



Genomics in Catalonia

November 2020

Technology snapshot

Genomics in Catalonia. Technology pill

ACCIÓ

Regional Government of Catalonia (Generalitat de Catalunya)



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Execution

ACCIÓ Strategic and Competitive Intelligence Unit

Collaboration

BIOCAT

Xarxa d'R+D+I en biotecnologia

ACCIÓ Innovation Unit

Catalonia Trade & Investment

Barcelona, November 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



- Drones
- Connected vehicle
- New space

TECHNOLOGY HYBRIDISATION



- Big data
- Connectivity – 5G
- Cybersecurity

TRANSVERSAL



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

BIOLOGICAL

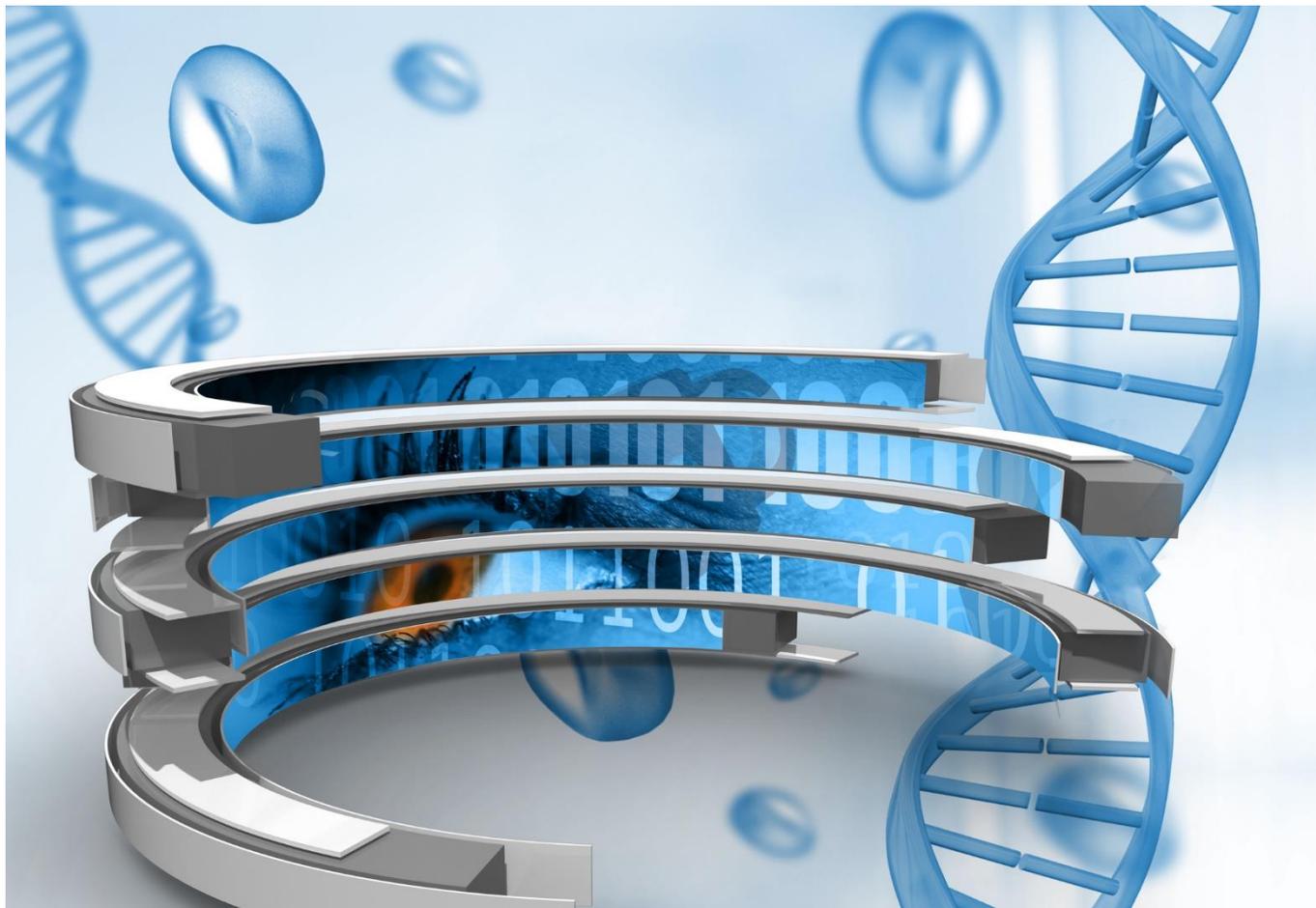


The reports published as of 1 July 2020 appear in blue. The reports pending publication appear in red.

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1. Definition of genomics



Gene, genetics, genome, genomics

A **gene** is a linear sequence of nucleotides in DNA or RNA that is essential for a specific function, whether in human development or the maintaining of a normal physiological function.

Genetics is a branch of biology that focuses on the inheritance and variation of organisms, i.e. the characteristics transferred from parents to children, from generation to generation.

The **genome** refers to the genetic material of an organism.

Genomics is a scientific discipline that deals in genetic mapping, DNA sequencing, and genome analysis.



