



Synthetic Biology in Catalonia

*Creating the next wave of biotechnology
innovation, and growth of the bioeconomy*

Technological snapshot

Synthetic Biology: Informe Tecnològic

ACCIÓ

Generalitat de Catalunya



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Execution

ACCIÓ Strategic and Competitive Intelligence Unit
UAB, Universitat Autònoma de Barcelona


Collaboration

ACCIÓ Innovation Unit

Barcelona, July 2020


Technology trends target

This study is part of a collection of reports on the different disruptive technologies detected in the ACCIÓ Technology Trends Target (2018), which are expected to have a great impact on Catalan society and its productive fabric in the years to come.




- Virtual reality and augmented reality
- Artificial intelligence
- Internet of Things
- DLT and blockchain

DIGITAL




- 3D printing
- Nanotechnology and new materials
- Robotics
- Quantum science and photonics

PHYSICAL




- Neuroscience
- Advanced drug design
- Omics
- Biotechnology and synthetic biology

BIOLOGICAL



- Big data
- Connectivity – 5G
- Cybersecurity

TRANSVERSAL

- Drones
- Connected vehicle
- New space

TECHNOLOGY HYBRIDISATION

The reports published as of 1 July 2020 appear in blue. Those pending publication appear in red.

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Synthetic biology



1. **Technology definition**
2. **Global market of Synthetic Biology**
3. **Applications of Synthetic Biology**
4. **Synthetic Biology in Catalonia**

Definition of Synthetic Biology

Synthetic biology is defined as the design and construction of biologically based parts, devices and entirely novel biological systems, or the reengineering of existing biological systems.

How?

- Using **existing biological building blocks** to create combinations not present in nature
- Creating **non-natural building blocks** to replicate natural functions, such as xeno-nucleic acids that encode and pass on genetic information.

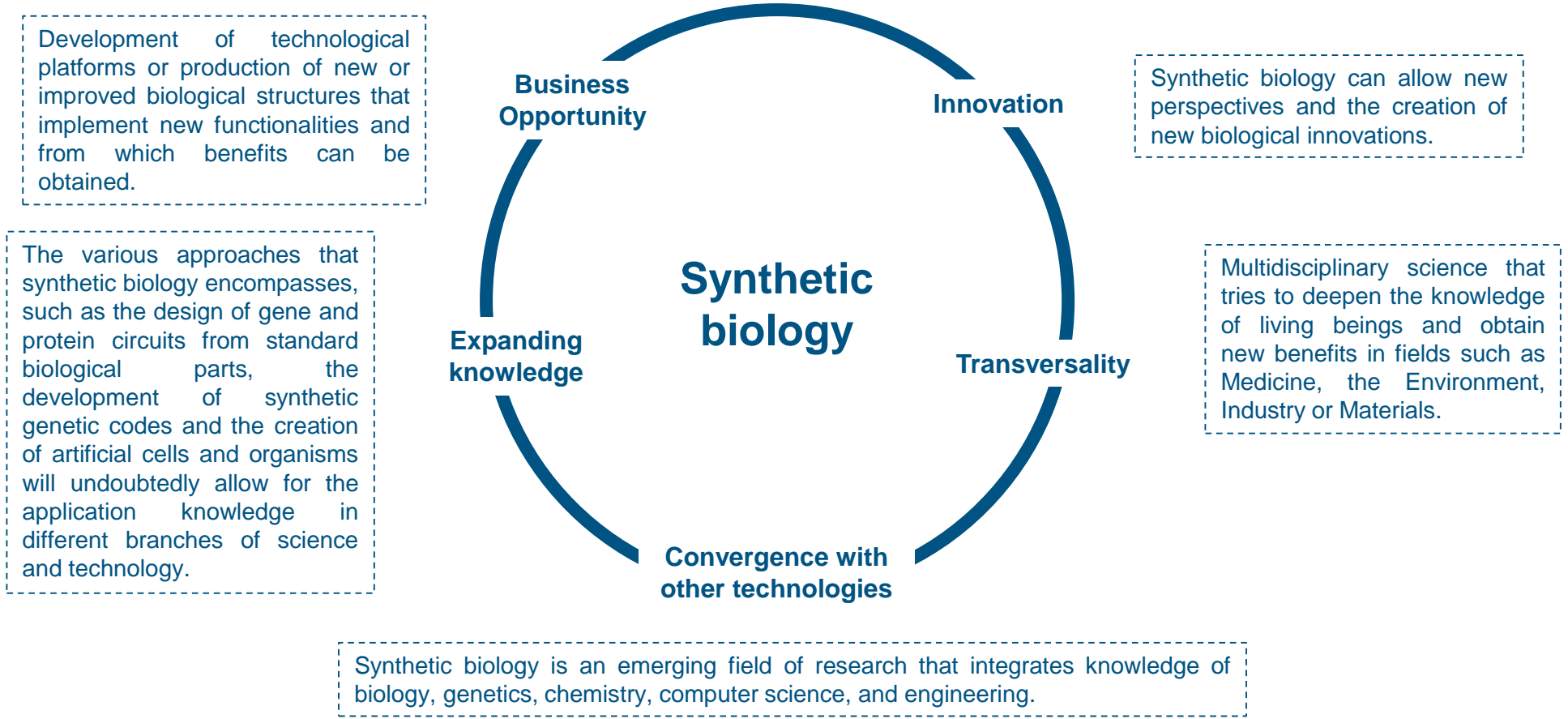
Goals?

