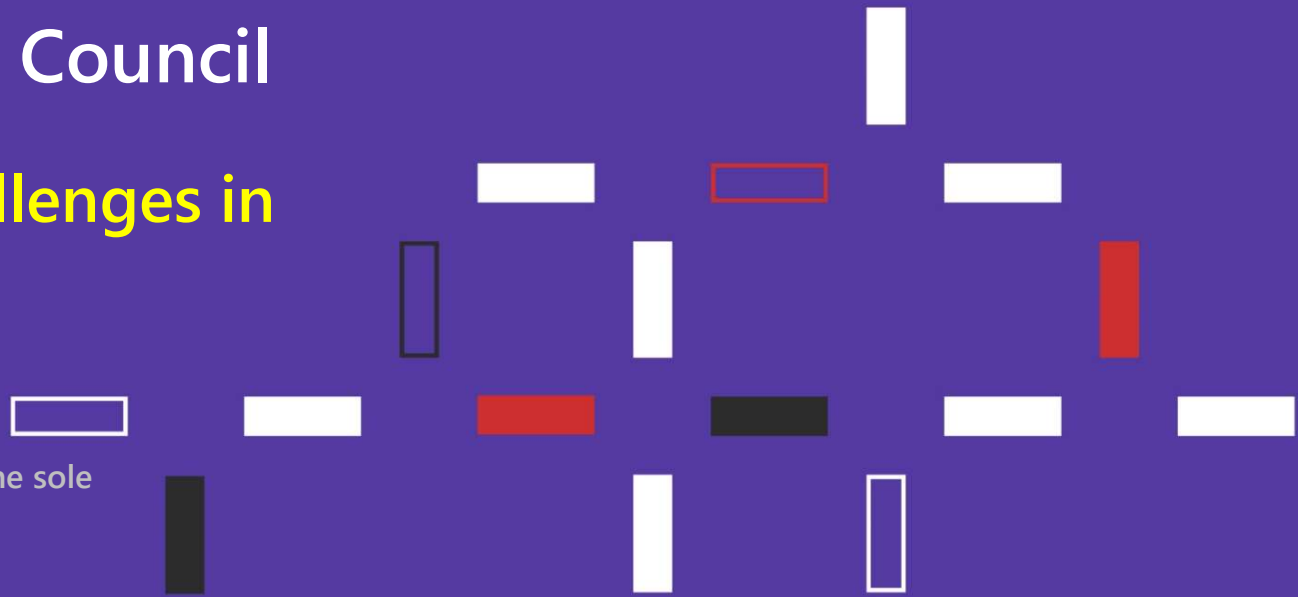
Backing visionary entrepreneurs

The European Innovation Council

For the Member States

Candidate topics for EIC Challenges in Health and Biotechnology

Iordanis Arzimanoglou



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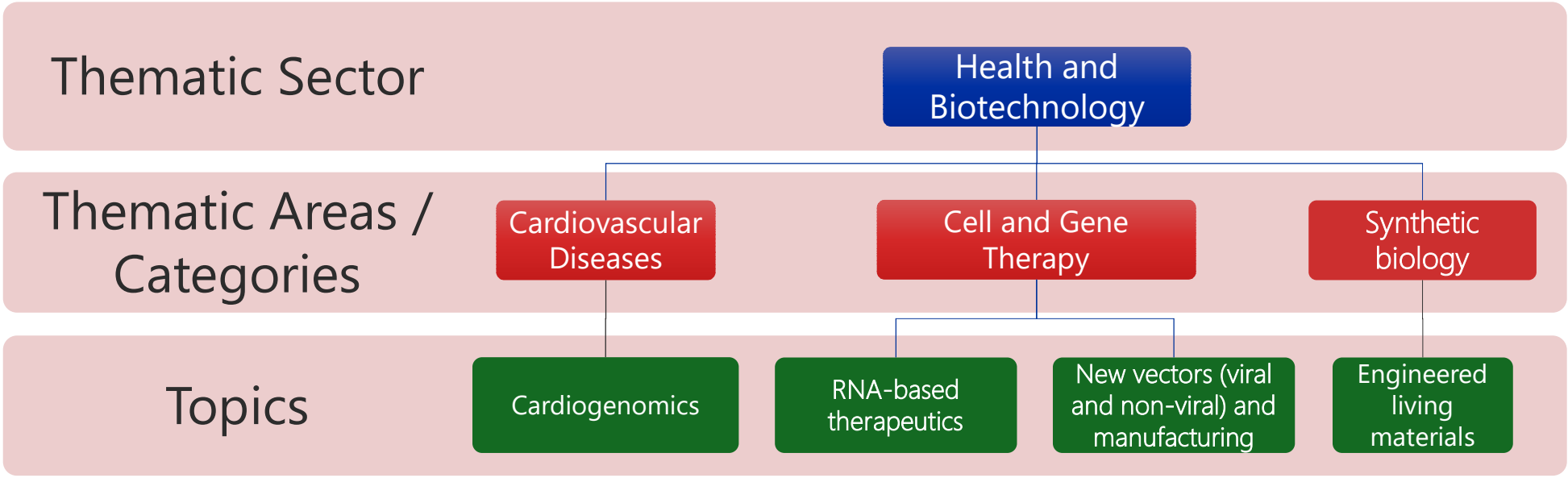
EIC Health and Biotechnology Strategy