Source: NIH

Definitions (I)

Omics

Omics are a group of **disciplines related to biochemistry and molecular biology** through which in-depth analytical knowledge can be ascertained of the characteristics and the overall contents of a biological sample. Omics include: genomics, metabolomics, proteomics, transcriptomics, pharmacogenomics, and others.

Genomics

Genomics involves the study of the contents, organisation, function and evolution of the genetic information in a complete genome. It studies the mapping, sequencing and analysis of the genome functions.

This analysis is used to diagnose genetic diseases and counselling, create personalised medicine and nutrition, perform evolution studies for species, identify micro-organisms or produce functional foods.



Gene therapies

Gene therapy can be defined as the transfer of genetic material to an individual for therapeutic purposes.

A new type of therapy that consists of using nucleic acid that is released in different ways, generally with a viral vector or synthetic lipid-based vectors to treat a disease.

Source: Omics report, ACCIÓ(2018); Spark; Spanish Society of Gene and Cell Therapy

Definitions (II). Personalised medicine

Personalised medicine adapts to the specific needs of each patient. It consists of adapting the dose and type of drug to each patient, because each person responds differently to the same treatment.

Advances in knowledge of human genetics have led to a shift in paradigm in the way in which medical science deals with disease. In this paradigm, the challenge does not lie in treating the disease but in the specific individual suffering from it, by adapting the treatments to the individual biological characteristics of each patient.

This new scenario indicates that personalised medicine seeks objectives from an individual perspective: understanding the disease molecularly, understanding how the response to treatment is produced, particularly pharmacological, specifying the response and having the capacity to foresee the individual risk of suffering a disease or of responding to certain medication.



Source: IBEC; Generalitat de Catalunya. Department of Health

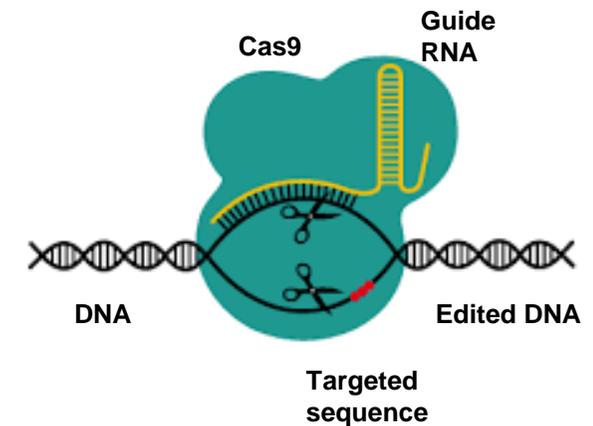
Definitions (III). CRISPR, genome editing

Genome editing has allowed for genetic modifications to be made at will in any gene of any organism. Although intentional genome modification has been feasible for some time, this has now expanded and been improved thanks to the discovery of the CRISPR system.

CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) is the name of a sequence of repetitive sequences present in the DNA of bacteria, which act as auto-vaccines. More specifically, CRISPR is a region of the DNA of some bacteria that acts as an immune mechanism to viruses, i.e. the bacteria surviving the attack stores the information on their aggressor. When the virus attacks again, the bacteria identifies the unwanted genes thanks to the information stored, and this memory enables it to destroy the virus.

Cas9 is an endonuclease associated to the CRISPR (an enzyme), known for acting as “molecular scissors” that cut and edit, or correct, the DNA associated to a disease in a cell. A guide RNA directs the Cas9 molecular scissors to the precise location of the mutation. Once these molecular scissors make a cut in the DNA, the additional cellular mechanisms and the DNA added exogenously will use the machinery of the cell itself and other elements to specifically “repair” the DNA.

CRISPR-CAS9 technology can offer the capacity to directly modify or correct the changes associated to the underlying disease in the genome and has great potential in medicine, food, agriculture, and the environment.



The **2020 Nobel Prize in Chemistry** was awarded to researchers Emmanuelle Fuster and Jennifer A. Doudna “for the development of a method for genome editing”, CRISPR/Cas9 technology.

Source: SINC Agency, Bayer, Genotipia

Definitions (IV). Bioinformatics

Bioinformatics is a field of computer science that analyses biomolecular sequences. It is normally applied to genes, to DNA, to RNA or to proteins, and is especially useful in comparing gene and protein sequences between different organisms to see the evolutionary relationships between organisms in search of the function of these genes and proteins.

Bioinformatics can be said to be responsible for the linguistic part of genetics. In the same way that linguists study language patterns, bioinformatics study the patterns in DNA or protein sequences.

Bioinformatics use computer software with a great many applications, such as determining the functions of genes and proteins, establishing evolutionary relationships, and predicting the 3D shaping of proteins.