SynBio is currently donating solutions to medical problems, food production and energy, remediation, scaling, and national security.

From the production of **drugs** and their targeted delivery and dosage, to **biofuel**, tissue engineering and genomically recoded **organisms**.

“The central idea of synthetic biology is that living cells can be programmed in the same way that computers can, in order to make them do things and produce compounds that their natural counterparts do not.”

Importance for Industry



Synthetic biotechnology breakthroughs

- In 2003, a fully synthetic PhiX174 chromosome was built in vitro in just 14 days at **J. Craig Venter Institute (JCVI)** led by Drs. Smith, Hutchinson and Venter.
- In 2004, a new “multiplex” DNA synthesis technique was invented George M. Church of **Harvard Medical School** and Xiaolian Gio of the **University of Houston** that will eventually reduce the cost of DNA synthesis to 20,000 base-pairs per dollar.
- In 2006, Dr. Jay Keasling, director of the **Berkeley Center for Synthetic Biology** discovers and re-engineers of a yeast containing bacterial and wormwood genes into a chemical factory to produce a precursor to artemisinin for use as an inexpensive anti-malarial drug.
- In 2007, the **JCVI** developed genome transplantation methods to transform one type of bacteria into another type dictated by the transplanted chromosome.
- In 2008, the **JCVI** created the first synthetic bacterial genome, *Mycoplasma genitalium* JCVI-1.0, representing the largest man-made DNA structure.
- In 2010, scientists at **JCVI** announced the world’s first synthetic life form; the single-celled organism based on an existing bacterium that causes mastitis in goats, but at its core is an entirely synthetic genome that was constructed from three chemicals in the laboratory. The single-cell organism has four “watermarks,” written into its DNA to identify it as synthetic.

Source: Biotechnology Innovation Organisation- archive.bio.org/articles/synthetic-biology-explained

Artemisinin, the first triumph of the field of synthetic biology

The anti-malarial drug that was the first triumph of the field of synthetic biology and an example of involvement of the whole industry chain



In 2006, **Dr. Jay Keasling** discovers and re-engineers of a yeast containing bacterial and wormwood genes into a chemical factory to produce a precursor to artemisinin



The spin-out company cofounded by Keasling bring the lab-bench discovery to the marketplace by developing and scaling-up the yeast strain



The pharmaceutical firm lead the production of chemical precursor of artemisinin.
In 2014, Sanofi launched the anti-malarial drug



The organization played a key role on looking after the drug that will save hundreds of millions of people in developing countries most of them children

Source: Info Own Design and data based on Synbiobeta- The Synthetic Biology Innovation Network; Biotechnology Innovation Organisation- archive.bio.org/articles/synthetic-biology-explained; and press release

Bioethics

Synthetic biology holds out the prospect of significant benefits to humanity however there are 3 main concerns according to bioethicists:

- Concerns about "*playing God*"
- Concerns about undermining the distinction between living things and machines
- Concerns about deliberate misuse of knowledge

WHO foresight unit aims to anticipate advances in life science specifically in synthetic biology. WHO holds The Global Summit of National Bioethics Committees independent guidance. WHO foresees to draw an expertise of ethicists and bioethicists to help drive impact on future biotechnical capabilities globally.

WHO established an expert advisory committee to develop recommendations on governance in human genome editing.

US Presidential Commission issued recommendations on ***The Ethics of Synthetic Biology and Emerging Technologies*** report. The commission urges monitoring and attend careful potential risks of Synthetic Biology advances.

Synthetic biology



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Global market of Synthetic Biology

- A number of international bodies - including the UK and US Governments, the EC and the OECD - are predicting that synthetic biology **will have a significant impact on the economy, growth and jobs over the coming years.**
- The global synthetic biology market is estimated to reach **\$100 bn by 2030.**
- The industry has raised **more than \$12.3B in the last 10 years.**
- Being **2018 the most staggering** so far with synthetic biology companies have been raising **\$3.8 billion** compared to just under \$400 million total invested less than a decade ago.

Source: Synbiobeta- The Synthetic Biology Innovation Network

Main regions (I)

Worldwide innovation hotspots in synthetic biology



Source: Own Design based on SynBioBeta Data-The Synthetic Biology Innovation Network

Main regions (II)

- The main regions where synthetic biology investments took place historically are based on **San Francisco/Silicon Valley and Cambridge/Boston regions.**
- In 2019, **San Francisco Bay Area led synthetic biology investment** at \$542M, followed by the Boston region at \$230M. The rest of the US totalled \$297M, and the rest of the world totalled \$147M.
- **North America is considered to be one of the dominating market.** In addition, Increasing R&D investments are also boosting the growth of the market.
- As shown in the map Canada is also a hotspot for synthetic biology in **Vancouver and Montreal.**
- **APAC (Asia Pacific Countries) region is growing at a highest rate** due to increasing research organizations.
- China and Asia-Pacific it is predicted to grow fast in synthetic biology market in the coming years.
- China and Singapore are increasing their research funding and it is projected to be \$38 billion by 2020
- In Europe, **UK and Ireland stand out as a hotspot for Synthetic Biology** start-ups and research centers and universities; **France, The Netherlands, Denmark, Switzerland and Germany** also stand up for research centers and synthetic biology companies to develop new generation products.