From sector to topic



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EIC Health and Biotechnology Challenge

Rationale behind

EIC H&B Challenges are selected topics in biomedical areas in which Europe has the opportunity to compete and sustain globally, and which can set the basis to establish a critical mass of disruptive bioinnovation-based activity, potentially leading to achieve European technological autonomy in these areas in the long run

EIC Health & Biotech portfolio
Current State

European Innovation Council

EIC 2021 Pathfinder Challenge (status: proactive management)

Emerging technologies in
cell and gene therapy

EIC 2022Transition Challenge (status: deadline Sep 28,2022)

RNA-based therapies and diagnostics
for complex or rare genetic diseases

Two Challenge Calls were issued in the context of strategically positioning EIC in Cell & Gene Therapy

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Proposed the idea that the EIC should strategically and systematically focus on CGT

First presentation for future candidature EIC Pathfinder

Screening of the ERC CGT portfolio data from ERCEA. Analysis results presented to ERC & EIC Board Members: CGT Workshop proposed

2020

July-August

September-October

October - November

Follow-up events to the workshop:
Dutch Medical Univ;
Nanomedicine network;
Danish Aarhus Univ;
Portuguese P-Bio

1st ever Workshop EIC – ERC Cell & Gene Therapy

EIC Pathfinder Challenge Call: Emerging technologies on CGT

October - December

June 29

June

2021

The importance of the Call was highly acknowledged by leading industry in the field, with a letter sent to the President von der Leyen

EIC Pathfinder Challenge Evaluation

French Ministerial Conference on Health Industries: "Strategic ambitions and European Vision, the keys to build an industrial health policy"

EIC Transition Challenge Call: RNA-based therapies and diagnostics for complex or rare genetic diseases

2022

January

March 3

4 May
28 September

April 12, 2022 : Editorial in Molecular Therapy, Vol. 30 No 5

EIC Health & Biotech portfolio:

Current State

EIC 2021 Pathfinder Challenge (status: proactive management)

Engineered living materials

(Barbara Gerratana and Iordanis Arzimanoglou)

Integration of expertise in:
Synthetic biology/Morphogenesis, Materials engineering/AI

EIC Health & Biotech portfolio

Topics initially considered to become EIC Challenges

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EIC Pathfinder

- Disease Modeling in Space

EIC Accelerator

- New biomarker-guided treatment in the era of precision oncology
- Monoclonal antibodies-based therapeutics for new variants of emerging viruses

