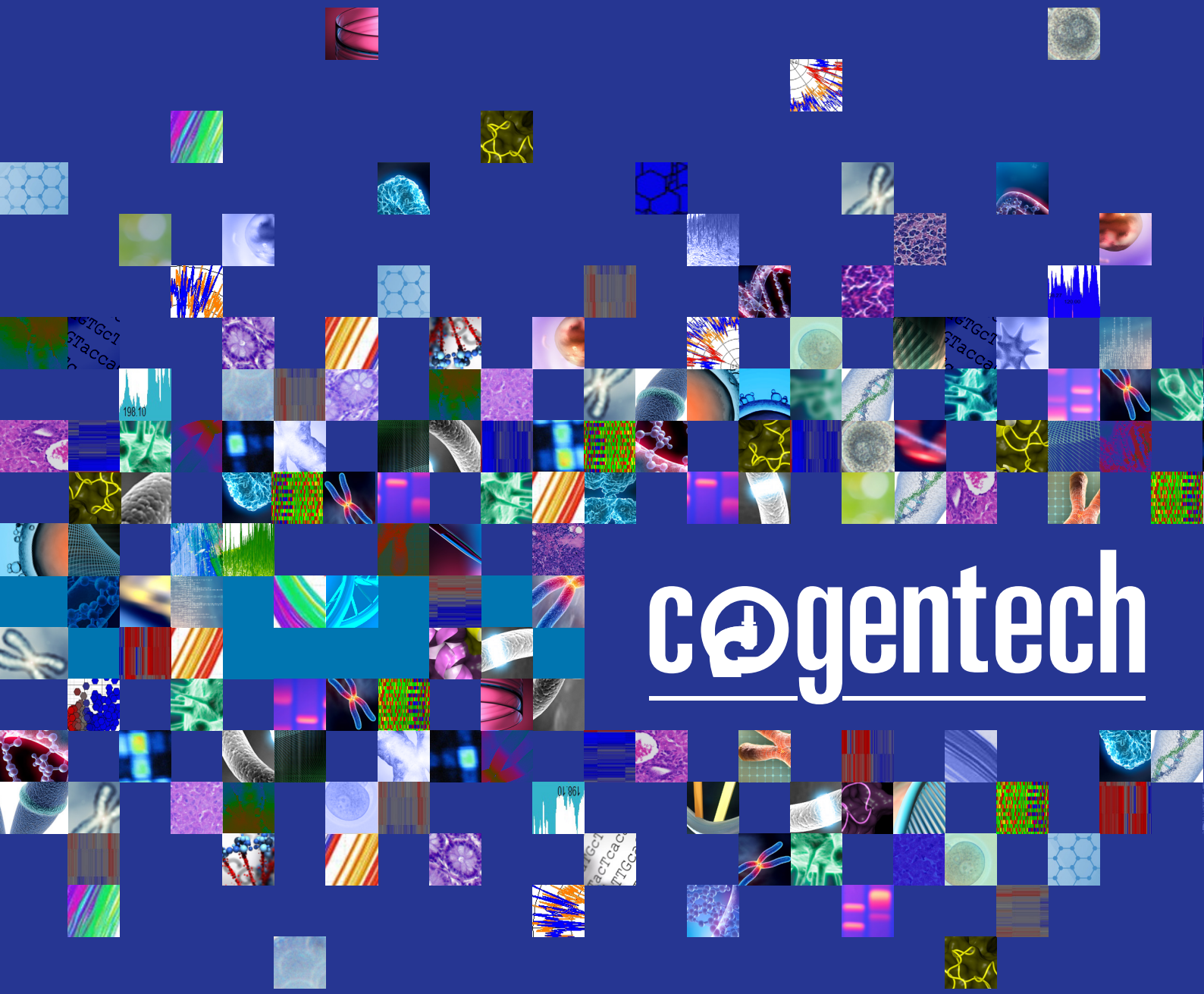

cogentech

IMPACT REPORT 2021

INDEX

Letter to stakeholders

Dearly beloved,

I am about to introduce the third "Impact Report" of Cogentech as a Benefit Corporation, in my very recent capacity as Chairman.

The contents of this report derive, in its vast majority, from the stewardship of the previous chairman, Professor Claudio Basilico, whom I thank for the great work he has done and the lucid vision with which he has given strong impetus to Cogentech's development in recent years.

Looking ahead to the challenges that await us in the coming years, it is therefore with enthusiasm but, above all, with a spirit of service, that I have accepted to lead the Society in this delicate period of transition.

The various changes that affect us, the most significant of which is certainly the change in Governance, also occur as a result of structural and management changes at AIRC and the IFOM Foundation, the sole shareholder and controller of Cogentech.

The pandemic, which so profoundly affected our work for the entire 2020s, leading us to face hitherto unthinkable difficulties, is still not over. On the contrary, in the last months of 2021 it showed a resurgence that brought us back to safety measures we thought were outdated. However, the intensity of the vaccination campaign, with particularly high coverage in IFOM and Cogentech, has allowed us to continue our work, without any interruption in service.

Unexpectedly, on June 15, 2021, an incredible accident with potential dramatic consequences occurred: a 15-meter drill fell from a nearby construction site onto an IFOM building. Fortunately, no one was injured; however, the Directorate building was declared temporarily unusable. This led us to face the reorganization of all offices, both IFOM and Cogentech, with some activities temporarily moved to remote locations.

Under these conditions, with the drill still firmly embedded in the affected building, the Accredia Surveillance Audit for confirmation of UNI EN 15189 accreditation was tackled, and brilliantly passed.

The presence of numerous construction sites, a source of vibration and consequent harmful effects on animals, is behind the relocation of one of the Mouse Facility's two enclosures. The enclosure activity is therefore partially outsourced to a partner with an international profile, allowing the research to continue without any impact.

The Cancer Genetic Testing Lab once again shows itself to be solid, thanks mainly to the very high professionalism and considerable experience of the staff. These values and the quality of the service provided have also been recognized by additional hospitals that go on to lengthen the list of Clients. Clients who, continue to score higher and higher in the annual Customer Survey. The laboratory, in addition to having handled the situation as well as possible during the pandemic, has increased the supply of genetic testing in the past year, thanks to the development of the new customized management system and the continuous improvement and automation of analytical processes. Looking ahead, the intention is to expand and refine the diagnostic offerings and continue the strong research collaboration with some high-profile partners.

Special mention should be made of the Genomic Unit, as the NGS technique is taking on an increasingly pronounced role in both diagnostics and R&D. In the latter area, the Unit's professional level is evidenced by the assignment of research projects with clinical spin-offs by such prestigious bodies as the Ministry of Health and ISS. Moreover, the bioinformatic analysis of these Projects has received the very valuable support of the bioinformatics group of the Catania Cogentech Sud office.

In relation to the latter, it is with particular satisfaction that we note an exponential growth in the activity of the laboratories engaged in the themes of the BiLiGeCT/PON Project, which involved the fine-tuning of pre-analytical methods in the histopathological context, the now routine use of NGS sequencing of eligible liquid biopsy cases, and the fruitful collaboration with the Milan Branch for the analysis of Variants of Unknown Significance (VUS) of BRCA genes.

However, all of Cogentech's facilities have confirmed their value, both in day-to-day and research activities.Within the document, ample space has been given to individual projects, the value they represent to the community, and the resulting publications.

So it is with the knowledge of a strong and motivated group like Cogentech's that I am going to face all the challenges (and opportunities) that 2022 will bring.

The Chairman

Methodological Note

In line with Italian regulations on Benefit Societies, Cogentech is preparing the Impact Report for the third consecutive year, adopting the year 2021 (January 1-December 31) as the reference period.

In this document, Cogentech reports on its social, environmental, and economic performance and, in line with the regulations, describes the specific goals set and actions implemented in pursuit of the Company's goals of common benefit.

The Impact Report has been prepared according to an external assessment standard developed by an independent third party, which meets the transparency and credibility requirements of the regulations. Based on the sector analysis and its own specificities, Cogentech chose to prepare its Impact Report according to the Global Reporting Initiative guidelines (GRI Sustainability Reporting Standards published in 2016 and updated to 2020), adopting the "Referenced" mode. For material issues for which Specific GRI Standards are not available, ad hoc indicators (hereinafter "No GRIs") have been developed that are representative of the specific business reality and sector within which Cogentech operates. The general principles applied in preparing the Impact Report are those established by the GRI Standards: relevance, inclusiveness, sustainability context, completeness, balance between positive and negative aspects, comparability, accuracy, timeliness, reliability, and clarity.

The process of drafting the Impact Report was initiated by conducting an internal analysis of the organization, which was also carried out by taking into consideration the interests of the company's various Stakeholders such as general management, employees and external collaborators, customers, suppliers, end users and the local community.

Subsequently, Cogentech was able to identify some pivotal issues on which to focus its efforts:

- Training and professional development of employees;
- Staff welfare;
- Relationship with the community;
- Customer satisfaction and service quality;
- Research and innovation;
- Environmental sustainability;
- Occupational health and safety.

Data collection followed a structured process with the involvement of the organization's internal contact persons. The 2021 Impact Report was subjected to Limited Assurance by PricewaterhouseCoopers Business Service Srl. The Impact Report is published on the Company's institutional website at https://www.cogentech.it/.

More information about the document can be obtained from the following e-mail address: press-desk@cogentech.it

Who we are

Our history and mission

Active since 2005, Cogentech in 2018 was reconfigured as an SRL Benefit Company with Sole Shareholder the nonprofit IFOM Foundation (FIRC Institute of Molecular Oncology), based in Milan.The Society is based at the IFOM-IEO Campus in which there are numerous other organizations involved in research and clinical applications in the field of oncology.

The mission of the Society is to provide technologically advanced and high-quality services to both researchers engaged in the development of basic research in oncology and Translational Medicine and to hospital facilities for the diagnosis and treatment of cancer diseases.

It was precisely to offer modern diagnostic solutions that Cogentech's Cancer Genetic Test laboratory, CGT Lab, was established. The CGT Lab, is a point-of-care Laboratory Medicine Service (SmeL) accredited by the National Health Service since 2011, and registered in the Regional Register of Accredited Facilities in the sub-branch of Medical Genetics. This means that the facility possesses both technical-professional and organizational, structural and relational quality requirements necessary for the protection of rights and user satisfaction.

Since 2019, Cogentech has been operating a new facility at the Science and Technology Park of Sicily in Catania, where new laboratories have been set up for the development of a project funded by the PON of the Ministry of Education, University and Research (MIUR) for a scientific project titled "BiLiGeCT - Liquid Biopsies for the Clinical Management of Tumors," which aims to provide a development opportunity for the area and an important opportunity for highly specialized scientific personnel.