Source: Synbiobeta- The Synthetic Biology Innovation Network: Synthetic Biology Investment Report 2019 Q2

Top tier companies

INDUSTRY APPLICATIONS	COMPANIES
BIOMEDICINE	Moderna Therapeutics, Synlogic, Caribou, Twist Bioscience, Evonetix, Ziopharma, Codex, Codexis, Codagenix, Editas Therapeutics, CRISPR Therapeutics, Vedanta Biosciences, Poseida Therapeutics, Beam Therapeutics, Precision Biosciences, DNA Script, Inscripta, Autolous, Triton, Eligo Bioscience, Synthorx**, AzarGen, Antheia, Epiobiome, BiomX, Tweewinot, Evolva, Intrexon, Horizon Discovery, Sanofi
AGRITECH & FOOD	Agrimetis, Agrivida, PivotBio, Plant Sensory Systems, Calysta, GEA Enzymes, Metabolix, Impossible Foods, Beyond Meat, Solar Foods, Motif FoodWirks, AquaBounty, Air Protein
NEW MATERIALS & FABRICS	Zymergen, Checkerspot, Pili, Genomatica, Bolt Threads, AMSilk, Spiber, Ecovative Design, Colorifix, Mango Materials
RENEWABLE ENERGY	Solazyme, Ginkgo Bioworks, Gevo, Amyris, DSM, LanzaTech, Joule, Industrial Microbes, BioAmber, Cargill, DuPont, Ecovia Renewables, EnEvolv*, Modular Genetics
ENVIRONMENT	Sapphire, Matrix Genetics, Green Biologics, Verdezyne, Biosintia, Myriant, Lygos, GreenLight Biosciences, Arzeda, CinderBio, ZymoChem, NatureWorks, Synthetic Genomics

* acquired by Zymergen; ** acquired by Sanofi

Source: Own design and data based on Synbiobeta- The Synthetic Biology Innovation Network, Synbicate and press release

Investment



- In **2018**, 98 synthetic biology companies collectively raised \$3.8 billion
 - **Moderna Therapeutics** and **Zymergen's** combined raised \$1 billion
- In the first half of **2019**, 65 synthetic biology companies raised \$1.9 billion in funding
 - **Impossible Foods** raised a funding round of \$300 million in 2019.



Required reading for the biological revolution.
Published by SynBioBeta, July 17, 2019

Top investments

The top higher investment rounds in Q1 and Q2 of 2019 are the following (in million dollars)

Impossible Foods	\$300M	meat, dairy and fish directly from plants
Poseida therapeutics	\$142M	Next-generation CAR-T cell therapies for cancer
Beam Therapeutics	\$135M	Base editors enable them to precisely and permanently rewrite a single letter of the genome
Precision Biosciences	\$126.4M	Delivering therapeutic-grade genome editing
Autolous	\$109M	T-cell programming and manufacturing technology for the treatment of cancers
Motif Ingredients* (rebranded: Motif FoodWorks)	\$90M	Engineering of nutritional proteins
Twist Bioscience	\$84M	Innovative silicon-based DNA synthesis platform enables the production of high-quality synthetic DNA
Synlogic	\$80M	Designing living therapeutics programmed to treat disease in new ways
Verve therapeutics	\$58.5M	Developing gene editing therapies to reduce risk of coronary artery disease in adults
Codexis	\$50M	Protein engineering company
Green Light Bioscience	\$50M	Creating RNA-based products can be used to more naturally and safely solve healthcare and agricultural issues
Sherlock biosciences	\$49M	Developing CRISPR-based diagnostics
Vestaron	\$40M	Proprietary, fermentation-based, peptide production platform that is leading to the development of a broad range of biological crop protection and trait products.
DNA script	\$38.5	Disruptive DNA synthesis company engineering biology to accelerate breakthroughs in life science

* Ginkgo Bioworks spin-off

Source: Own Design and data based on Synbiobeta- The Synthetic Biology Innovation Network. SynBioBeta - Synthetic Biology Investment Report 2019 Q1 SynBioBeta - Synthetic Biology Investment Report 2019 Q2