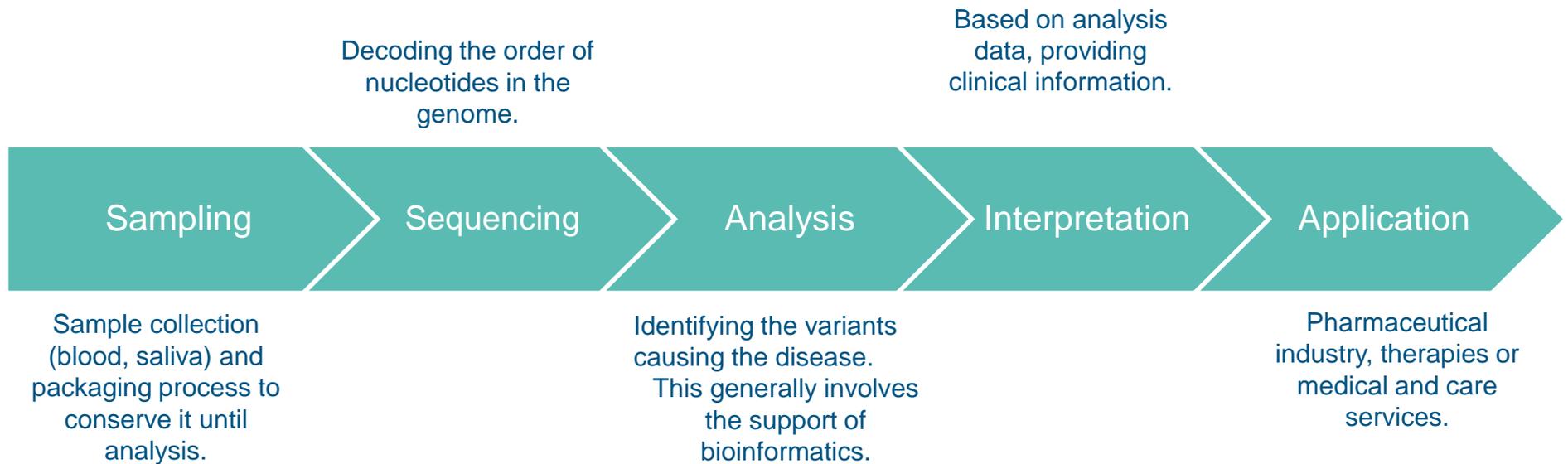
Bioinformatics is one of the scientific disciplines with most repercussions over recent years, even more so in 2020 with the essential task involved in handling and interpreting data on SARS-CoV-2.

Among the most relevant problems benefiting from the development of genomics and bioinformatics are the study of rare genetic diseases, the identification of tumour-associated mutations, the identification of the pathogen causing an outbreak of infection, or the discovery of new viruses, such as SARS-CoV-2.



Source: Instituto de Salud Carlos III, National Human Genome Research Institute

Value chain



Source: Preon Capital, Deloitte (2018)

2. The world genomics market



The world genomics market

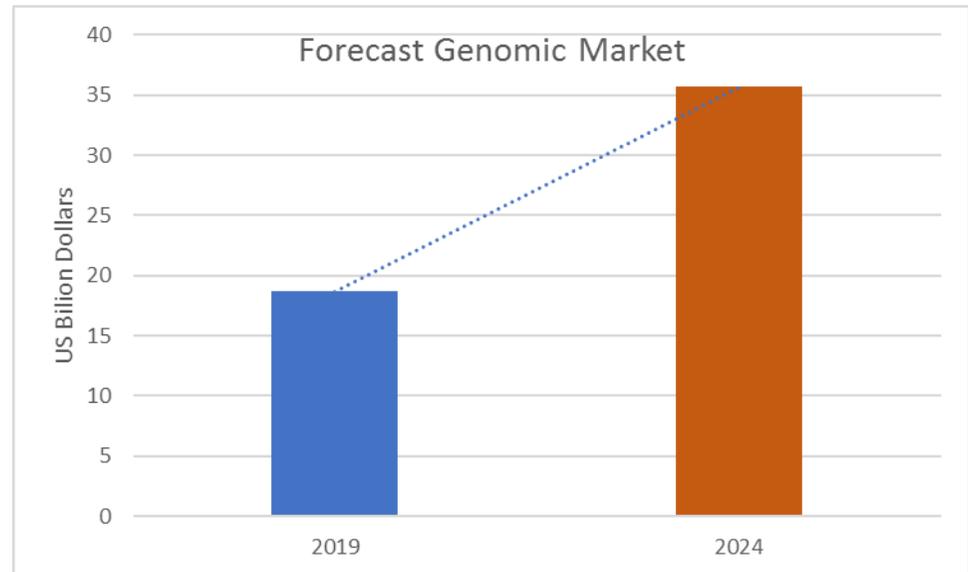
The world genomics market is calculated to reach **35.7 billion dollars by 2024**, as of 18.9 billion dollars in 2019, at a compound annual rate of **13.5%**.

The United States was the principal area of the genomics market in 2018.

Factors such as the increase in funding and investments by governments, the growth in the number of projects, the decrease in sequencing costs, the increase in areas of application, and the entry of new players and new companies in the field of genomics might promote its growth.

However, the high cost of equipment may also put a restraint on this growth.

Non-invasive cancer detection research is one of the main factors in promoting the genomics industry. Investigators from different areas are taking part in the development and establishing of protocols for clinical trials to identify the DNA mutations causing cancer that that could be detected early in this way.



Traditional genome editing technologies are intensive in terms of time, but the appearance of new technologies such as CRISPR/Cas9 or ZFN might help streamline genome editing and the appearance of personalised therapies.