Since 2014, Cogentech has had a Code of Ethics, which, in addition to outlining general ethical principles, governs all areas of the company's actions, from ensuring impartiality and transparency, to relations with the community, public administration and internal staff.

The actors with whom Cogentech interfaces can be divided into two macro-categories: customers and suppliers. Regarding customers, there are four different types. Hospitals that turn to Cogentech for genetic testing; "internal campus" customers; external academic customers; and external commercial customers interested in the research services offered by Cogentech.

The Society also deals with suppliers of both research technology products and services.

The composition of corporate governance

Cogentech's organizational model is inspired by principles of quality and professionalism. The fundamentals on which it is based are:

- Equal rights of users;
- The impartiality of the staff, inspired by criteria of objectivity and justice;
- Continuity, effectiveness and efficiency in service delivery.

The Company Mission, defined by the Company's Management, is strongly oriented toward scientific-technological advancement, on the quality of service provided, and on the positive return for the Community, understood as Workers, the Medical-Scientific World, and Society.

In the Quality Policy, the corporate Mission is defined, concordant with the Articles of Association, as well as the goals that the Organization itself sets.

Management consistently carries out monitoring of the achievement of quality objectives by conducting in an integrated manner an analysis of the context in which Cogentech operates, an assessment of the needs of the various stakeholders, and an evaluation of the risks associated with the specific activities performed. Through ongoing audits, with the support of staff functions, management thus identifies corrective and improvement actions, which are timely implemented and communicated internally. The construction of an in-depth SWOT analysis allows the Management to highlight the strengths (Strenghts) of the System, as well as the weaknesses (Weaknesses), opportunities (Opportunities) and risks (Treaths): the mentioned parameters thus go to constitute the pivotal elements on which future planning is designed.

In 2021 Cogentech experienced a renewal of its Governance. As already described in the Letter to Stakeholders, Prof. Marco Alessandro Pierotti, Director of the CGT Lab, succeeded Prof. Claudio Basilico in the role of Chairman. Dr. Alessandra Della Porta joined the Board as a Director, while Dr. Luciano Baielli retained his role as CEO.

The organization is thus headed by a president, a chief executive officer, and a board of directors, which is composed as follows:

Board Members	women	men	total
less than 30	0	0	0
between 30 and 50	0	0	0
more than 50	1	2	3
Total	**1**	**2**	**3**

Tabella aggiornata al 31/12/2021

Since 2014, Cogentech has had an Organizational Management Model pursuant to Legislative Decree No. 231/01, legislation that introduced the administrative liability of entities into the Italian legal system. In 2020, Cogentech's Organizational and Management Model pursuant to Legislative Decree No. 231/2001 was updated by providing for the new types of crimes introduced in the catalog of 231 offenses, and in January 2021, the updated version of the Model was published on Cogentech's website.

Cogentech also appointed its Supervisory and Control Body (SB), composed of Lawyer Andrea Gottardo, Dr. Alberto Bettinardi and Dr. Ambrogio Brambilla.

The task of the SB is to supervise the operation of and compliance with the Model, as well as to ensure that it is updated periodically

In addition to the provision of mandatory 231 training, the personnel department, in an email dated January 18, 2021, invited all staff to view the updated Model, posted on the company website (https://www.cogentech.it/chisiamo.php)

The services we offer

Cogentech is designed to offer technology services that meet the needs of the scientific community as well as those of clinical entities, which intend to make use of these technologies for diagnostic purposes.

The preparation of the staff, who have extremely refined know-how, the innovative technologies available, and the vast array of instruments are indispensable elements, to meet the needs of both the researcher and the clinician.

Diagnostic services for the clinic: Cancer Genetic Test Lab

Cogentech acts in an area ranging from research to diagnosis, from treatment to prevention.

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The Cancer Genetic Test (CGT Lab for short), in particular, offers a specialized laboratory medicine service devoted entirely to genetic testing.

With an experience of more than 15,000 genetic tests performed, the CGT Lab guarantees its academic and clinical partners efficiency and accuracy, thanks to the expertise of highly qualified staff, a large and up-to-date technology pool, supported by a scrupulous and documented Quality Management System.

The CGT Lab, has in fact achieved several certifications and accreditations over time.

It is in fact found to be: Accredited with the National Health Service; Enrolled in the Regional Registry of Accredited Facilities in the sub-branch of Cytogenetics and Medical Genetics for Molecular Genetics activities; UNI EN ISO 9001:2015 Certified; SIGUCERT Certified by the Italian Society of Human Genetics; Accredited UNI EN ISO 15189:2013 with ACCREDIA for Medical Genetics examinations.

Obtaining these certificates demonstrates an ongoing commitment to excellence in the field of molecular diagnostics of cancer diseases.

The accuracy of the services provided and the development and implementation of new diagnostic methodologies have as their only goal an ever-improving support to the physician and, consequently, to the people he or she cares for.

Throughout the pandemic we are still experiencing, the CGT Lab, consistent with its mission, has never interrupted its activities, aware of how timely diagnosis in oncology can make a difference. More precautionary protocols have obviously been adopted because of the type of samples analyzed.

Research and Technology

IFOM scientists have been engaged in the study of major issues in cancer research for years.

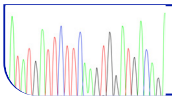
Researchers work in the belief that knowledge of the biological mechanisms responsible for cancer development and progression (from primary tumor to metastasis) will lead to the design of new and rational methods for prevention and personalization of treatment.

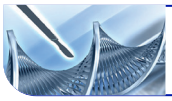
The most original and innovative research concerns the topic of genomic instability of cancer cells and the role of the chemical and physical properties of the microenvironment in which the tumor develops (mechanobiology), which are particularly important for metastatic spread.

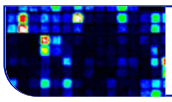
Cogentech supports oncology research with cutting-edge technologies dedicated to the development of new strategies for the identification of neoplastic molecular targets (genes, proteins, protein groups, and mechanisms that play key roles in cancer and that, if pharmacologically altered, can reduce or even regress the disease). Great space is also being gained by Translational Medicine, which makes use of both the expertise and technology park of Cogentech.

Scientific Services

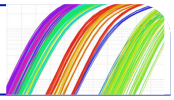
Close collaboration with state-of-the-art scientific institutes has enabled Cogentech personnel to achieve a level of specialization that enables them to support clients at every stage of research, from proper experimental design to performing specific analyses and interpreting results.

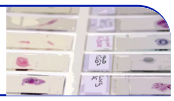

DNA Sequencing

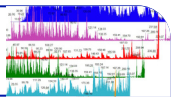

Genome Editing


Microarray/NGS


Mouse Genetics

Quantitative PCR


Histopathology


Proteomics


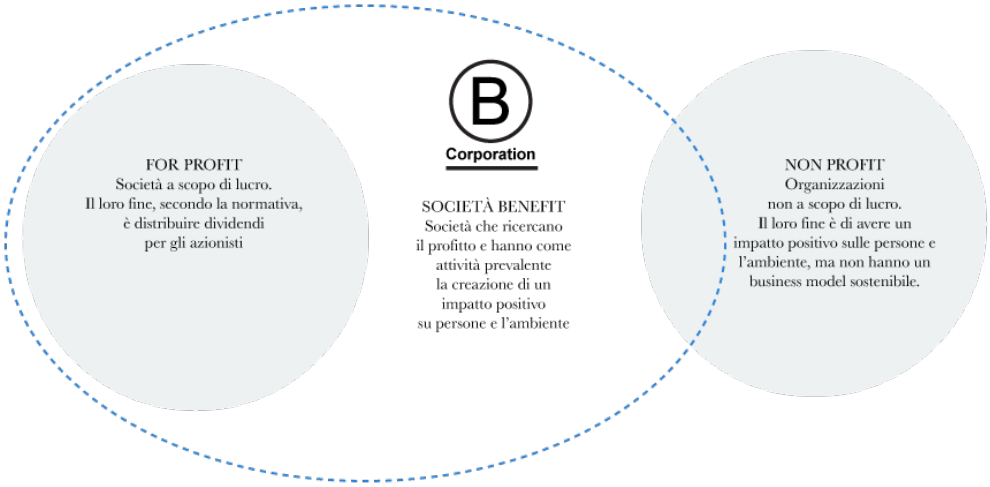
Zebrafish


Our commitment

Benefit societies

Italy, through Law No. 208 of Dec. 28, 2015, recognized and regulated corporations with the purpose of common benefit: Benefit Societies.

These are corporate forms that allow entrepreneurs, managers, shareholders and investors to protect the company's mission and, at the same time, to distinguish themselves in the market from all other corporate forms through a virtuous and innovative legal form. In fact, Benefit Societies integrate profit goals into their corporate purpose, while operating in a responsible, sustainable and transparent way, in order to have a positive impact on people, communities, territories and the environment, cultural and social goods and activities.



Fonte: https://www.societabenefit.net

Cogentech, in 2018, changed its corporate name, choosing to become a Benefit Society S.r.l., having IFOM as its sole shareholder.

As a Cogentech Benefit Society, it is annually required to prepare and publish an Impact Report outlining how the Society is pursuing and achieving the common benefit purposes set forth within its Articles of Incorporation.

The goal is to adopt an increasingly effective evaluation model that allows for a concise, clear and comprehensive Report.

The purposes of common benefit

As a Benefit Society, Cogentech is committed to pursuing the common benefit purposes outlined below, which are at the heart of its day-to-day activities.

Promote and support personalized medicine as a "model," including social, for improving health by taking advantage of advances in the field of genomics that open new opportunities to personalize therapeutic strategy, and/or to determine disease susceptibility, and/or to deliver timely targeted prevention interventions.

- Promote people's health and well-being through the development of education, awareness and prevention initiatives designed to promote a healthy lifestyle.
- Raise stakeholders' awareness of the value of scientific research and the significance of its positive impacts on people's health and quality of life.
- Actively contribute to national and international scientific debate, including by collaborating with agencies and various scientific entities, and carry out basic research and in the field of diagnostics, developing innovative models that ensure greater prevention and better protection of people's health.
- To disseminate good sustainability habits and practices to all stakeholders in order to incentivize their social and environmental engagement.

Scientific Research and Innovation

Scientific research and innovation are fundamental to the welfare of the entire country system as the basis of social and economic progress.