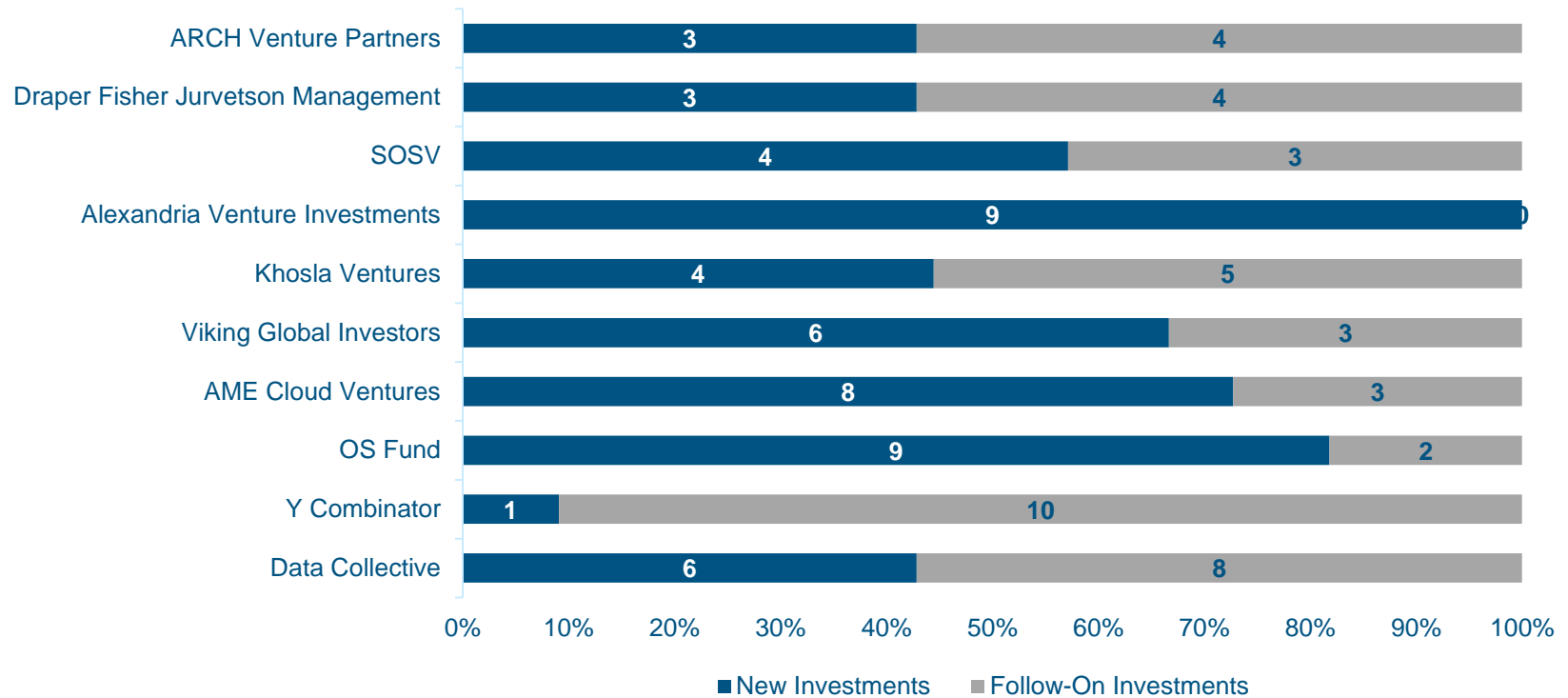
Who's investing?

- **Private Equity and Venture Capital** funding accounted for 40% of all the money raised
- **Over 500 investors** funding *synbio* startups
- The number of new investors in the space exploded in 2019
- New investors coming to synthetic biology
 - **Tech Venture Capital firms** are joining the sector because of the potential in combining computation and biology
 - **Impact investors** that see the environmental and human impact when companies get their product to the market
 - Charitable groups
 - Family Offices
 - **Tech Titans funders** are investing through their own investment firms
 - **Corporations**

Source: Synbiobeta- The Synthetic Biology Innovation Network; Forbes: Meet eight Tech Titans investing in Synthetic Biology, 2019

Some keyplayers

Top investors -by number of deals- in synbio firms



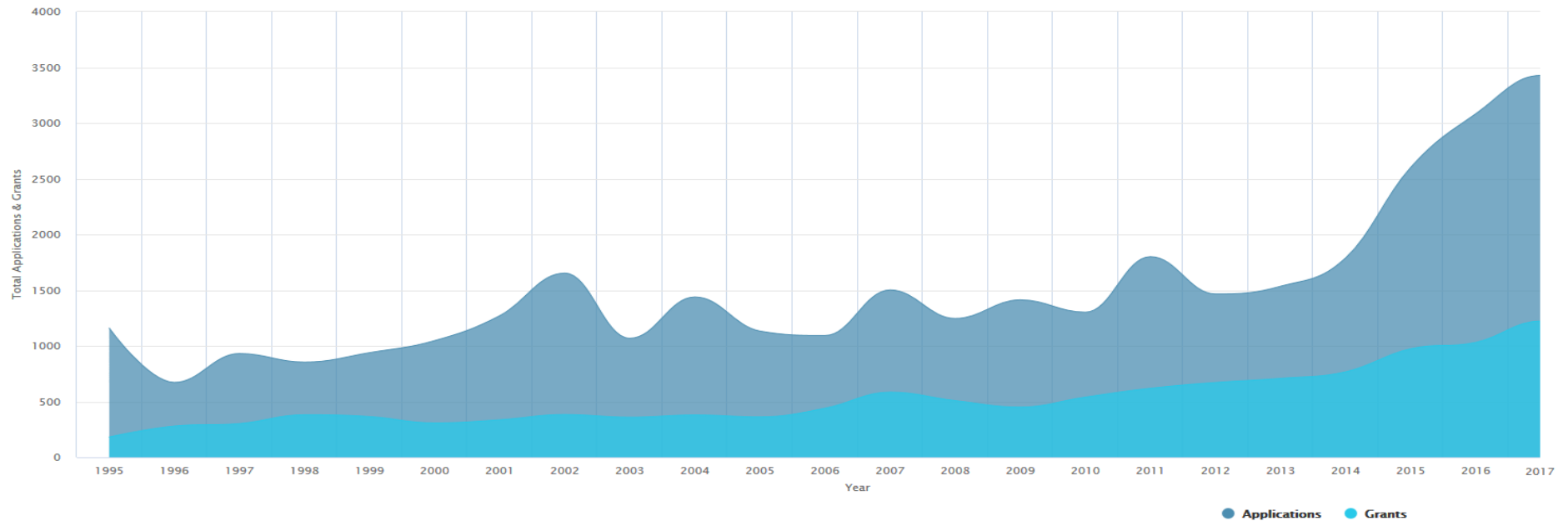
Others: Sofinnova Partners, SR One, Roche Venture Fund, Pfizer Venture Investments, Syncona Partners Capricorn Venture Partners, Lundbeckfonden Ventures, Mercia, Arix Bioscience, Woodford Equity Income Fund, Draper Esprit, UKI2S Innovate Accelerator, Start Codon accelerator

Source: Synbiobeta- The Synthetic Biology Innovation Network. SynBioBeta - Synthetic Biology Investment Report 2018; Synbicitic.