Source: Markets and Markets (2018)
grandviewresearch

Main regions and relevant hubs



North America, a possible leader

The United States is foreseen as being the dominating region in this market, given the significant investment into research made by the governmental organisations and the advanced infrastructure in medical care. The presence of key companies such as Bio-Rad Laboratories, Inc., Tecnologías Agilent, Illumina, Genomic Health and Bluebird Bio, who are leading the way in the fields of genome sequencing, genetic diagnosis, and gene therapies.



Europe: initiatives within the European Commission

Through the initiative European '1+ Million Genomes, a collaboration mechanism to obtain at least 1 million genomes sequenced by 2022 with the goal of improving disease prevention, allow for more personalised treatments, and provide a sufficient scale for new clinical research.



Asia-Pacific: *Early adopters*

Asia-Pacific is expected to grow most quickly over the coming years. China is developing an essential role in the growth of the region's market with initiatives such as the *Precision Medicine Initiative (PMI)* for use of the genome in medical case since 2017.

Source: ACCIÓ based on Grand View Research and the European Commission

World leading genomics companies

Country of origin	Company
	
	
	
	
	
	
	
	
	
	

 Present in Catalonia

Main genomics startups

Country of origin	Company
	
	
	
	
	
	
	
	
	
	

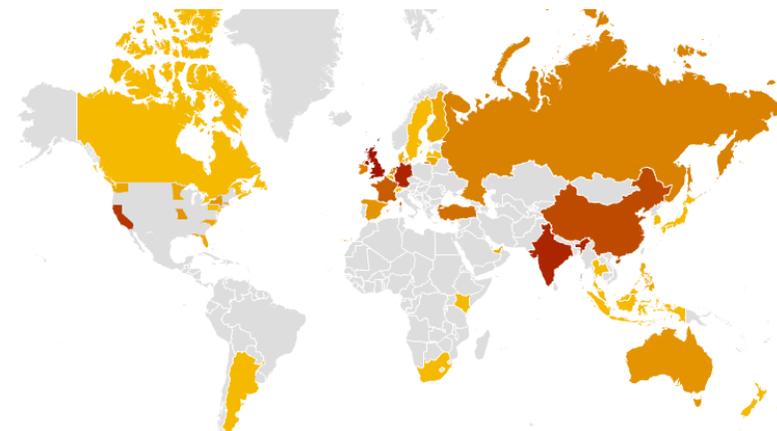
Source: Biospace, The Medical Futurist; Medical Startups

Foreign investment in genomics (2015-2019)

Country of origin



Target country



Country of origin	Projects	Capex (€M)	Jobs created
United States	46	971.0	3,118
China	19	1,195.7	2,204
The Netherlands	12	63.7	465
Malaysia	11	2,762.2	5,572
United Kingdom	9	47.2	237
France	4	108.7	277
Japan	4	63.4	320
Israel	4	45.0	115
Switzerland	4	26.4	71

Destination	Projects	Capex (€M)	Jobs created
United States	28	761.0	1,758
Singapore	11	145.6	640
United Kingdom	10	402.0	1,543
India	9	211.3	1,071
Germany	9	154.1	453
China	7	433.2	1,284
France	6	40.0	121
Turkey	5	5.4	67
Ireland	4	688.2	811

Source: fDi Markets (2015-2019). The countries in the table are the top 10 countries in numbers of projects. The maps illustrate the historic series (the intensity of projects in the United States is shown subdivided into states)

Main companies investing in genomics

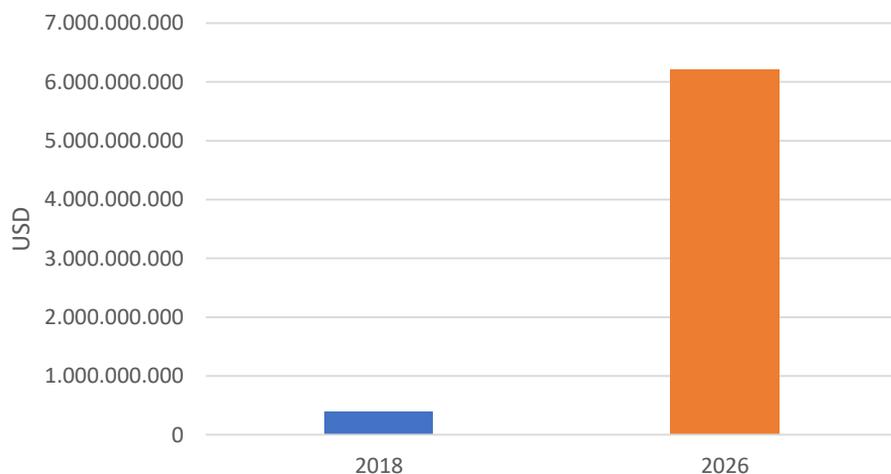
Country of origin	Company	Projects	Capex	Jobs
	Abbott Laboratories	48	2,413.8	7,347
	Monsanto	38	1,080.2	4,432
	Sigma-Aldrich	24	348.4	816
	Genting	21	15,938.4	14,416
	Qiagen	18	265.9	1,547
	WuXi PharmaTech	16	1,239.8	1,986
	BGI (Beijing Genomics Institute)	11	232.7	584
	Eurofins Scientific	7	57.0	559
	Illumina	6	46.6	278

Source: fDi Markets (2015-2019). The countries in the table are the top 10. The maps illustrate the historic series

World gene therapy market

The world gene therapy market was valued in **393.3** million dollars in 2018 and is expected to reach **6,205.85** million dollars by **2026**, with a compound annual rate of 34.8% from 2019 to 2026.