It is important to emphasize the importance of both knowledge creation and its application and dissemination. In this regard, it should be noted how the recent pandemic and consequent crisis in some sectors of the NHS, have dramatically underscored the country's lack of significant autonomy in the conception and production of diagnostic health care preps. This fact is the consequence of a gap, which has always characterized our biomedical system, between the creation of excellence, globally often at competitive levels, and its application.

Cogentech has always been committed to the reduction of this gap, and its Mission is to provide technologically advanced, innovative and high quality services, both to researchers engaged in the development of basic research (in the oncology and non-oncology fields) and to hospital facilities, for the diagnosis and treatment of cancer diseases.

The research and development projects and investments undertaken by Cogentech, which during 2021 committed the company to approximately 38.7 percent of total investment spending for the year, (compared to 25 percent in 2020), were aimed at creating an original and innovative proprietary position, which allows the company to maintain:

- one's competitive role
- develop new tools
- Develop new analysis techniques.

All planning is always geared toward continuous improvement in the ability of diagnostics and investigation to hereditary predisposition to the disease, thus enabling the timely delivery of interventions, both diagnostic and preventive.

One of Cogentech's strengths is the strong competence of its staff, the result of many years of experience in the specific field as well as a continuous training program aimed at maintaining a state-of-the-art level of preparation.

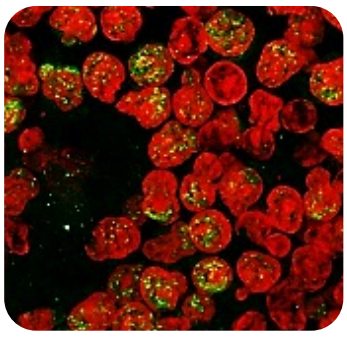
Associated with this is the strong technical and scientific collaboration link with the parent company IFOM, which can be called the "factory of ideas" to be developed and applied through Cogentech.

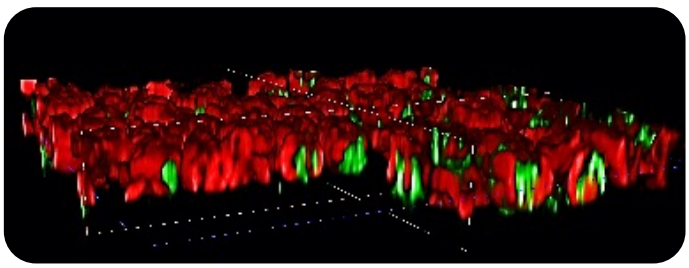
With this in mind, the research and innovation produced by Cogentech staff lead to the development of new strategies useful for identifying genes, proteins, and molecular mechanisms that play key roles in the development of neoplastic pathology and beyond.

These could then become the target of pharmacological molecules, which can reduce or even reverse the disease.

In this way, the knowledge obtained through the virtuously established synergy between the new scientific knowledge developed in IFOM and the technological expertise of Cogentech can be transferred to the health services market for the benefit of the community.

From the medical-scientific point of view, Cogentech's Benefit rationale is to promote clinical and translational oncology research, enabling immediate application in clinical practice of the advances in scientific knowledge occurring in the laboratory. This is also and especially in areas that, due to their niche nature, do not find significant interest and investment from commercial companies.





Confocal microscope image acquisition with 2D and 3D deconvolution - Histopathology Facility

Targets achieved in 2021

Cogentech, by its nature, has interest and necessity in keeping up with scientific and technological evolution.

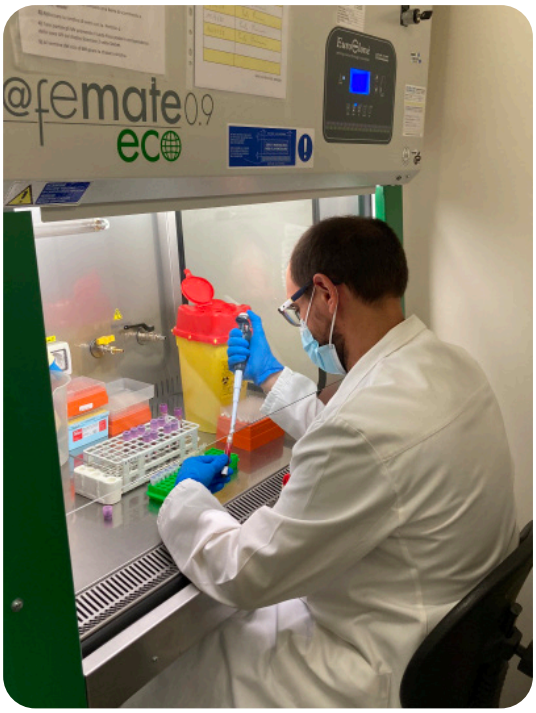
As a natural consequence, many of the goals achieved are the result of actual Research Projects that are prerequisites for understanding basic biological mechanisms as well as technological implementations, diagnostics, and therapeutic hypotheses.

Evolution of the Oncopan panel

In some types of heredo-familial cancers (breast/ovarian, pancreas, prostate, Lynch Syndrome, Familial Polyposis) the clinical manifestations are not always so well defined and are, in some respects, overlapping. The introduction of multi-gene panels for Next Generation Sequencing (NGS) allows an extremely advanced and original "one-step" approach, which allows simultaneous analysis of multiple genes. This strategy is particularly useful in cases of genetic heterogeneity of risk factors for a given cancer. It appears, in fact, increasingly evident that analysis alone, conducted on material extracted from blood, of the major susceptibility genes for each of the heredo-familial malignancies is limiting, reducing the rate of genetic risk detection.

For this purpose, the OncoPan® panel developed by the CGT Lab, was expanded by adding additional susceptibility genes for tumor development. In addition, genes of prognostic utility, specific for the analysis of endometrial cancer, and therapeutic utility, useful, if the investigation is performed on DNA extracted from tumor tissue, for their predictive value of response to therapy in various tumor types, were introduced.

The first version of the multigenic OncoPan® panel for NGS analysis of hereditary-familial tumors proposed to the market was developed by Cogentech's CGT Lab staff in 2019 (version 2): an innovative and competitive offering in the field of oncology molecular diagnostics!



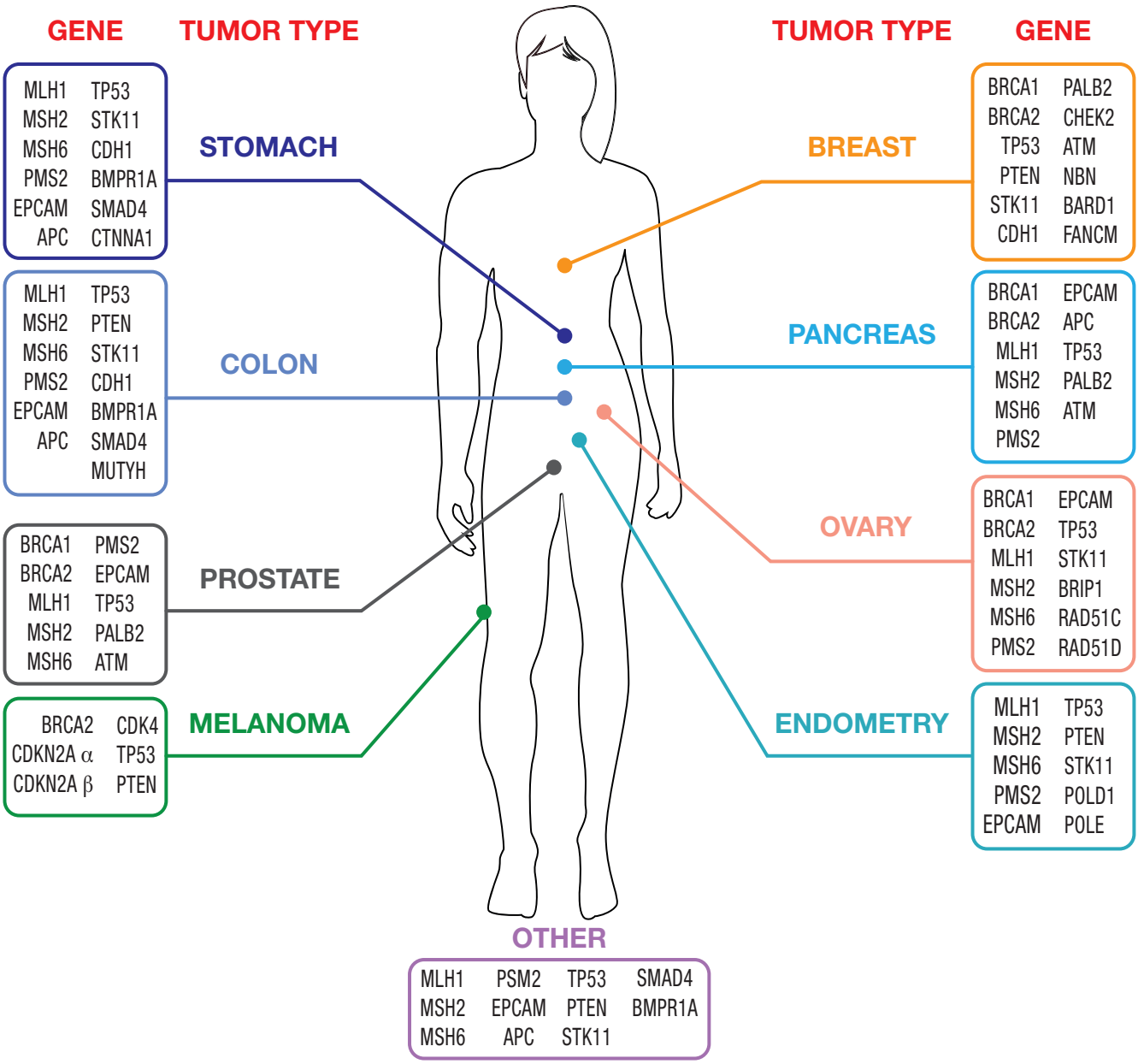
The research and development activity carried out in that 'year, focused on the validation of the panel for germinal analysis while, in 2020, this line of research was further expanded with the validation on somatic material of the OncoPan® panel (version 3).

Finally, this new version of the panel allows the analysis of several hundred nucleotide variations (SNPs) whose combined effect, termed Polygenic Risk Score (PRS), can modulate the risk conferred by the major susceptibility genes BRCA1 and BRCA2. The PRS-derived coefficient constitutes an added value of the OncoPan panel v3 that makes it peculiar compared to commercially available panels, and will allow personalizing the risk of developing cancer of patients analyzed with the panel.