EIC Health & Biotech portfolio

Challenge topic retained and included in the draft 2023 EIC WP

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EIC Accelerator

New biomarker-guided treatment in the era of precision oncology

2023 EIC Accelerator Challenge

New biomarker-guided treatment in the era of precision oncology

- Scope
- Key Objectives
- Rationale
- Underpinning Evidence
  - Selected examples of predictive, prognostic and companion diagnostics (CDx) biomarkers at the preclinical validation and/or initial clinical testing level potentially applicable to cancer treatment
  - Selected examples of new concepts/ideas that can influence cancer treatment
- No overlap with Health Cluster Group and the Innovative Health Initiative (IHI) Calls
- Complementarity/Synergy with the Cancer Mission

Iordanis Arzimanoglou, PhD ©

2023 EIC Accelerator Challenge

Scope – Expected Impact

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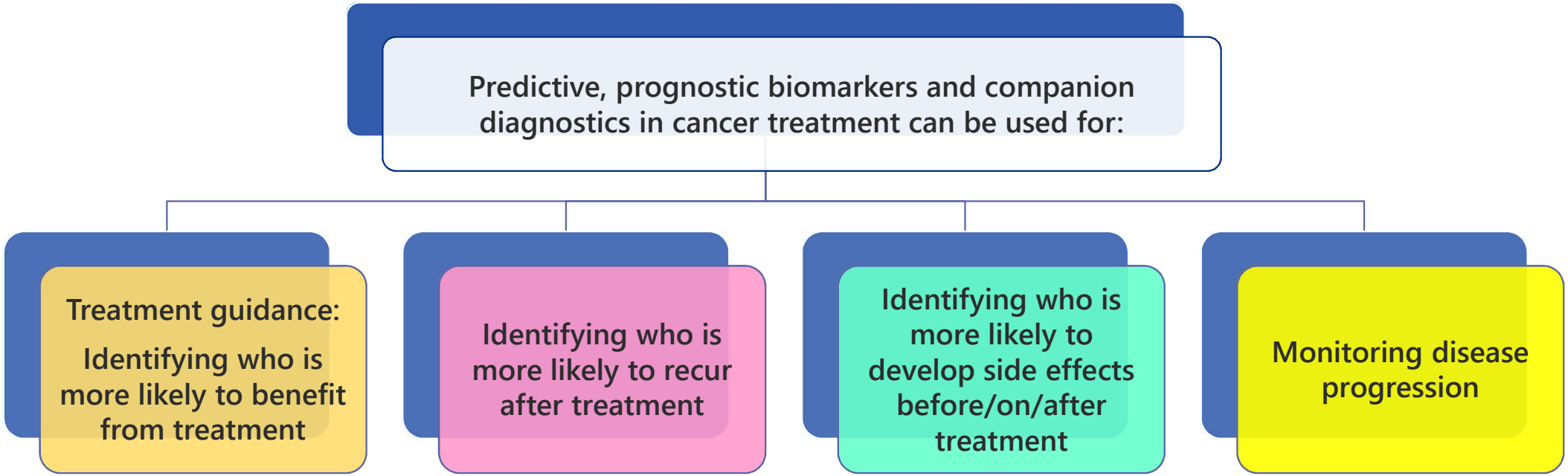
Scope: The development of new more accurate predictive, prognostic biomarkers and companion diagnostics that will contribute to improve the effectiveness of cancer treatment

Expected impact: Clinical establishments, industry and investors will all benefit in one way or another, from biomaker-based tests to guide and monitor oncology treatment in patients with refractory cancers

2023 EIC Accelerator Challenge
Key Objectives:



2023 EIC Accelerator Challenge

Relevance of the objectives to EU policies and initiatives

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The objectives of the proposed Challenge are relevant to specific strategic goals of

- the Europe's Beating cancer plan,
- EU Cancer Mission implementation plan and
- Innovative Health Initiative-2

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*cancers with a 5-year overall survival of less than 50% from time of diagnosis

2023 EIC Accelerator Challenge
Rationale

European Innovation Council

Through the preclinical validation and clinical work funded by this Challenge, we will gain critical insights how to design novel and effective ways to predict, monitor and guide targeted cancer treatment to patients afflicted by refractory cancers*. This approach is fully in line with the concept of precision oncology.