Technological patent surveillance (I)

Technology surveillance report in synthetic biology patents published*

The following graph shows patent applications and granted patents during the last 20-25 years in synthetic biology. The graph reports a clear tendency in an increasing number of patent applications and granted patents within this field. Moreover the graph shows that almost 50% of patent applications are granted.



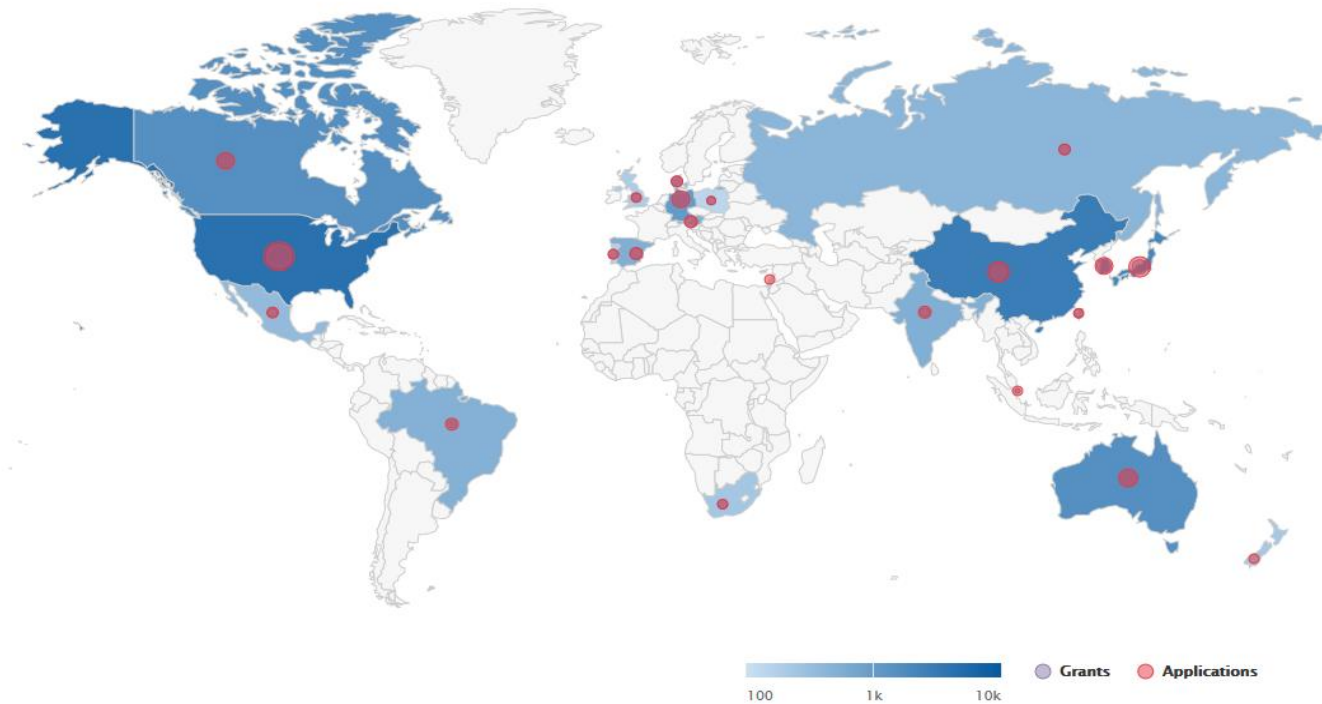
* Data on 2018 and 2019 is not shown in the graph because of the lack of consistency, due to the publication confidential period of patent applications of 18 months

Source: Own analysis using patbase database- analysis on synthetic biology in January 2020

Technological patent surveillance (II)

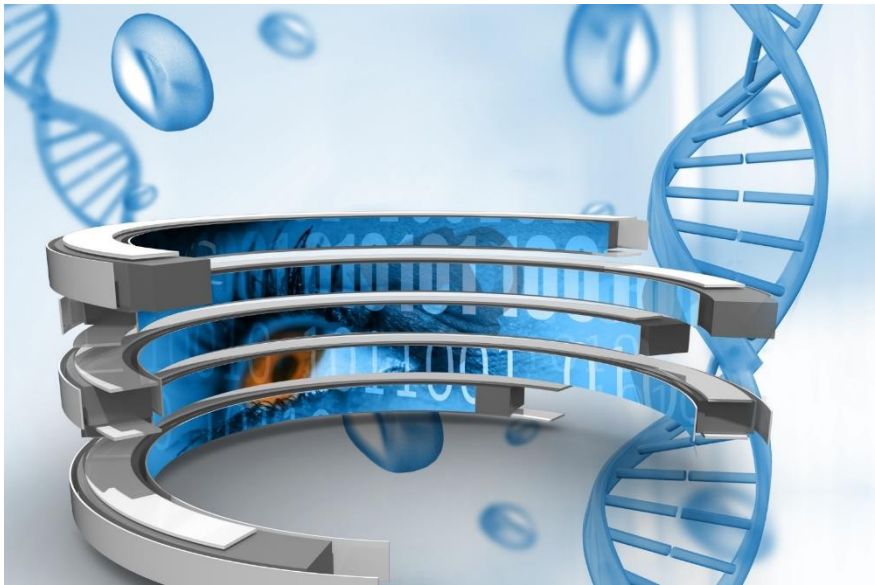
Technology surveillance report in synthetic biology patents

Geographically US is the most active in patent applications within the field of synthetic biology followed by China, European patent office and Japan.