Gaining new insights into the genes identified by our researchers as potential new diagnostic and/or therapeutic markers will be instrumental in facilitating their development in the clinical setting and further updating the OncoPan® panel with new gene regions of interest.

The need to improve the timing of report release, minimize errors, and optimize processes prompted the laboratory to automate protocols, through the use of robotic systems, consisting of automated dispensers integrated with programmable equipment. This has had a positive impact on the analytical process and optimized sample processing times.

The conception and validation phase of the OncoPan® panel v3, involved Dr. Sara Volorio, Dr. Valeria Pensotti, Dr. Stefano Fortuzzi, and Dr. Paolo Mariani.

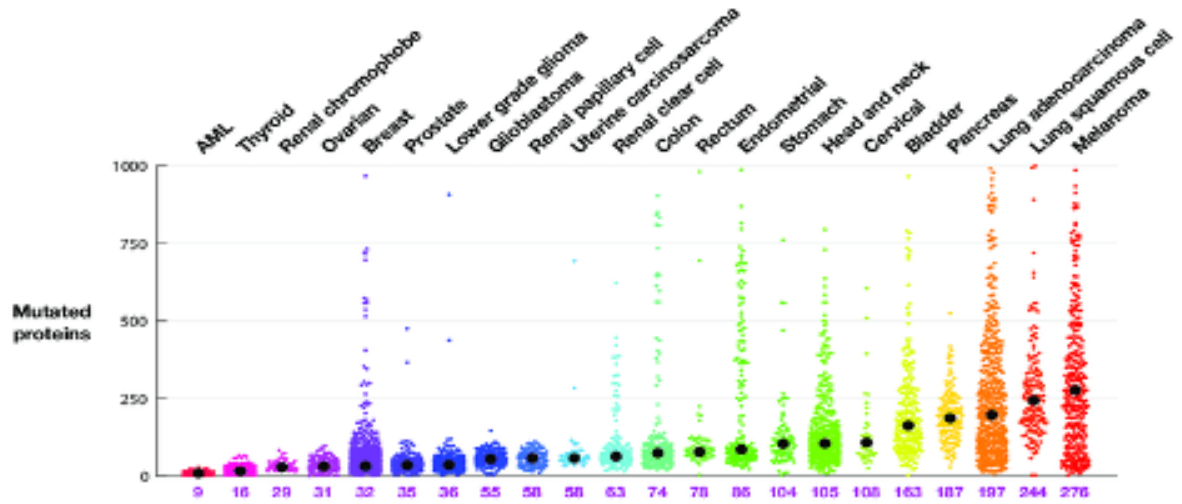

GENE
TUMOR TYPE
TUMOR TYPE
GENE
MLH1 TP53
MSH2 STK11
MSH6 CDH1
PMS2 BMPR1A
EPCAM SMAD4
APC CTNNA1
STOMACH
BREAST
BRCA1 PALB2
BRCA2 CHEK2
TP53 ATM
PTEN NBN
STK11 BARD1
CDH1 FANCM
MLH1 TP53
MSH2 PTEN
MSH6 STK11
PMS2 CDH1
EPCAM BMPR1A
APC SMAD4
MUTYH
COLON
PANCREAS
BRCA1 EPCAM
BRCA2 APC
MLH1 TP53
MSH2 PALB2
MSH6 ATM
PMS2
BRCA1 PMS2
BRCA2 EPCAM
MLH1 TP53
MSH2 PALB2
MSH6 ATM
PROSTATE
OVARY
BRCA1 EPCAM
BRCA2 TP53
MLH1 STK11
MSH2 BRIP1
MSH6 RAD51C
PMS2 RAD51D
BRCA2 CDK4
CDKN2A α TP53
CDKN2A β PTEN
MELANOMA
ENDOMETRY
MLH1 TP53
MSH2 PTEN
MSH6 STK11
PMS2 POLD1
EPCAM POLE
OTHER
MLH1 PSM2 TP53 SMAD4
MSH2 EPCAM PTEN BMPR1A
MSH6 APC STK11

Personalized medicine pilot project on thyroid cancer patients: Toward personalized therapy.

Genetic characterization of an oncologic disease, both at the level of the primary tumor and any secondary sites, can prove critical in the identification of the causes of the disease and the subsequent identification of targeted pharmacological strategies (personalization of therapy).

In this project, in collaboration with the University of Pisa, and aimed at the genomic characterization of medullary thyroid tumors (MTC), two approaches were integrated: the first, consisting of the search for genetic alterations at the level of tumor DNA and the second aimed at analyzing the gene expression profile (thus at the RNA level) peculiar to tumor tissues compared with their healthy counterparts.

In two patients (P1 and P2) with TCM, alterations in the coding portion of the human genome were sought by very high processivity sequencing (WES, whole exome sequencing), comparing tumor tissue, metastases, and normal tissue. This was done in order to monitor the possible activation of pathways amenable to drug treatment, and to validate alterations found by genomic analysis.

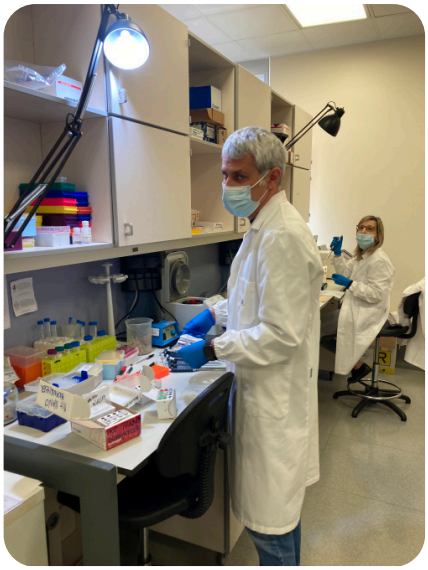


The number of identifiable mutated proteins in a tumor sample (Tumor Mutational Burden, TMB) is not constant, but varies depending on the tissue of origin; Genomic Unit).

TMB (Tumor Mutational Burden) or mutational burden of the tumor, an indicator of the genetic damage accumulated by the tumor and varying from tissue to tissue, was also calculated (see image). This biomarker allows patients to be stratified according to the efficacy of response to immunotherapy treatment, which is shown to be more effective in tumors characterized by a high number of mutations.

A RET gene variant (M918T variant) believed to be directly causative of cancer disease was identified in patient P1. This tumor variant (biomarker of pathology) confers sensitivity to drug treatments with specific inhibitors. This evidence was confirmed and further complemented by transcriptional analysis on RNA.

In contrast, patient P2 is characterized by medium to high Tumor Mutational Burden (TMB), with a mutational profile correlated with alterations that impact the efficiency of DNA damage mechanisms ('DNA mismatch repair deficiency'). A high TMB index increases the likelihood of positive response to immunotherapy treatment.



Molecular study of “weakly positive" COVID-19 swabs to define their clinical framing

The Covid-19 pandemic has affected as an event of exceptional urgency every working, health and scientific reality and has concretely placed Cogentech in the need to activate its technological units in the service of improving scientific knowledge on the subject.

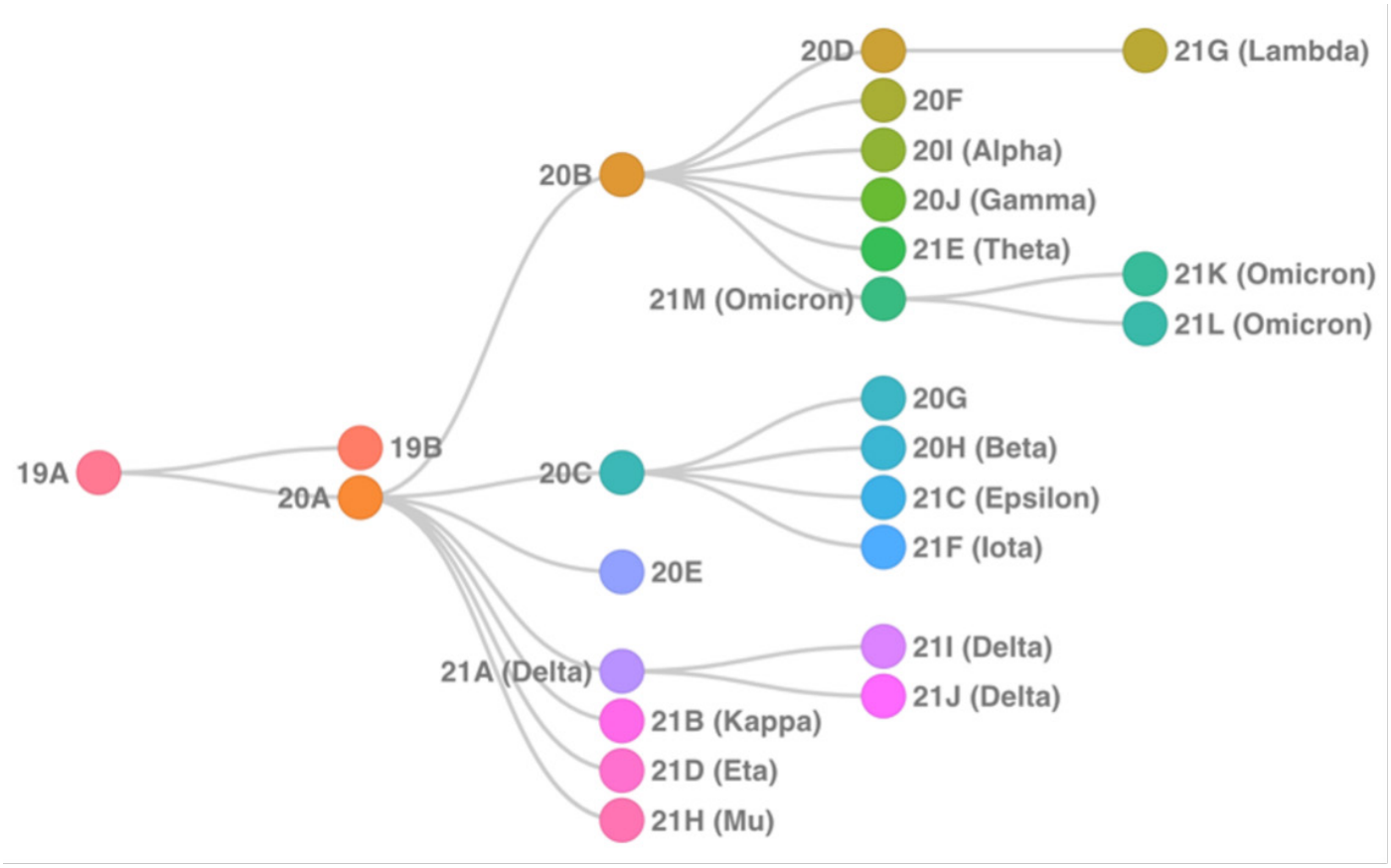
QPCR and Cogentech's Genomic Unit have been working in synergy in order to improve knowledge of COVID-19 infection and its multiple variants.