Despite ample participation of health-tech startups in Health Cluster calls, the outcome of this Challenge is essential for Europe to establish a globally competitive biotech portfolio composed of startups and scaling up SMEs targeted to the development of new predictive and prognostic biomarker-based tests that have the potential to effectively guide cancer treatment. In addition, the portfolio could set the basis for a future critical European mass, potentially leading to gain technological sovereignty in this field.

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*cancers with a 5-year overall survival of less than 50% from time of diagnosis

Underpinning Evidence 1st example:

Tiny amounts of ctDNA can inform about the need for additional treatment in bladder Ca

https://www.nature.com/articles/s41586-021-03642-9

- Detection of tiny amounts of circulating tumor DNA (ctDNA) to identify the risk of cancer recurrence and guide precision treatment in bladder cancer following surgery
- Patients with urothelial cancer who had ctDNA fragments that escaped into their bloodstream following surgery to remove their tumor, had a higher likelihood of cancer relapse. **These patients could benefit from subsequent treatment with an immunotherapy** called atezolizumab.

Underpinning Evidence 2nd example:

Detection of ultra low risk for recurrence would allow breast Ca patients to skip chemotherapy

https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045%2821%2900007-3/fulltext

- Through the EU-funded MINDACT trial, Agendia has delivered new data showing its MammaPrint genomic diagnostic can help identify patients at an ultralow risk of recurrence
- 99% of breast cancer patients in this category survived at least 8 years, regardless of other clinical risks-while 97% saw no distant tumor metastases over the same amount of time
- "The Ultra Low threshold identifies patients who may be candidates for further de-escalation of treatment. The MINDACT study enrolled nearly 7,000 patients with newly diagnosed breast cancer. After a median follow-up of nearly 9 years, 46% of patients shown to be at a clinically high risk for recurrence-but who had a low-risk result from the MammaPrint test-**were able to skip chemotherapy entirely without hurting their outcome**.

Underpinning Evidence 3rd example:
Predictive biomarkers in Barrett's esophagus

https://www.nature.com/articles/s41467-022-29767-7

- WGS to contrast genomic alterations from 40 patients with stable Barrett's esophagus compared to 40 Barrett's patients who progressed to esophageal adenocarcinoma (ESAD)
- It was found that the same somatic mutational pattern (focal chromosomal alterations and similar mutational signatures) were active in Barrett's tissue regardless of outcome
- The critical distinction between stable Barrett's versus those who progress to cancer was the acquisition and expansion of cell populations with TP53−/−, complex structural variants and high-level amplifications, which are **detectable up to six years prior to a cancer diagnosis**

Underpinning Evidence of new concepts/approaches that can influence cancer treatment

European Innovation Council

Genetic alterations in a single pathology slide can guide cancer treatment

https://www.nature.com/articles/s43018-020-0085-8

- Information gained from accurately screening of cancer patient biopsies for certain genetic alterations may inform about their treatment options and likelihood to respond to specific therapies
- Ability to detect these genetic alterations almost instantly from a single slide (with the help of AI too), instead of requiring additional testing post-biopsy, has the potential to significantly improve the effectiveness of treatment across cancer types, provided that this model is validated and deployed at scale

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Underpinning Evidence of new concepts/approaches that can influence cancer treatment

Fighting Cancer with Sound-Controlled Bacteria

Nature Communications, 13 doi:10.1038/s41467-022-29065-2

New idea/approach to potentially tackle the long lasting problem of chemotherapy (side effects):

- Genetically engineered, sound-controlled bacteria that seek and destroy cancer cells.
- Two sets of genes (temperature-dependent and therapeutic nanobody) were inserted in a bacterial strain that only produced the tumor-suppressing nanobodies when warmed to a trigger temperature of 43 C. Since normal human body temperature is 37 degrees C, these strains do not begin producing their anti-tumor nanobodies when injected into a person. Instead, they quietly grow inside the tumors until an outside source heats them to their trigger temperature.
- It was found that mice treated with this strain of bacteria and ultrasound showed much slower tumor growth than mice treated only with ultrasound, mice treated only with the bacteria, and mice that were not treated at all. However, some tumors did not shrink