World gene therapy market; forecasts



World gene therapy leaders		
		<i>Kite Pharma</i>
		<i>BioVex</i>
		<i>Novartis</i>
		<i>Spark Therapeutics</i>
		<i>Bluebird Bio</i>
		<i>Sangamo</i>
		<i>Dimension Therapeutics</i>
		<i>Adverum Biotechnologies</i>
		<i>Celladon</i>

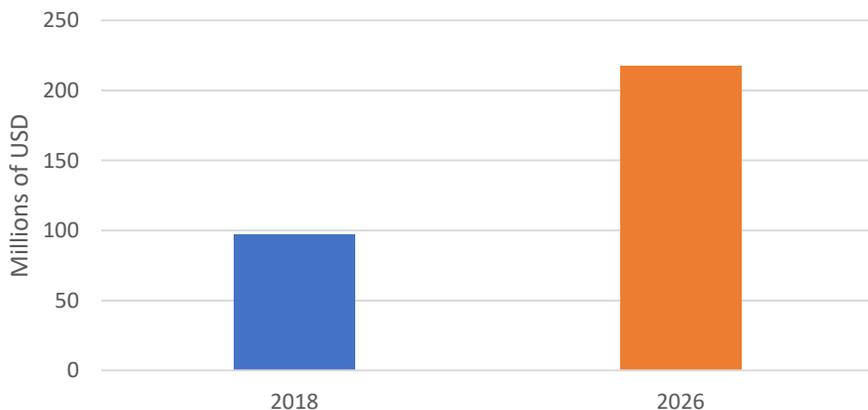
Source: Allied Market Research. Gene Therapy Market Outlook - 2026

The world personalised medicine market

The personalised medicine market was valued at 96.97 million US dollars in 2018 and is expected to grow 10.67% between 2019 and 2026 to reach 217.90 million US dollars.

The main vectors for adopting these personalised therapies include the significant impact of different types of cancer, the second cause of death worldwide, and the lesser side effects of the medication. The main challenge that might slow down market growth, however, is the relatively unstable legal and regulatory framework.

Forecasted evolution of the personalised medicine market



World leaders in personalised medicine		
	 Abbott	Abbott Laboratories
	 MERCK	Merck & Co
	 AstraZeneca	AstraZeneca
	 Pfizer	Pfizer, Inc.
	 gsk	GlaxoSmithKline PLC
	 NOVARTIS	Novartis AG
	 AMGEN	Amgen, Inc
	 BAYER	Bayer AG
	 Mylan [®]	Mylan N.V
	 <i>Lilly</i>	Eli Lilly

Source: Grand Review Research. Personalized Medicine; Verified market research

3. Applications of genomics



Applications of genomics

Life sciences, pharmaceutical industry, and health:



Genomics allows for more precise diagnoses for early treatment or surgery.



Genomics allows for personalised medicines to be developed and, therefore, more effective treatments.

Agriculture



With the growth of the world population and environmental pressure, there is a pressing need to speed up the production of new crops with higher production levels, drought or tolerance to heat, and a lower use of pesticides. The advances made in genomics offer the potential to speed up the crop development process with promising agronomic features.

Extraction of materials and treatment of ecosystems



- Bioleaching is the process of extracting material from living organisms. It is a cheaper and more effective technique. Genomics also allows for more respectful mine closure practices.
- Genomics provides solutions in water treatment.

Food industry



- The applications of **nutritional genomics** include the identification of dietetic signs that increase immunity to eliminate the need for antibiotics in animal feed, as well as the development of crops or animal products with higher levels of healthy phytochemicals. They are also used to promote improvements in the transformation, security and quality of feed.

Source: Brown L, van der Ouderaa F. Nutritional genomics: food industry applications from farm to fork [published correction appears in Br J Nutr. 2007 Aug;98(2):446]. Br J Nutr. 2007;97(6):1027-1035

Genomics and SDGs OBJECTIUS DE DESENVOLUPAMENT SOSTENIBLE (II)

Terrestrial ecosystem

The new genetic and genomic approaches have great potential to use the natural genetic variation to promote forest health and productivity, especially in light of world disruptions such as climate change, land fragmentation, and emerging afflictions and diseases.



Zero hunger

The genomics applied to agriculture can help increase the efficiency, competitiveness, and shock resistance or sustainability of the environment to contribute towards food safety, nutrition, economic development, or the sustainable management of natural resources. It can also help provide tools for the agricultural sector to mitigate the impact of climate change on crop production.



Climate action

Effective action against climate change: analysis of the way in which the environmental stress factors such as climate change affect the populations of wildlife through advanced genetic analysis.



Health and well-being

Development of drugs to help patients with Alzheimer's, leukaemia or other rare and minority diseases. It also allows for earlier diagnosis and personalised therapies.

Innovation

The introduction of genomics may generate new business and innovation models in different areas.



Clean water and sanitation

Genomics and genetic modification of micro-organisms can help in the treatment of urban and industrial wastewater.