A company screening conducted during 2020-2021 included an oro-pharyngeal swab performed by the company physician, RNA extraction, and subsequent molecular RT-PCR assay to detect the possible presence of SARS-Cov-2 viral sequences in the samples. Out of about 350 study participants, 30 positive samples were detected.

In some circumstances, it was noted how a swab reported “negative" by ATS (Health Protection Agency), was “positive" or, more often, “weakly positive" on internal molecular testing.

In the wake of these observations, a project was designed and implemented to better understand the reasons for this discrepancy and, more importantly, to grasp its possible implications.

A viral RNA enrichment kit was used in positive or weakly positive buffers to characterize by NGS sequencing the integrity of the viral genome and define its membership in a particular strain. The viral genome was characterized with an average of 300,000 reads per biological sample. Interpretation of the sequencing data was performed using Viralrecon, an automated analysis procedure, developed by Nf-Core (https://nf-co.re/), a group of scientific developers that creates and makes available to the scientific community free analysis software.



In addition to the identification of variants and alterations that allowed each buffer/sample to be associated with a specific viral strain, the interest of the evaluation was to understand whether the entire viral genome or only incomplete sequences were present in the swabs detected as “weakly positive," with obvious reduction in the subject's potential risk of infectivity.

Sequencing reads aligned with respect to the Genomic sequence of Sars-Cov-2: we show the completeness of the viral genome in the top panel, and only partial coverage in the two panels below, all related to the same patient at different times of infection (Source Genomic Unit Facility)

In the study, we showed correlations between the Ct (cycle-threshold*) shown in RT-PCR and the viral genome integrity found through NGS.

Analyzing the RT-PCR results in light of the NGS results, we appreciate the high sensitivity of the kit used for RT-PCR assays that nevertheless defines as "weakly positive" subjects that by NGS sequencing are found not to have complete viral genome integrity and are likely not infectious.

These observations make it possible to suggest a lowering of the threshold for defining "positivity" of the RT-PCR assay, which at present appears to have a very high sensitivity, possibly exceeding the very principle of health safety.

Design, development and deployment of a new application software for managing laboratory activities: the LAG (Laboratory Genomic Analysis) project

The CGT Lab's activities in recent years have become increasingly complex due to the development of new analysis techniques and the increasingly articulated demands from customers.

Managing laboratory activities using reliable and versatile software that reduces the risk of errors and maintains data traceability while complying with GDPR is a fundamental requirement for a biomedical laboratory's processes.

Therefore, since 2018, the CGT Lab, and in particular, Dr. Giovanna De Vecchi, have been designing innovative application software from scratch, supported by the specialized firm BCS (Biomedical Computering Systems s.r.l.).

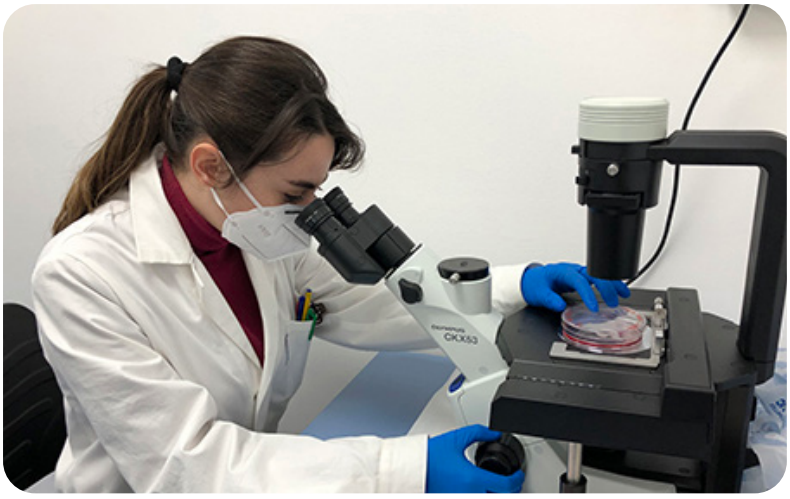
In 2020, the development of the final program structure was completed, retrieved the historian from the previous management with a reverse engineering process, to move, in 2021 to the final testing and validation phase of Priamo LAG.

Since April 2021, the management system has gone into production, and to date about 2,000 requests have been processed.

Evaluation of liquid biopsy for clinical management of hereditary breast and/or ovarian cancer

In 2019, Cogentech was awarded a prestigious PON (National Operational Program "Research and Innovation" 2014-In 2019, Cogentech was awarded a prestigious PON (National Operational Program "Research and Innovation" 2014-2020) grant from the Ministry of Education, University and Research (MIUR) for the project entitled "BiLiGeCT - Liquid Biopsies for Clinical Management of Tumors." Cogentech is the lead partner in this ambitious project, carried out in collaboration with five other prestigious Italian entities (Carebios srl, Consorzio Interuniversitario Nazionale Metodologie e Processi Innovativi di Sintesi - CINMPIS, Istituto Oncologico del Mediterraneo S.p.a., Istituto Superiore di Sanità and Università degli Studi di Torino). In its role, Cogentech organizes quarterly meetings to share results with with the participation of all partners

With this study, Cogentech aims to answer still open questions in the clinical management of subjects carrying mutations in the BRCA1/2 genes (with greater genetic predisposition to the onset of breast/ovarian cancers), socially weak subjects



whose protection is not always readily recognized by social and health institutions. At the same time, the project, taking advantage of the prerogatives of subjects with defined genetic risk of developing cancer disease ("risk patients"), intends to evaluate the possibility of implementing early cancer diagnosis through a non-invasive methodology such as liquid biopsy.

Specifically, the project aims to use liquid biopsy for early detection of disease onset or recurrence and to monitor disease and appropriate therapy use in BRCA mutated individuals. Also planned is the development of innovative cell-based assays to study the functionality of BRCA1/2 gene variants of uncertain significance (Variants of Unknown Significance, VUS).

This project has important social, political and economic implications in historically and geographically disadvantaged areas of Southern Italy. Cogentech, in fact, operates within the project through the new Operating Unit, at the Science and Technology Park of Sicily, while fostering a fruitful exchange of technical-scientific knowledge with local authorities.

To this end, 10 technical/scientific professionals have been hired to work on the project. One part of the group is dedicated to bioinformatics activities while the other part of the group carries out experimental activities for the development and application of new protocols.

In 2021, with the completion of the set-up of the new laboratories and the delivery and testing of the instrumentation dedicated to the project, experimental activities finally began at Cogentech's new facility in Catania.

Already, the first interesting results have been obtained from a project, which aims to develop new diagnostic tools for individuals carrying mutations in the BRCA1/2 genes and cancer patients in general. The ultimate goal is not only early detection of cancer onset or possible recurrence, but also monitoring of therapy.

Enhancement of computational capacity of the Catania Laboratory

In order to help maximize the speed of execution of calculations of relevant scientific interest, especially those related to histopathological image analysis, such as mathematical models, numerical simulations, machine learning and artificial intelligence applications, a special HW implementation was introduced in 2021: a Tesla A100 multi-GPU cluster.

This allows researchers to process huge amounts of calculations in parallel in a very short time.

More effectiveness and more time to devote to research!

Development of database for quality data management (NGSource)

In order to improve, speed up and track some steps of the processes that lead to the 'issuance of reports, a database has been developed that collects the quality values of NGS runs (NGSource) and at the same time allows extrapolating statistics for the periodic indicator reports required by the certifications held by the CGT Lab (UNI EN ISO 9001:2015, SIGUCERT and UNI EN ISO 15189:2013). NGSource is a database installed on an internal server at Cogentech that is accessed only by authorized personnel and also allows for quick verification of workflow activity regarding the Next Generation Sequencing (NGS) part of the experiments.

Development of methods in nanoLC/MS for metabolomic analysis of biological samples

Metabolomics is the study of low molecular weight molecules present in different biological matrices. The metabolomic approach allows the study of intermediates and products of cellular metabolism that can be analyzed from a variety of sample types: tissues, biological fluids, cells, and cellular constituents. Metabolomic analysis reflects the physio-pathological state of the model studied, thus allowing a metabolic fingerprint to be drawn that can be used to understand important biological mechanisms underlying disease or to intervene therapeutically in disease states.

Among the many instrumental techniques, the most widely used in metabolomics is mass spectrometry coupled with liquid chromatography (LC/MS). This instrumental approach, of which the Proteomics Unit, directed by Dr. Angela Bachi has internationally recognized expertise, allows the separation of different metabolites and their accurate identification and quantification.

The development of high-sensitivity methods thus makes it possible to analyze the metabolic status, qualitatively and quantitatively, of valuable and low abundance biological samples.

During 2021, in the Proteomics Unit of Cogentech, activities were carried out to optimize the conditions of analysis to increase the number of detectable and quantifiable metabolites in biological samples.

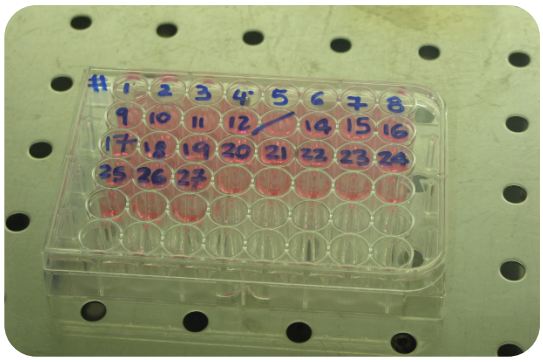
The development of metabolomics techniques is particularly relevant in the study of various diseases, including cancer, which are characterized by significant metabolic alterations, very often underlying the aggressiveness of the disease itself.

Development of isogenic cell models by "genome editing" methodologies for the functional study of specific BRCA1/2 variants and their sensitivity to targeted therapies

It is known that individuals who carry certain germline mutations in the BRCA1/2 genes involved in the DNA damage repair process have a significantly higher risk than the rest of the population of developing cancer, especially breast and/or ovarian cancer, during their lifetime.

Indeed, there are variants capable of generating alterations in the structure and/or function of BRCA1/2 proteins, termed pathogenic. In addition to these, about 15 percent of the variants detected have uncertain clinical significance (Variants of Unknown Significance or VUS) for which there is no data associated with an increased risk of developing the cancer pathology. This uncertainty poses an important problem about the most appropriate prophylaxis and treatment of the disease in these individuals. In fact, the diagnosis of these variants still remains very unsatisfactory because it does not provide a clinically useful response to individuals who carry these variants and their family members.