2023 EIC Accelerator Challenge
No content overlap with relevant Health Cluster Calls

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- HORIZON-HLTH-2021-DISEASE-04-01: Improved supportive, palliative, survivorship and end-of-life care of cancer patients *closed 21.09.21*
- HORIZON-HLTH-2021-CARE-05-02: Data-driven decision-support tools for better health care delivery and policy-making with a focus on cancer *closed 21.09.21*
- HORIZON-INFRA-2021-EOSC-01-06: FAIR and open data sharing in support of cancer research *closed 23.09.21*
- HORIZON-INFRA-2021-SERV-01-01: Research infrastructures services to support research addressing cancer *closed 20.10.21*
- HORIZON-MISS-2021-CANCER-02-01: Develop new methods and technologies for cancer screening and early detection *closed 26.04.22*
- HORIZON-MISS-2021-CANCER-02-02: Develop and validate a set of quality of life and patient preference measures for cancer patients and survivors *closed 26.04.22*
- HORIZON-MISS-2021-CANCER-02-03: Better understanding of the impact of risk factors and health determinants on the development and progression of cancer *closed 26.04.22*
- DIGITAL-2022-CLOUD-AI-02-CANCER-IMAGE: Federated European infrastructure for cancer images data *closed 17.05.22*
- HORIZON-MISS-2022-CANCER-01-01: Improving and upscaling primary prevention of cancer through implementation research
- HORIZON-MISS-2022-CANCER-01-03: Pragmatic clinical trials to optimise treatments for patients with refractory cancers

2023 EIC Accelerator Challenge
No content overlap with relevant IHI Calls

European Innovation Council

- Innovative Health Initiative Calls
  - Next generation imaging and image-guided diagnosis and therapy for cancer
  - Personalised oncology: Innovative people-centred, multi-modal therapies against cancer

- Content wise, the focus of the IHI Calls is on image-guided and multi mode therapeutic approaches, whereas the EIC Challenge aims to support individual SMEs focused on preclinical and first clinical evidence of new biomarker and novel concept-based guided cancer treatment

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2023 EIC Accelerator Challenge
Complementarity with the Cancer Mission

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- The Cancer Mission has four specific objectives aimed at benefitting cancer patients: (1) understanding, (2) prevention, including screening and early detection, (3) optimize diagnosis and treatment, and (4) quality of life
- This EIC Challenge is complementary and contributes to the EU Cancer Mission, and specifically to the objective 3 of the Cancer Mission implementation plan: "*Optimize diagnostics and treatment*", and in particular to the specific aim: "*To ensure that more patients have access to the latest treatments adapted to their conditions, and with minimal secondary effects*".

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European Innovation Council

EIC H&B portfolio:

Vision for the Future State

2024 Candidate EIC Pathfinder Challenge

Disease Modeling in Space

PMs (Iordanis Arzimanoglou and Stela Tkatchova)

2024 Candidate EIC Pathfinder Challenge:
Disease Modeling in Space: New therapies

European Innovation Council

Stem cell-based investigations focused on: **Stroke therapies**, conducted by researchers at the Mayo Clinic and **Heart disease therapies**, were sent to ISS National Lab on SpaceX CRS-10

Flight experiments that will help develop 3D models to observe muscle and bone cell organization into tissues in order to study **musculoskeletal disorders e.g. sarkopenia** and evaluate potential therapies

If space-based R&D allows researchers to make breakthroughs in **oncology** compounds, for instance, the insights could save millions of lives (McKinsey Technology Trends Outlook)

2024 Candidate EIC Pathfinder Challenge:

Disease Modeling in Space:

Cell changes due to microgravity

Picture: https://www.issnationallab.org/

In space, several profound changes take place in cells, including changes in:

- cell signaling
- Cell aggregation
- The physics of fluid movement due to microgravity
- Leveraging microgravity (e.g., protein crystallization) to improve pharmaceuticals

These cellular changes **provide opportunities for discoveries that cannot be made on Earth.** In this context, ESA may provide space condition platforms to develop experimental models to better study diseases such as those affecting the heart, immune system, bones and muscles