Source: Own analysis using patbase database- analysis on synthetic biology in January 2020

Synthetic biology



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Applications

Synthetic biology has extraordinarily diverse applications and the potential to develop whole new markets.

Biomedicine

Medicine will be one of the areas that most will benefit from advances in Synthetic Biology, specifically the areas on which the new discipline will have a greater impact will be the smart drug development, medicine personalized, gene therapy, repair and tissue regeneration, cell reprogramming and in vivo drug synthesis. The development of new metabolic pathways is also interesting.

Renewable Energy

Synthetic Biology will be one of the keys to the design of new biochemical routes that allow the conversion of Biomass into Energy sources. There are three main fields of research in terms of bioenergy production through Synthetic Biology, the production of hydrogen or ethanol, the efficient conversion of waste into energy and converting solar energy into hydrogen.

New Materials & Fabrics

The areas related to new materials that will benefit the most from the development of Synthetic Biology will be biomedical materials, sensors, materials for energy conversion, microelectronics and ICT and composites.

Agritech & Food

Investments and research in synthetic biology are mainly focus on products and processes that aim to improve agriculture, for example more crops resistant to diseases, droughts or adapted climatic changes

Environment

In this field, work is being carried out on bacteria that can degrade plastics, in bioremediation of soils, biosensors or in the recovery of minerals.

Main recent applications (I)



Therapies for COVID-19

A company enabling customers to succeed through its offering of high-quality synthetic DNA using its silicon platform has announced a collaboration with **Vanderbilt University Medical Center** to supply **synthetic genes and antibodies for the development of therapies for COVID-19**



Novel enzymes for manufacturing pharma&healthcare products

CodeEvolver[®] protein-engineering synbio platform is used to create unique enzymes for use in manufacturing drugs that work faster or more efficiently. Codexis's proteins are used across a broad variety of industries, but recently has done some great work in the development of **proteins as a therapeutic, having partnerships with GSK and Merck**



Desktop DNA platform

The synthetic biology company developing a **desktop DNA platform** for scalable, high-fidelity and rapid gene synthesis early in 2020 has raised series B funding. This platform will facilitate and enable the rapidly growing field of synthetic biology, with application across industries: healthcare, pharma, biotech, food and agriculture and data storage

Source: Own design and data based onSynbiobeta- The Synthetic Biology Innovation Network; and Press release

Main recent applications (II)



CAR-T therapy targeting B-cell maturation antigen tumors

Leading CRISPR genome editing company has signed a collaboration with ProMab Biotechnologies to utilize the scFv of ProMab in the development of Caribou CB-011 program, an allogeneic CAR-T therapy targeting BCMA-positive tumors including multiple myeloma



Nucleotides X and Y generate a more efficient cancer drug

In 2014, Dr Romesberg's in his lab at Scripps Research La Jolla synthesized a couple of extra base pairs in DNA alphabet, adding synthetic nucleotides X and Y to the standard lineup of A, C, G, and T. In collaboration with SynBio spin-off Synthorx, they entered into the drug discovery to make a less toxic and more effective version of an anticancer drug called interleukin-2. In 2019, Sanofi acquired Synthorx to reinforce its immuno-oncology pipeline for \$2,5B

Source: Own design and data based onSynbiobeta- The Synthetic Biology Innovation Network; and Press release

Main recent applications (III)

 **zymergen**


The Genome Engineering Company

Faster Biomanufacturing

Recently, **Zymergen** has acquired **enEvolv**, establishing a combined platform that promises to speed up R&D in biomanufacturing. Zymergen will use enEvolv's ultra-high-throughput technology to screen and select individual cells from among millions, finding those rare cells with just the right genes and properties needed in biomanufacturing applications. enEvolv says it can do in a single month what would take 30 of today's high-speed robots 2,000 years to do.

 **gevo**[®]

Renewable diesel

A leading renewable fuels and chemicals manufacturer has developed proprietary, breakthrough processes that converts either low-carbon isobutanol or low-value "fusel oils," into renewable diesel. This renewable diesel is expected to compete head-to-head on price with natural and petroleum-based equivalents, while reducing particulates and CO2 emissions.

Source: Own design and data based onSynbiobeta- The Synthetic Biology Innovation Network; and Press release

Main recent applications (IV)

Lactoferrin for infant formulas



Discovery and development of a sustainable proprietary lactoferrin protein that mirrors the nutritional properties of lactoferrin from breast milk. The first-of-its-kind natural lactoferrin protein is produced via fermentation process at commercial-scale. Conagen's lactoferrin closely matches those in breast milk, better than lactoferrin found in cow's milk

Meat made by plants



"What makes meat taste like meat?" Heme is what makes meat taste like meat. It's an essential molecule found in every living plant and animal, most abundantly in animals. Impossible Foods plant-based heme is made via fermentation of genetically engineered yeast

Source: Own design and data based onSynbiobeta- The Synthetic Biology Innovation Network; and Press release

Main recent applications (V)