The main goal of the project is to develop an innovative in vitro cell model for functional characterization of VUS and for screening PARP inhibitors, new therapeutically active molecules.



To achieve the goal, CRISPR/Cas9 genome editing technology was used to generate cellular models suitable for the functional study of gene variants of BRCA1/2 genes with as yet uncertain clinical significance. The expertise of Cogentech's "Genome Editing" unit in introducing targeted mutations into the genome proved essential for achieving the experimental goals described.

During 2021, the Genome Editing Unit's activity focused on the development of new isogenic cell models. This R&D activity, is also closely related to the project entitled "BiLiGeCT: Liquid Biopsies for Clinical Management of Tumors" (covered elsewhere in the Report).

After fine-tuning of all experimental conditions, this protocol will be rapidly applied to the new VUS identified by Cogentech's CGT lab to supplement the molecular data produced by the lab.

An essential feature of the model cell line for this type of experiment is the nonlethality of the phenotype induced by the absence of the BRCA1 gene. Following gene deletion experiments in several candidate lines, we identified the MCF-7 cell line as meeting this prerequisite.

In order to rapidly introduce the VUS mutations to be studied, these cells were engineered by targeted deletion of two of the three copies of the BRCA1 gene present in this line resulting in so-called hemizygous cells. Several MCF-7 BRCA1 hemizygous clones were then genome-wide analyzed by NGS sequencing to check for potential CRISPR/Cas9-induced genetic alterations in other cancer genes.

The results obtained lay the foundation for the generation of isogenic lines for the functional study of VUS variants of the BRCA1 gene and the possibility of testing the sensitivity of these variants to known anticancer drugs, as well as for the development of new molecules, with enormous application potential.

The experiments of the various research lines involved the participation of several Cogentech researchers: Dr. Mario Cinquanta and Dr. Marisa Aliprandi (Genome Editing Unit); Dr. Laura Tizzoni and Dr. Valentina Dall'Olio (Quantitative PCR Service); Dr. Paolo Mariani and Dr. Sara Volorio (Sequencing Service). Dr. Giovanni Carapezza, Dr. Tania Velletri and Dr. Annalaura Cordaro (Cogentech Catania) also collaborated.

The project is carried out in collaboration with Dr. Paolo Radice (National Cancer Institute, Milan) and under the supervision of Dr. Marco A. Pierotti.

New Goals for 2022

Extension of the Scope of ISO9001 Certification to Training Delivered

In view of the quality and level of technical scientific depth of the courses provided, Cogentech has started the process of extending ISO9001 certification to Training (Sector 37) as well.

The Scope of Application will therefore include the Design and delivery of training courses for the qualification and scientific-technical upgrading of researchers, professionals and specialists.

This scope is already extensively detailed within the Articles of Association of Cogentech, which aims, among other things, to organize training courses for the creation and retraining of professional figures in the area of health, veterinary and agribusiness.

Our goal starts from the knowledge that the delivery of training has always been one of the flagship activities of the Mouse Genetics Service, with experience in courses of various types, internal and external, involving learners from very different fields.

Obtaining ISO 9001:2015 certification for the training delivery process will enable:

- Delivering quality, effective and tracked training.
- Increase attractiveness to external customers.
- Lay the groundwork for embarking on the path to becoming a CME provider.
- Extend the Mouse Genetics Service's expertise in training to all Cogentech entities.

Extension of ISO9001 certification to the Local Unit of Cogentech Catania

By 2022, the process for ISO9001 certification of PON laboratories will be initiated.

The process will involve all activities of the Catania Unit and will be implemented similarly to other Cogentech facilities, with the involvement of all staff.

The ISO9001 certification of the new Unit, strengthened by the Commitment of Cogentech Management, will enable greater control of processes, with a view to Continuous Improvement. This will help open up new prospects for affirmation in the Territory, such as the provision of diagnostic services.

Transcript analysis for evaluation of the effect on RNA splicing of variants of unknown significance (VUS).

The advent of next-generation sequencing (NGS) has greatly enhanced the process of identifying predisposition variants for cancer development, also giving the possibility of identifying a large number of potential new cancer predisposition genes with a significant impact on prevention strategies.

However, it is difficult to assess the clinical significance of some variants.

Some of these variants of uncertain significance (VUS) confer pathogenicity through an effect on mRNA splicing and can be classified with high efficiency by in vitro assays.

Cogentech's CGT Lab intends to collaborate with the U.O. "Hereditary Tumors of the Digestive System" of the IRCCS Istituto Nazionale dei Tumori (Milan, Italy) to evaluate the effect on mRNA splicing of variants of uncertain significance in digestive tract cancer predisposition genes, with the aim of classifying them and thus improving the identification of individuals genetically predisposed to cancer, allowing them to be targeted through precision medicine for personalized surveillance and risk reduction measures.

Evaluation of liquid biopsy for clinical management of hereditary breast and/or ovarian cancer

One of our future goals, for the Catania site, is to 'widen the circle of our clinical collaborators so as to include biopsies from Sicily in the project. The material provided by the latter, together with that already collected in 2021, will be dedicated to the experimental activities envisaged by the project to achieve the set goals:

- Development of new diagnostic tools for individuals carrying mutations in BRCA1/2 genes and cancer patients in general;
- Early detection of cancer occurrence, its eventual relapse, and its treatment.

Extension of PriamoLag

The innovative PriamoLag software, developed to manage laboratory activities, has been further implemented, with the creation of the Request Management Portal (Priamo PGR) that will be put into production in early 2022.

Priamo PGR will allow physicians to complete requests directly online, avoiding the need for paper forms. By also allowing referrals to be downloaded once available, the flow of information will be made even faster and more secure.

With the extension of PriamoLag, Cogentech increases its flexibility and competitiveness in the public and private diagnostics market. At the same time, with a view to greater environmental sustainability, Priamo PGR will enable a significant reduction in paper and ink consumption, indicative of a clear "digital transition" in Cogentech's business.

Possible association between breast prosthetic implantation and development of anaplastic large cell lymphoma (BI-ALCL)

Genomic Unit project commissioned by Ministry of Health and carried out in collaboration with ISS (Istituto Superiore di Sanità).

In a small minority of cases there is development of anaplastic large cell lymphoma in breast implant recipients, for reasons not yet identified but related to possible genetic predisposition. The aim of the present project is to investigate its possible associations in case series of 82 subjects, including 41 who developed lymphoma following implantation of prostheses and 41 controls who, despite the presence of prostheses, did not develop any pathology.

DNA is extracted from blood samples and used for fragment library generation and ultra-high-processivity exonic portion sequencing (NGS or Next Generation Sequencing) in order to identify germline (carried by 100% of cells) and somatic (carried by only a small fraction of cells) molecular alterations present in affected subjects and absent in healthy subjects that predispose to and participate in the pathogenesis of breast implant-associated anaplastic large cell lymphoma (BI-ALCL). Ongoing Study.

Identification of germline molecular alterations that may be a possible risk factor for non-small cell lung cancer (NCLC) in non-smokers.

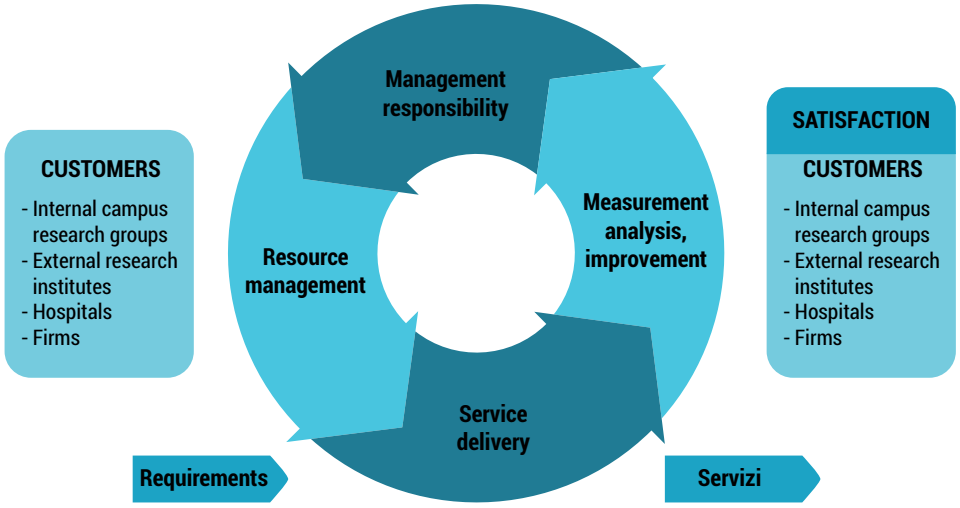
Genomic Unit project in collaboration with INT (National Cancer Institute, Dr. Manuela Gariboldi)

Retrospective study carried out on case series of 60 subjects who, despite being non-smokers (never smokers) developed lung cancer (NSCLC); study aimed at identifying germline molecular alterations (carried by 100% of cells) that constitute risk factors and predispose to the onset of the disease. The study involves the search and identification of germline mutations in the exonic portion of DNA (exome) that predispose to the development of the disease and was carried out by generation of fragment libraries and sequencing of the exonic portions at very high processivity (NGS or Next Generation Sequencing), followed by bioinformatics analysis of the data obtained. Ongoing Study.

A quality service

Due to the criticality of the services offered, Quality has always been a pivotal element for Cogentech. It manifests itself in the careful verification of both internal and goal-oriented processes required by the client, within an ever-growing context.

CONTINUOUS IMPROVEMENT QUALITY MANAGEMENT SYSTEM



The Processes approach, the analysis of Risks and Opportunities, the drive by Management, the continuous attention to the needs of the Customer, and Continuous Improvement are the fundamental principles that Cogentech is inspired by.

Attention to customers' needs is concrete, with the understanding that every interaction can prove to be a useful opportunity to give rise to new opportunities and to create value for society.

Cogentech is therefore committed to understanding both the present and future needs of customers in order to win their trust. The company's attention is, of course, also directed to the needs of all stakeholders, such as partners, associates and suppliers.

With the aim of constantly monitoring and always managing its Quality Management System to the best of its ability, Cogentech has identified indicators to evaluate the performance of the services provided. Specifically, customer response time, average rating obtained in the customer survey, and the number of complaints received are subject to analysis.