2024 Candidate EIC Pathfinder Challenge:

Disease Modeling in Space: Gene Expression in Space

European Innovation Council

"**Genes in Space Program**" is a US-based program founded by Boeing and miniPCR bio™ companies and supported by the International Space Station/U.S. National Laboratory. The winning proposals are developed into flight projects that are sent to the space station. In this program, crew members can make copies of specific segments of DNA onboard the ISS using a miniaturized polymerase chain assay (PCR) developed by miniPCR bio™

2024 Candidate EIC Pathfinder Challenge

Disease Modeling in Space: Bioprinted tissues in Space

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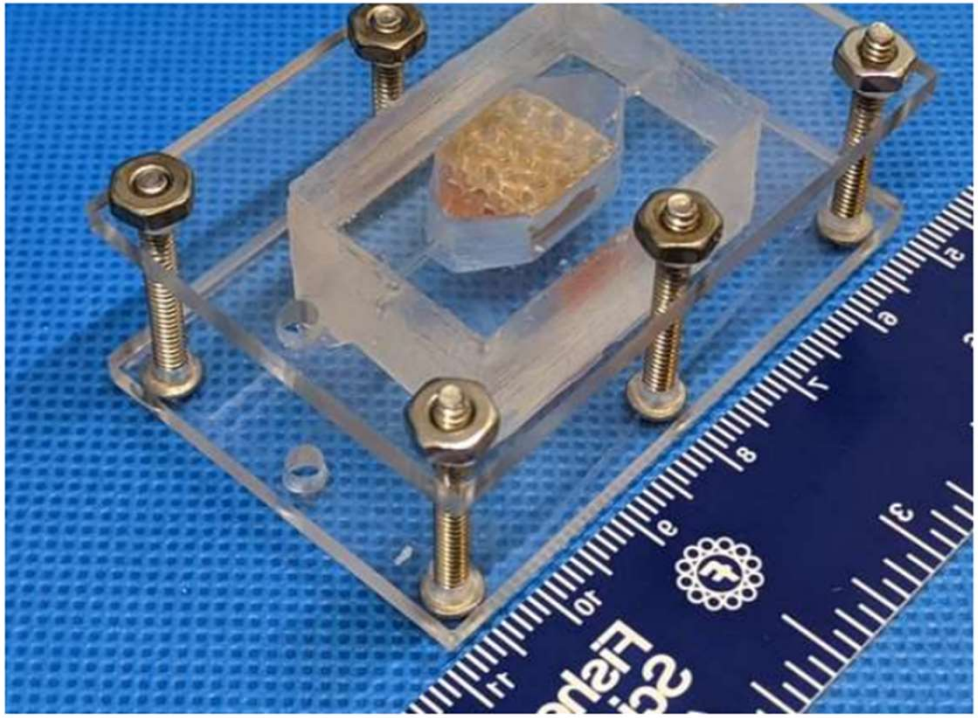
MIT Technology Review

Space

NASA inches closer to printing artificial organs in space

Researchers used 3D-printing to create human liver tissue that could soon be tested on the International Space Station.

by **Tatyana Woodall** June 18, 2021



Liver tissue created by team Winston for NASA's Vascular Tissue Challenge.

WAKE FOREST INSTITUTE FOR REGENERATIVE MEDICINE

Technological solutions that can tackle the hurdles in the formation of functional thick human tissue in a space station environment and conditions such as, the ability to generate a vascular network in bioprinted tissues

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EIC H&B portfolio:

Vision for the Future State

2024 Candidate EIC Accelerator Challenge

Monoclonal antibodies-based therapeutics for new variants of emerging viruses

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Why monoclonal antibodies (mAbs)?
mAbs are potent antivirals

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- According to CEPI but also current evidence suggests that mAbs, are promising antiviral approaches complementary to vaccination for many outbreaks in the coming years.
- Proofs of potential targets have been shown through the SARS-CoV2 pandemic
- Intense research activity on mAbs across infectious diseases: WHO is working on mAbs in areas such as influenza, respiratory syncytial virus, HIV etc