New clothing made by microbes

Their microbes can produce fatty acids with unique chemical properties found nowhere else. Checkerspot's materials will likely be available soon in the form of new clothing

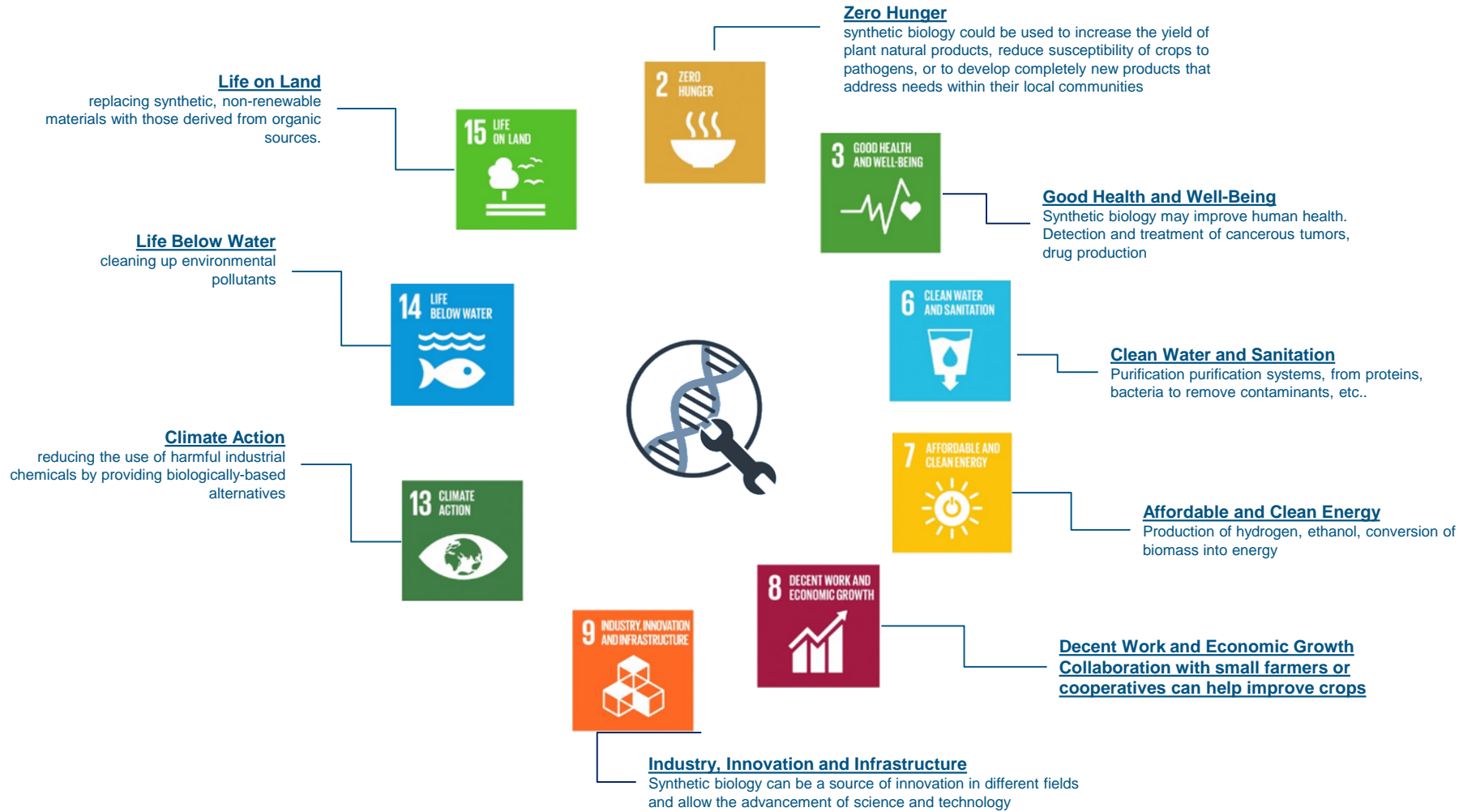


Bread for consuming off-earth

The Finnish company developed Solein, a wheat flour-like substance comprised of 50% protein that they have made out of CO₂, water, and electricity, and microbes. The idea born at NASA and developed by researchers at VTT and Lappeenranta University of Technology. Solein is produced via an entirely carbon-neutral process that doesn't require arable land and is ready for consuming worldwide and off-Earth

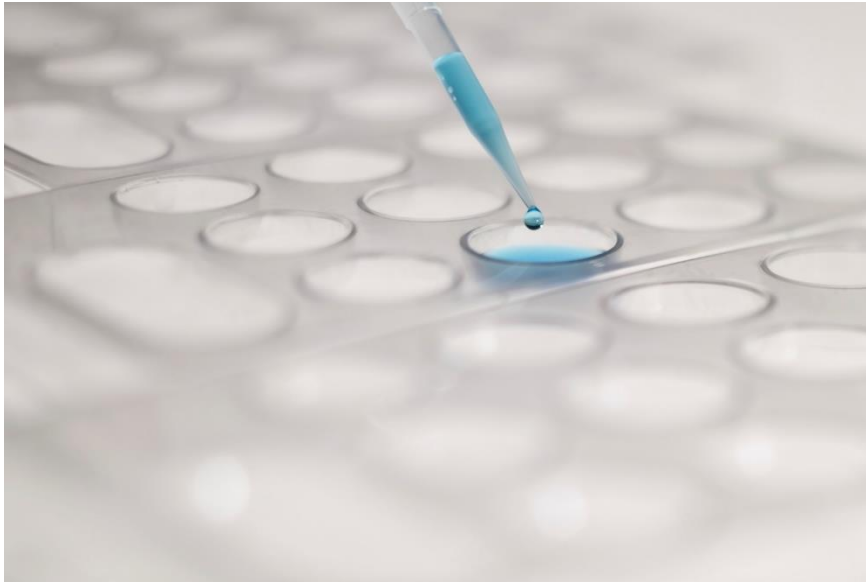
Source: Own design and data based on Synbiobeta- The Synthetic Biology Innovation Network; and Press release

Synthetic Biology and the SUSTAINABLE DEVELOPMENT GOALS



Source: EIC (DGI-ACCIÓ), based on data from McKinsey.