The most significant moment for the operation of the QMS is the Management Review: here various elements are analyzed, including, for example, the degree of customer satisfaction, indicators, context analysis, risks and opportunities encountered i.e., a precise and up-to-date overview of the consistency of the services offered by Cogentech, which is useful for formulating new objectives and contributing to continuous improvement.

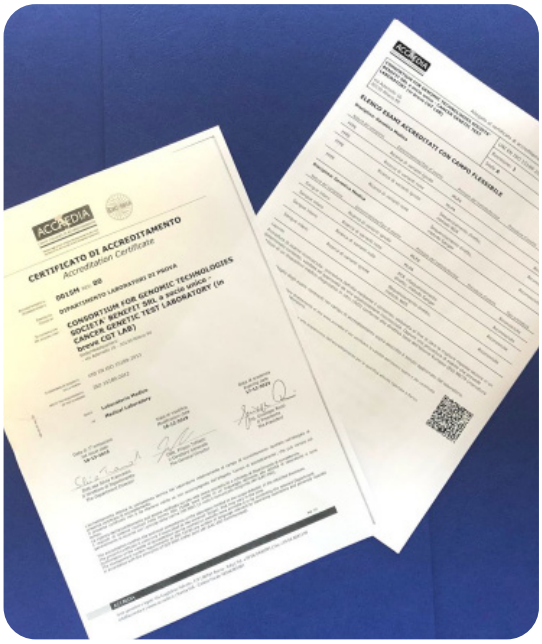
The quality management system (QMS), has been structured over time through continuous adaptations to mandatory regulations, to the changing environment, as well as to the requirements of the standards with which, over time, Cogentech has been certified and/or accredited, thus leading to tangible benefits in business performance.

Cogentech, obtained certification in accordance with UNI EN ISO 9001:2015 issued by Bureau Veritas Italia spa on 08/08/2017 (Certificate No IT256850), renewed on 24/08/2020 for the following services: Cancer Genetic Test Lab (CGT Lab), Sequencing Service, QPCR Service, Microarray Service, Mouse Facility, Histopathology Service.

Since 2011, CGT Lab has been accredited with the National Health Service (Resolution No. 929 ASL Milano), and is listed in the Regional Register of Accredited Facilities (Registration No. 1118) in the sub-branch of Cytogenetics and Medical Genetics for Molecular Genetics activities. Since 2015, the CGT Lab has also been certified by the Italian Society of Human Genetics (SIGUCERT Certificate No. IT282620).

In addition, in 2019 CGT Lab achieved UNI EN ISO 15189:2013 accreditation by ACCREDIA (number 0015M) for Medical Genetics examinations, with a steady increase in the number of accredited examinations in Flexible Field.

As also stated on CGT Lab's Service Charter, Cogentech has entered into an agreement with ACCREDIA in which mutual obligations are defined; maintaining accreditation involves ACCREDIA's periodic assessment of the laboratory's technical and managerial competence in accordance with the requirements of UNI EN ISO 15189:2013 and additional ACCREDIA requirements.



To achieve all these ambitious goals, it is essential that the people who work for Cogentech are competent, trained, and eager to make their own contribution, feeling Quality as a true added value.

Quality has a cost, both for those who offer it and for those who demand it.

In the field of Scientific Research, obtaining reliable, reproducible, correctly interpreted data on time provides incalculable support to researchers.

Often the sample to be analyzed is valuable, the reagents are expensive, the technique to be applied is extremely refined, the scientific question difficult...in this situation, resorting to a highly specialized facility equipped with advanced, validated and certified protocols is the best choice.

And here the "cost" incurred becomes "gain" if all the parameters just remembered are carefully evaluated.

Of course, reliability and timeliness are even more significant in the health care setting, where delaying a diagnosis a few days can compromise a treatment protocol. And here even more so, a participatory Quality Management System lends additional credibility to the laboratory.

People at the center

Cogentech is committed daily to valuing its professionals, operating safely and offering professional and personal services that ensure the satisfaction and well-being of employees. It is important that all people feel part of an overall project, in which each person is aware that he or she constitutes a partial element, but equally essential to the whole. And it is people, with skills yes, but also with their emotions and sense of belonging that enable Cogentech to offer its services in accordance with the highest industry standards.

As also stated within the Code of Ethics, Cogentech promotes a climate of mutual respect where everyone must interact with others with honesty and dignity.

Respect for the individual, as a founding value, in its fullest sense, is also reiterated. And thus: non-discrimination, transparency, individual empowerment and trust.

Accordingly, Cogentech is committed to safeguarding workers from acts of psychological violence and seeks to counter any attitude or behavior that is discriminatory or personally injurious, strongly condemning sexual harassment and urging the avoidance of behavior or speech that may disturb a person's sensibilities. Anyone who believes that he or she has been subjected to harassment or has been discriminated against for reasons related to age, gender, sexuality, race, health status, nationality, political opinions and religious beliefs may report the incident to the Supervisory Board, which will assess the actual violation of the Code of Ethics.

In 2021, as in 2020, no reporting occurred.

As of December 31, 2021, Cogentech has 38 employees, 1 more than in 2020. The workforce is predominantly composed of women (57.9 percent) and young workers between the ages of 30 and 50 (65.8 percent). Out of 38 employees, 28 have permanent contracts (11 men and 17 women) and 10 have fixed-term contracts (5 men and 5 women). Only one employee (female) is part-time. In addition, Cogentech cooperates continuously with 4 external consultants, 3 men and 1 woman, who are over 50 years old. 99% of Cogentech's workers have full-time contracts.

	2021			2020			2019		
Headcount as of 12/31	**Women**	**Men**	**Total**	**Women**	**Men**	**Total**	**Women**	**Men**	**Total**
Squares	**3**	**3**	**6**	**3**	**3**	**6**	**1**	**2**	**3**
of which less than 30 years old	0	0	0	0	0	0	0	0	0
Of which age between 30 and 50 years old	1	1	2	1	1	2	0	1	1
of which are over 50 years old	2	2	4	2	2	4	1	1	2
Employees	**18**	**13**	**31**	**16**	**14**	**30**	**16**	**10**	**26**
of which less than 30 years old	4	1	5	2	3	5	1	0	1
Of which age between 30 and 50 years old	11	11	22	11	10	21	11	8	19
of which are over 50 years old	3	1	4	3	1	4	4	2	6
Workers	**1**	**0**	**1**	**1**	**0**	**1**	**1**	**0**	**1**
of which less than 30 years old	0	0	0	0	0	0	0	0	0
Of which age between 30 and 50 years old	1	0	1	1	0	1	1	0	1
of which are over 50 years old	0	0	0	0	0	0	0	0	0
Total	**22**	**16**	**38**	**20**	**17**	**37**	**18**	**12**	**30**

100 percent of employees are covered by CCNL.

The development of human capital

Cogentech's Personnel, each within the scope of their role, are invited and supported to undertake a path of continuous improvement, throughout their working careers.

Indeed, Cogentech's management is aware that the continuous and constant development of its Human Capital is one of the cornerstones on which the improvement and definition of new strategies, to be applied in both the research and diagnostic fields, rests.

All this finds concrete application in management systems aimed at integrating different roles and professions, valuing and recognizing individual contributions and professional growth.

Cogentech worker training

Employee development is a process through which all workers, in harmony with the job description and personal aptitudes, improve existing skills, acquiring new skills useful for improving the effectiveness and efficiency of work. Training sessions are also an opportunity to receive input and ideas from each individual worker and, more importantly, are a crucial time to strengthen the bond between worker and Company.

Training courses are organized by Human Resources, Safety Management or Quality Office or facilities. Or they may be courses organized by external entities. All courses are formally structured with an attendance register and, depending on the type of training event, there may be a final test and subsequent issuance of a certificate.

Cogentech staff are required to participate in both legally required courses (e.g., CME) and other internally organized training events, depending on their role within the Organization and their area of expertise.

Average hours of training	2021			2020			2019		
	Women	Men	Total	Women	Men	Total	Women	Men	Total
Squares	65,15	26,00	45,58	82,00	14,30	48,20	0,00	8,00	5,33
Employees	26,44	15,19	21,87	29,30	15,40	22,80	28,19	14,60	22,96
Workers	8,00	0,00	8,00	2,00	0,00	2,00	2,00	0,00	2,00
Total	**30,69**	**17,21**	**26,16**	**35,80**	**15,20**	**26,40**	**25,17**	**13,50**	**20,50**

Below is a table showing the average hours of training, broken down by professional category and gender, provided during 2021 to all internal Cogentech employees:

Each facility and office provides its own annual Training Plan, including internal and external courses. Courses held within Cogentech's facilities are held under the responsibility of the Facility Manager and may include courses preparatory to accessing the various facilities as well as courses aimed at training or the proper use of laboratory instruments and compliance with the prescribed safety measures.

In preparing the Annual Training Plan, ISO9001-certified facilities provide specific training courses. CGT Lab, as a healthcare facility, must also consider mandatory CME (Continuing Medical Education) credits, required by law by a national program, active in Italy since 2002.

Training courses provided to employees

Training courses provided to employees	2021	2020	2019
231 Organization and Management Model	16	16	9
Courses in Health and Safety	146,5	74	50
Privacy Course (196/2003)	8	18	3
Quality Certification Course	74	57	100
Specific professional training courses	663,5	811	407
Total training hours provided to employees	**916**	**976**	**569**

In addition, to promote a climate of cooperation and transparency, training events are organized to improve knowledge of issues of common interest, such as, for example, proper waste management and maintaining Quality Management System requirements.

In 2021, we were finally able to deliver some Emergency Squad refresher courses that had been stuck due to Covid-19.

About 20 staff members between IFOM and Cogentech also enthusiastically participated in the training and education course for the use of self-contained breathing apparatuses-an extra garrison to cope with the under-oxygenation risk.

In 2021, a number of Fire and First Aid officers were also trained for the Catania office, which now has a full-fledged autonomous Emergency Response Team.

Thanks in part to all these specialized courses, the number of Safety-related training hours has more than doubled since last year and nearly tripled since 2020.

Within the IFOM-Cogentech campus, it is possible to participate almost daily in high-level scientific-technological seminars with prominent speakers from the international scientific world. The prolongation of the Covid-19 issue even in 2021, has unfortunately slowed down this activity, as well as the organization of in-person events. In spite of this, these valuable seminars still continued, but in a different guise: the in-person meeting was replaced by meetings via the various digital platforms, still allowing for the cultural enrichment of the staff.

As was the case in 2020, the wide range of thematic webinars offered by various organizations, which are often free of charge and of short duration (1-2 hours maximum), has made it easy to take advantage of them without the complication due to travel and without interrupting work activities. Even at the demise of some restriction measures, the “webinar” or “videoconference” formula is now a widely exploited and established mode.