Source: Euforgen, Orizon, International Food Policy Research Institute (IFPRI)

4. Genomics in Catalonia



Genomics in Catalonia: main mapping conclusions



49 companies



€276.22 million

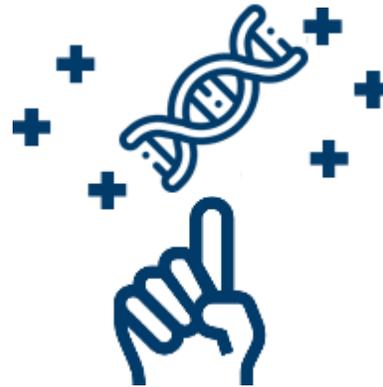


742 jobs

77.55% of the total are **SMEs**



38.77% of companies have a turnover of **more than one million euros**, and 28.57% have a turnover of **more than ten million euros**



55.10% of the companies are less than ten years old



40.81% of these companies are startups

Average degree of internationalisation:



40.81% of the companies are exporters

The main application of the sector is biomedicine.
Furthermore, the ecosystem is formed by a large network of research centres and leading hospitals.

Source: Acció according to Orbis, ACCIÓ Directories, Biocat, ASEBIO, Spain Biotech 2018 data

The genomics ecosystem in Catalonia

Partial illustrative table

COMPANIES						SECTORS OF APPLICATION
						Health and life sciences 
						
						Food 
						
						
						
						
						
						
						

Note: these brands are used solely for informative purposes. The brands mentioned in this report belong to their respective owners and are under no circumstances the property of ACCIÓ. This is a partial representation in order to illustrate the main companies belonging to the genomics ecosystem in Catalonia, but there may be other companies that have not been included in the study

Source: ACCIÓ according to BIOCAT and BIOTECH Spain

Others players in the genomics ecosystem in Catalonia



Technology and research centres



Universities, research and training centres



Hospitals



Associations, clusters and federations



Source: ACCIÓ

Business case in Catalonia

Esteve is an international pharmaceutical chemical group that focuses on innovation and excellence in the area of health.

In collaboration with other organisations, it focuses on promoting the development of gene therapies and on research into products in the area of pain management.

In collaboration with the UAB (Universitat Autònoma de Barcelona), a gene therapy platform has been developed that researches products for the treatment of mucopolysaccharidosis and Sanfilippo Type A and B diseases, and Hunter's syndrome.



GEN inCode specialises in risk assessment and the prediction of cardiovascular diseases, which are the main cause of death and disability in the world and account for one in every four deaths in Spain.

The GEN inCode genome technology combines patented clinical algorithms and artificial intelligence to offer an advanced assessment of the risk to each patient in order to predict the appearance of diseases.

This technology, which combines traditional clinical measures and genetic information on patients, is made available to health professionals. The goal is to provide a full assessment to determine the most effective treatment in each case (personalised medicine). This means that patients can be informed of the existing risks to their health in order to make changes to their habits and lifestyles before a cardiovascular disease appears.



Source: EIC (DGI-ACCIÓ) based on the press, White paper on advanced therapies

Health and life sciences in Catalonia



1,060
COMPANIES (2017) related to the health and life sciences sector.

3.4% of the Catalan GDP.

Complete value chain

The densest pharmaceutical ecosystem in Europe



4.6% of European FET Flagships H2020 funds attracted (with only 1.2% of the population of the European research area).

Among the top 10 in Europe in **clinical trials** (top 5 in oncology).



40 research centres.

780 research groups in life sciences.

18 university hospitals.

3 leading science facilities.

14 science and technology parks.