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Main mapping conclusions

Synthetic Biology in Catalonia

12 companies that work with Synthetic Biology in Catalonia have been detected.

Most pure players are start-ups.

11 companies have a line of business in this area



The main application sector is biomedicine.

There is potential for growth in this area, because the life sciences, food and agritech sector are very important in Catalonia.

Ecosystem in Catalonia

Partial illustrational table



Note: The use of these brands is merely for information purposes. The brands mentioned in this report belong to their respective owners and under no circumstances are they the property of ACCIÓ. This is a partial representation for the purpose of illustrating the main companies that belong to the photonics ecosystem in Catalonia, but other companies may exist that have not been included in the study.

Source: EIC (DGI – ACCIÓ)

Business cases in Catalonia (I)

The logo for Pulmobiotics, featuring the word "Pulmobiotics" in a blue, sans-serif font with a trademark symbol.

Pioneering live biotherapeutics
in the respiratory tract

Pulmobiotics is a spin off of the Center for Genomic Regulation of Barcelona (CRG) which specializes in the discovery of treatments and vaccines for lung diseases based on synthetic biology.

Investigate a treatment for pneumonia associated with the use of mechanical respirators (NAV).

The goal is to develop a product that reduces the use of antibiotics to treat NAV and may be available to enter the clinical phase from 2023..

The logo for BrickBio, featuring a stylized orange and blue geometric icon followed by the text "BrickBio" in a blue, sans-serif font.

BrickBio Inc., biotechnology company, empowers next-generation unnatural amino acid coupled protein conjugation with its site-specific and site-selective platform.

The platform technology spans prokaryotic and eukaryotic expression systems, enabling the development of unique biologics and protein therapeutics with enhanced characteristics, including improvements to half-life, dosage and efficacy. With the broadest toolkit of bioconjugation handles, BrickBio can optimize any conjugate and is uniquely situated to push the frontier of biologics with the selective modification of multiple distinct sites on a single protein. BrickBio is working with partners to develop best-in-class therapeutics and RUO kits with its proprietary bioconjugation strategies.

Source: EIC (DGI – ACCIÓ)

Business cases in Catalonia (II)



Peptomyc is a company focused on the development of a new generation of cell penetrating peptides (CPPs) targeting the Myc oncoprotein for cancer treatment. Myc is found deregulated in the majority of human cancers, where it holds a non-redundant function without which tumors cannot survive and grow, while normal cells can. Hence, targeting Myc is a terrific therapeutic opportunity. However, although Myc plays a central role in cancer, there is currently no Myc inhibitor in the market.

Omomyc is the lead compound of Peptomyc and is an inhibitor of Myc that has already shown positive results in preclinical studies in mice. Clinical trials testing Omomyc's safety and efficacy in cancer patients are forecasted to start in 2021.

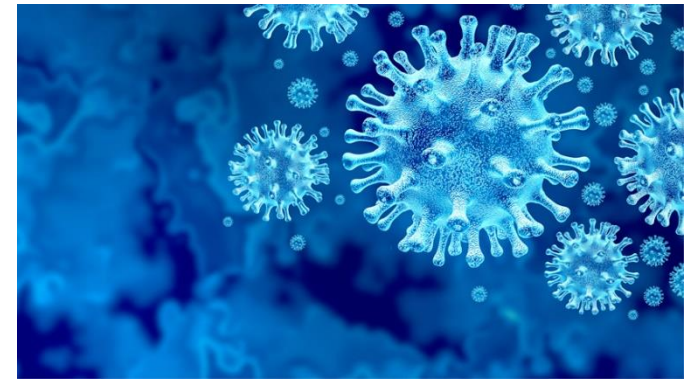
Source: EIC (DGI – ACCIÓ)

COVID-19 response

With today's coronavirus outbreak, synthetic biologists are applying cutting-edge tools and technology to help responders go from detection to cure with unprecedented speed and scale

Computational approach finds the unique molecular features on the surface of a range of different pathogens, then uses antibody the immune response against the parts of those pathogens that do not mutate over time.

Moderna also announced a new collaboration with CEPI to produce a vaccine against coronavirus. Moderna has a mature technology platform, fully integrated manufacturing site and development experience, and established relationship with the NIH, which situates it well to respond to public health threats.



Source: Synbiobeta, EUSynBioS



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Read the full report here:

<http://catalonia.com/.content/documents/synthetic-biology-in-catalonia.pdf>

More information on the industry, related news and opportunities:

<http://catalonia.com/industries-in-catalonia/sectors/health-well-being-and-life-sciences-industries/biotechnology.jsp>



For the full technological report, please send an e-mail to irodriguez@catalonia.com