Why monoclonal antibodies?
Advantages of monoclonal antibodies over vaccines

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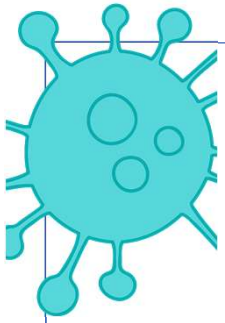
Immediate protection	• ➔ induced in immunosuppressed individuals who are often at the highest risk of infection
Generic manufacturing process	• ➔ switch on production of a mAb with minimal lead time, enabling rapid availability of a product in an outbreak; and
New technologies could simplify the production or administration of monoclonal antibodies	• ➔ extending the half-life of the antibody or injecting mRNA coding for a monoclonal antibody

Variants of the virus and mAbs
US FDA statement about mAbs (Jan 2022)

European Innovation Council



Viruses evolve and new variants may emerge. Therefore, there is a need to rapidly detect new variants of the virus for which existing vaccines may not be sufficiently effective

HERA

HERA aims at the rapid detection and analysis of virus variants, in coordination with relevant international systems and networks. This will ensure that the development of new vaccines and treatments (e.g. mAbs) targets the variants of high concern. Some of the new variants of high concern might exhibit decreased susceptibility to the mAbs

FDA

FDA revised the authorizations for two mAbs treatments, combined administration of bamlanivimab and etesevimab and REGEN-COV (casirivimab and imdevimab)-to limit their use to only when the patient is likely to have been infected with or exposed to a variant that is susceptible to these treatments. In other words, these mAbs had no effect against the Omicron Variant

2024 Candidate EIC Accelerator Challenge

mAbs-based therapeutics for new variants of emerging pathogens

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In the era of pandemic preparedness and precision medicine, EIC Challenge proposal aims to innovative solutions in the development and production of effective mAbs-based therapeutics against new variants of emerging pathogens, as a line of defence complementary to new vaccines. The Challenge can address:

- More effective mAbs (inter-individual variability)
- Preparation of mechanisms in advance to accelerate the development of mAbs-based therapy after break out of viral diseases
- Technological Innovations to tackle issues related to the production of mAbs
- Administration of mAbs to outpatients with mild disease in overwhelmed hospitals
- Hypersensitivity to treatment

EIC H&B portfolio:

Vision for the Future State

European Innovation Council

2024 or after Candidate EIC Accelerator Challenge

Gene therapy clinical trials: In vivo efficacy and safety

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2024 or after Candidate EIC Accelerator Challenge

Gene therapy clinical trials: In vivo efficacy and safety

Cell and gene therapy (CGT), holds a potential for transformative effect meaning to stop or slow the effects or even cure diseases by targeting them at the genetic level. When the genetic driver for a disease is known, patients can be molecularly matched to therapies (World Medical Innovation Forum May 2021). However, at least two main challenges remain:

- **Safety:** (https://www.genengnews.com/news/adverum-confirms-patient-loses-sight-in-eye-treated-with-its-gene-therapy)

- **In vivo efficacy**: (*Setback for Biogen's ophthalmic gene therapy aspirations as XLRP program misses in Phase II/III trial*)

2024 or after Candidate EIC Accelerator Challenge:

Gene therapy clinical trials: Strategies to mitigate the technological and supply chain risks

Multiple companies are performing more clinical trials so there is a capacity shortage currently. Unprecedented global increase in demand

From local administration to systemic delivery, which requires higher doses

Patient populations are getting larger as gene therapy applications are no longer only targeting rare diseases

EIC H&B portfolio:

Vision for the Future State

European Innovation Council

2024 or after Candidate EIC Transition Challenge

Industrial Biotechnology: Scaling up synthetic biology-based applications,

in collaboration with the Programme Managers for Environment, Energy and Food

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2024 or after Candidate EIC Transition Challenge

Scaling up synthetic biology applications: Medical and Industrial Biotechnology

The Challenge can cover a range of synthetic biology applications from Medical (cancer therapeutics, Gut Microbiology) to Environmental Surveillance bio-based applications

Technological innovation that would enable to **scale-up manufacturing of synthetic biology applications,** will provide Europe with critical know how and domestic capabilities to manufacture critical bio-based resources