Clusters



Local champions



International champions



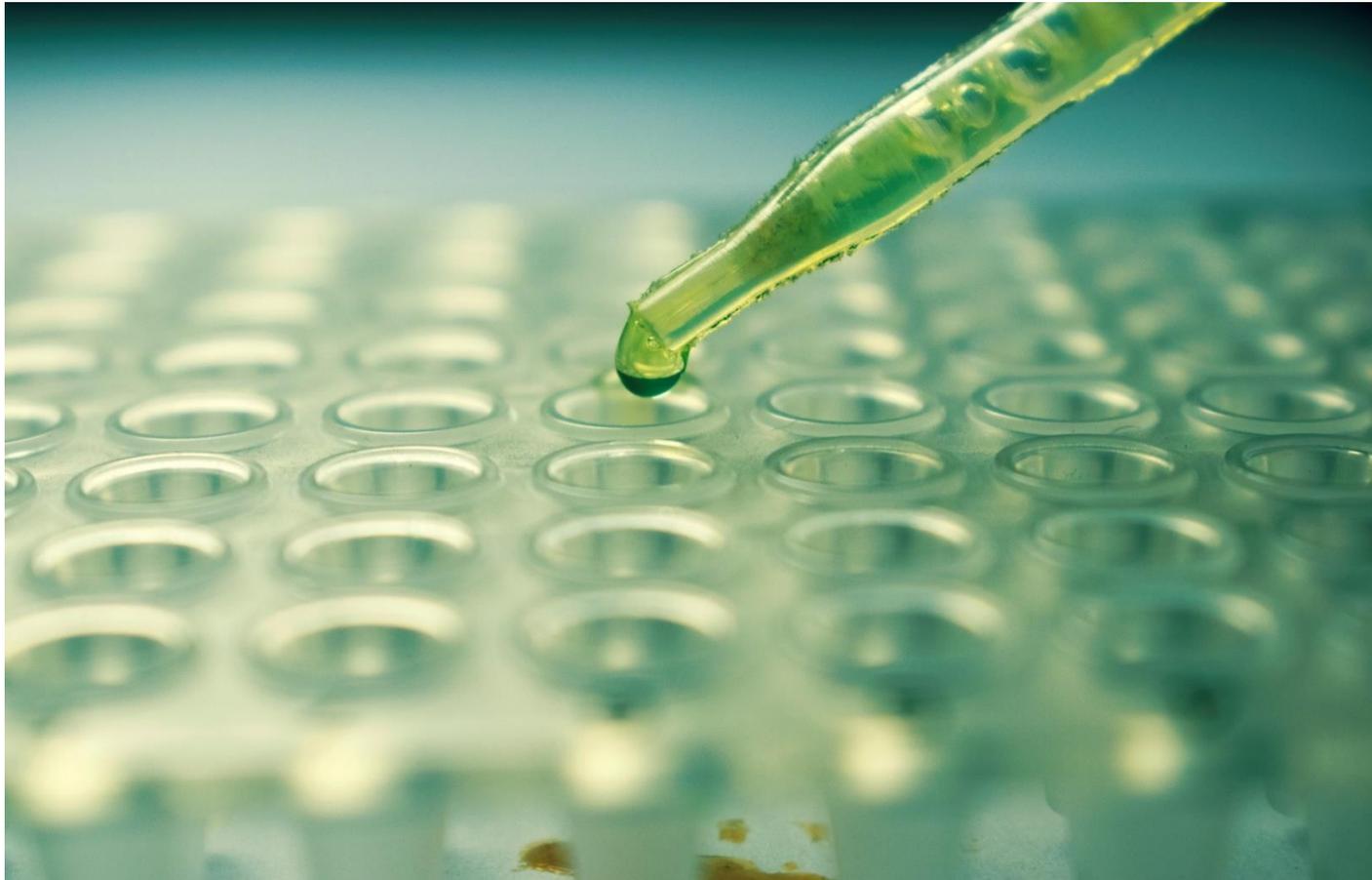
Top tech centers



Hospitals



5. Genomics, the key to finding solutions for COVID-19



Applications of genomics for COVID-19



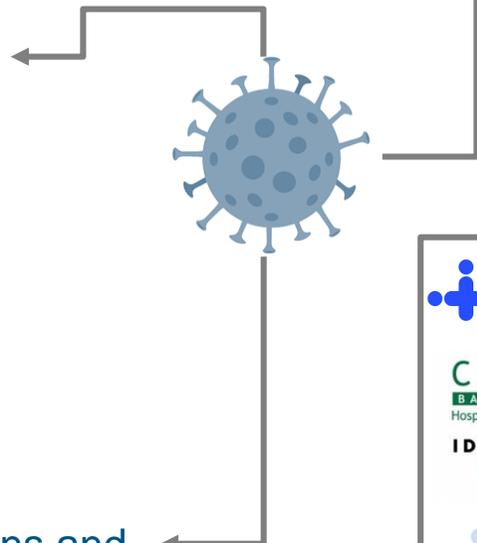
DIAGNOSIS

PCR (polymerase chain reaction) test to detect a fragment of genetic material of a pathogen or micro-organism. This test detects the genetic material of the virus.



RESEARCH

Genome sequencing for the virus to understand mechanisms, forms of possible treatment, and epidemiological studies.



TREATMENT

Design of medications and vaccines.

Success stories

Logos included in the Success stories grid: Vall d'Hebron, ORYZON, Hospital del Mar, Parc de Salut MAR, SEQUENTIA, CLÍNIC BARCELONA Hospital Universitari, upf. Universitat Pompeu Fabra Barcelona, CRG Centre for Genomic Regulation, IBEC Institute for Bioengineering of Catalonia, UAB Universitat Autònoma de Barcelona, IDIBAPS Institut d'Investigacions Biomèdiques August Pi i Suñer, UNIVERSITAT DE BARCELONA, INSTITUT FOR RESEARCH IN BIOMEDICINE, eureka! Centre Tecnològic de Catalunya, UPC, QIAGEN, qgenomics, and Floxxixics.

Source: compiled by author based on “Global efforts on vaccines for COVID-19: Since, sooner or later, we all will catch the coronavirus (2020)” and press

Felipe García, investigator at the **Hospital Clínic in Barcelona (IDIBAPS)**, is heading a project that seeks to develop and test in preclinical trials a new vaccine for SARS CoV-2 that induces long-term responses to the virus by the immune system.

The proposal is to design a vaccine based on the mRNA (messenger ribonucleic acid) of the virus, which is a promising alternative to the conventional vaccines thanks to its great potential, fast development, low-cost production, and safe administering.

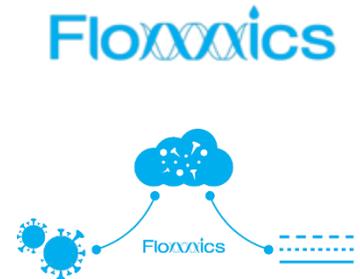
Investigators are to use computational methods to identify the parts of the virus that provoke a greater response by the immune system and will design the vaccine, considering these regions to ensure long-term immunity from the virus.

Traditional vaccines are made up of small or inactivated doses of the organism that cause the disease or the proteins producing it, which are introduced into the body to cause the individual's immune system to trigger a response. mRNA vaccines “trick” the body into producing certain viral proteins, using the messenger RNA that has the information to build a protein. In order to product an mRNA vaccine, a synthetic version of the mRNA of the virus is created. Once introduced into the body, the immune system detects these viral proteins and starts to produce a definitive response.



Flomics Biotech is a young biotechnology company that operates in the field of liquid biopsies. It comes from the Biomedical Research Park of Barcelona and its mission is to translate the latest research into genomics and cell-free circulating nucleic acids into clinical practice. Flomics is currently working with hospitals around the world in the fields of oncology and infertility. More recently, it has also collaborated in the fight against the coronavirus pandemic.

Flomics has joined forces with international biotechnology partners specialising in next-generation sequencing tests to develop a cloud-based data analysis solution to detect and investigate COVID-19. By combining the unique characteristics of the different experimental sequencing kits available to detect SARS-CoV-2, we are able to maximise the information extracted from each experiment performed in a reliable, sensitive and automated manner. The platform helps hospitals, clinics and research laboratories transform unprocessed data into interpretable clinical information, which will help manage this pandemic without the need for computer infrastructures or experience in bioinformatics.



Source: EIC (DGI-ACCIÓ) based on the press, Clínic and Spanish Ministry of Health websites

Oryzon Genomics focuses on the development of drugs for cancer and other diseases of the nervous system (Alzheimer's multiple sclerosis, and certain psychiatric diseases), and has also developed a molecule, vafidemstat, with a mechanism of action that has an anti-inflammatory effect with certain benefits to severely ill COVID-19 patients, avoiding progression of the acute respirator distress syndrome (ARS) and reducing the patient's inflammatory response.



According to the World Health Organization (WHO), COVID-19 diagnosis tests are essential in tracking the spread of the virus and avoiding its transmission.

qGenomics joins the fight against COVID-19 through its RT-qPCR diagnosis testing.

The qCOVID-19 RT-qPCR test by qGenomics is based on the RT-qPCR molecular method. It is used for the qualitative detection of the presence of the virus RNA causing acute respiratory distress syndrome of the Coronavirus 2 (SARS-CoV-2 or nCoV-2019), which is responsible for the 2019 Coronavirus (COVID-19) pandemic. Detection involves biological samples obtained from the respiratory tract of individuals suspected of suffering from COVID-19. The RNA of the SARS-CoV-2 can generally be detected in the respiratory tract during the acute phase of infection.



Sequentia Biotech provide support for R&D into COVID-19 through the production of GAIA, its microbiome analysis software capable of detecting and analysing SARS-CoV-2 NGS data with great precision and sensitivity, in a rapid, simple manner.

- It detects SARS-CoV-2 with great precision and sensitivity.
- It identifies strains of SARS-CoV-2, even in complex viral matrices.
- Updated and stored SARS-CoV-2 databases.
- Works with amplicon and shotgun sequencing.
- Works with any biological sample.
- Works with data from any NGS platform (Illumina, Oxford Nanopore, PacBio and IonTorrent).



Source: EIC (DGI-ACCIÓ) based on the press

An innovative therapy for COVID-19 based on circular RNA.

This project seeks to generate and validate in cell culture and in mouse models circular RNA (circRNA) that become hybrid and interfere in essential structures of the SARS-CoV-2 genome, rendering it inactive.

The work group has successful prior experience with circRNA that inhibit the replication of other RNA(+) viruses, and the existence of RNA-based therapies already in use and of spray-administering systems support the viability of the proposal.



The company Qiagen has developed the “QIAstat-Dx Respiratory 2019-nCoV Panel” system for the fast detection of SARS-CoV-2, a molecular diagnosis kit that differentiates between the coronavirus and 21 other respiratory pathogens (bacterial and viral) in approximately one hour, to be able to diagnose people infected by the novel coronavirus.



Source: EIC (DGI-ACCIÓ) based on the press, Clínic and Spanish Ministry of Health websites

Researchers at Vall d'Hebron hospital have sequenced the genome of the SARS-CoV-2 virus

The impact of COVID-19

- Medical research is a fundamental part of understanding and finding solutions regarding the detection and cure of the pandemic. The disciplines related to biochemistry and molecular biology can provide innovation in this field.
- Researchers at Vall d'Hebron hospital have sequenced the genome of the SARS-CoV-2 virus. This means that sequences can be compared among different populations and countries around the world to analyse the changes in the virus as it spread among the population. This knowledge will be useful in predicting what might happen in the coming years and the action to take. Obtaining the complete genome of the SARS-CoV-2 virus in every individual opens the doors to studying its variability and evolution, as well as prognostic factors in patients. Based on the study of these sequences, the best targets for the design of vaccines and direct-acting antivirals can also be determined.



Source: EIC (DGI-ACCIÓ), H. Vall d'Hebron

ACCIÓ

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www.accio.gencat.cat
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See the report here:

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

More information on the sector, 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