Training delivered by Cogentech staff

Mouse Genetics

Training Course	Hours 2021	2020 Hours
Enclosure access course (online and in-person)	181,5	218,5
Course "Update on Mouse Genetics service quality management system according to UNI EN ISO 9001:2015" (in attendance)	6	0
Course "Update regarding Operational Instruction 7.14B.35 Laboratory Supply" (in-person) (online)	3	0
*Course "What should you know about your rodent facility?" (online)	315	189
*Course "Fundamentals of management for a modern rodent enclosure" (online)	178,5	189
*Course "Introduction to microbiological monitoring in rodents facilities" (online)	329	0
Tecniplast employee course	0	18
Course "Autoclave use and cart handling in the Building 13 enclosure"	0	2
Total training hours provided externally	1013	616,5

**Courses provided with the Guido Bernardini Foundation.*

Below is the table containing the training courses provided by Mouse Genetics staff (online, in-person or blended modes).
The first three courses cover access to the facility and continuing education within the ISO 9001:2015 system.
The other courses are organized by the Guido Bernardini Foundation, a nonprofit, independent organization that aims to disseminate education in the field of laboratory animal science, helping to spread the principle of the 3Rs, or Replace, Reduce & Refinement.

In summary, it is the principle taken up by the European legislation that Legislative Decree 04/03/2014, whereby for animal experimentation the need for animal use, the numerosity and the model to be used must always be carefully justified.

The head of Mouse Genetics is among the Foundation's historical faculty. In 2020 there were 378 hours of training organized with the Bernardini Foundation, in 2021 there were as many as 822.5 going to underscore the staff's commitment to publicizing the proper and ethical use of animals for experimental purposes.

Overall, in 2021, Mouse Genetics devoted as many as 1013 hours to training delivery, an increase of more than 60 percent over 2020.

All of this demonstrates that despite the persistence of the Covid-19 pandemic, training for the purpose of proper enclosure access and ethical use of animals for experimental purposes is definitely a priority for Cogentech.

Webinar event

In March 2021, in collaboration with EnGenome, Cogentech organized an online seminar, which was attended by more than 70 specialists from all over Italy.

In this very technical-specialist seminar, Dr. Sara Volorio, Bioinformatics Analysis contact person in the Sequencing Unit of Cogentech, explained the approach used to validate NGS data in the reality of oncology diagnostics, particularly for the analysis of CNVs (Copy Number Variations).

Health and safety protection

The Code of Ethics of Cogentech Srl SB, has among its fundamental principles the constant commitment to spread and consolidate the culture of safety, developing awareness of the risks of hazards in the workplace and consequently promoting responsible behavior by all employees.

Cogentech offers all its workers a safe, welcoming, clean and well-maintained work environment in compliance with current regulations.

Following the COVID-19 pandemic, a series of interventions were activated for worker safety aimed at verifying and maintaining optimal sanitation and operating conditions of fancoils and splits in addition to carrying out a series of useful projects to address the Covid risk (e.g., swab campaign and serological examinations).

Workplace safety, however, is not seen as a mere list of regulations to be met: rather, it is experienced as a shared responsibility. Cogentech workers, in fact, are active participants in company safety. Upon detecting a potentially dangerous situation (near miss), everyone is aware of the need to promptly report what has been noticed, in order to be able to implement all necessary measures to prevent the recurrence of similar situations, thus contributing to building a safer workplace every day.

The Prevention and Protection Service, which assesses and manages the risks present in the company, consists of easily accessible people whom all workers can contact at any time, either in person or via dedicated e-mail.

The working group, joint IFOM and Cogentech, in addition to the figures of RSPP, ASPP, Medical Officer and Safety Manager is composed of attentive RLSs with a deep knowledge of the environment and possible critical issues. They are joined by knowledgeable and responsible Supervisors, carefully identified by the LD. Supporting them is a large Emergency Team, whose employees are well distributed among the different buildings of IFOM and Cogentech. During in 2021, Cogentech's Emergency Team did not perform the classic evacuation test because, together with IFOM employees, it was tested by a real and unexpected emergency. In fact, on June 15, 2021, a drill working at a construction site next to our headquarters fell on an IFOM building. The reaction of the staff, past the first moments of bewilderment, was unprecedented. Emergency Teams immediately activated to facilitate evacuation from offices and laboratories. Staff spontaneously and quickly gathered at the Gathering Point for roll call. In this context, the presence of the Company Physician helped to reassure those present. At the same time, the Maintenance Teams intervened on the facilities (gas interception, water supply interruption, electricity disconnection...) to contain the effects of the incident. By the time the Law Enforcement and Emergency Vehicles (Fire Brigade, Civil Defense, Police, ATS, Ambulances) arrived, the securing was well underway and the necessary documentation available.

The team then cooperated productively, with preparation, efficiency, and the necessary lucidity, providing help where it was needed and giving support to the law enforcement agencies that intervened.

At this juncture we all had tangible evidence of how the time spent over the years in conducting evacuation tests was a fruitful investment.

During 2021, out of 62,854 hours worked (both in the Milan office and at the local unit in Catania), there were no occupational accidents or commuting accidents.

The only near miss recorded concerns a report on placing more emphasis on the use of common dispensers at a time when the focus to be placed on Covid -19 risk management must be kept high.

The company intranet, already exploited for Safety Data Sheets and Procedures (Safety Space), was further exploited in 2021, creating a dedicated space, shared between IFOM and Cogentech, for information, procedures and documents useful for Covid emergency management. Applications have also been developed over the years to facilitate access to documents and speed up the registration of the use of hazardous substances.

Awareness and sensitization to safety issues relies heavily on education and training, which aim to keep the attention of all workers high and constant on issues related to occupational safety and hygiene. The training, delivered in an interactive mode, asking learners to contribute questions and observations regarding the topics covered, is often based on creative examples, photos and videos that are perfectly cast in the daily reality of the researchers.

The careful assessment and containment of chemical risk was also done through the application of the CLP (Classification, Labeling and Packaging of Substances and Mixtures) regulation. On each bottle of internally prepared solution there are pictograms related to the hazards of the substance, and there is a QR code that when framed by one's cell phone, allows the operator to obtain information related to the recipe and access the safety data sheets of the individual components of the solution.

During 2021, despite the daily effort to manage the Covid-19 emergency, health and safety management activities continued at full speed, allowing almost everything that had been planned to be completed. At the Regular Meeting in early December, the following Risk Assessment Documents (DVR) were presented for the Milan office: the General DVR (including all risks present in Cogentech), the Carcinogenic Risk DVR, and the Electromagnetic Fields DVR. Data useful for the reworking of the Chemical Risk DVR, which is being finalized, were also collected.

General DVR, Chemical DVR; Carcinogenic DVR and Biological DVR were also prepared for the Catania site. A definitely extensive and thorough assessment, considering that the start of activities is quite recent!

Covid-19 Health Emergency Management

The arrival of SarS-CoV-2 into our daily lives in early 2020 has left relevant repercussions worldwide, highlighting personal, community and economic fragilities.

Since early 2021, with the availability of effective vaccines, new strategies have been introduced nationwide to address this emergency situation, such as, a progressive vaccination campaign and the subsequent introduction of Green Pass and Super Green Pass.

IFOM and Cogentech workers, each according to his or her expertise, have steadily and carefully pursued both scientific research and diagnostics, both of which are at the core of our mission.

To this end, Cogentech has activated new projects to continue the "Safety in the Workplace" campaign in 2021.

The first activated project, started in 2020 and continued in 2021, was the gold-pharyngeal swab campaign, with the aim of promptly detecting and isolating every Covid-positive, asymptomatic individual in the institution. This was made possible with the invaluable assistance of the Medical Officer and a specialized Cogentech laboratory.

Over time, the initial project, combining rapid serologic tests with molecular swabs, turned into a clinical study in collaboration with the National Cancer Institute of Milan, titled "Strengthening preventive measures in the workplace during the pandemic through identification and monitoring of asymptomatic/paucisymptomatic subjects using comparatively validated rapid serologic swabs and tests."

Following the start of the vaccination campaign, Cogentech management, initiated an additional project with the aim of monitoring and quantifying the antibody response in people who underwent vaccination.

For both the vaccination and the third booster (Booster), strong adherence by staff was achieved, thanks in part to outreach by the Medical Officer.

The Company Physician, Massimo Maria Pegorari, in such a critical and long-lasting situation, was and is a key figure. With his almost daily presence, sure indication and clarifications when needed, he enabled IFOM and Cogentech to overcome the most critical moments with unexpected serenity. At the first stage, the Company Physician supported us in outlining the correct hygienic, prophylactic and procedural measures; at a later stage, when cases and contacts between acquaintances and family members began to occur, to safely manage each situation. Quarantine management was extremely flexible, especially as the extent of it changed over time in relation to vaccination status. Again, the collaboration between HR and Medical Officer was very close and seamless.

The Personnel Department has always done its best to provide assistance as the caseloads and critical issues increased: paid leave for family needs, activation of smart-working...all to make the organization of work morè streamlined and safe, while facilitating, at the same time, the daily lives of our employees and their families. Just to bring an example, when

the red zone in Lombardy was re-introduced in March 2021, the daily activities of IFOM and Cogentech continued, safely. However given, the temporary suspension of in-person teaching activities, parents with children under the age of 14 with organizational difficulties were given the opportunity to take advantage of the smart-working mode.

Whenever necessary, timely awareness and update notices were sent to Cogentech workers. At the same time, the dedicated company intranet area was kept up-to-date.

New limits were confirmed or established, security measures put in place, (PPE, distances, sanitation, access verification methods, ...). IFOM and Cogentech management decided to take on the burden of verifying all access to the Campus, contractors, suppliers and guests included. In this way, only individuals with the required documentation (Green Pass and/or Super Green Pass) were granted access.

The measures adopted to deal with the Covid emergency, described in detail in dedicated reports attached to the DVR, were "validated" by the results obtained in the monitoring campaign with molecular swabs and the consequent activity of tracing the close contacts of positive cases. In fact, it is observed that only in rare cases did the infection occur "in house," while in the vast majority the positive individuals turn out to have been infected externally to the campus, tending to be in family environments or in moments of socialization.

Wellfare: beyond the laboratory

For Cogentech, protecting the health and safety of its employees is not "limited" to work activities alone. Over the years, management has promoted various company initiatives that aim to improve quality of life, promoting healthier lifestyles and supporting sustainability.
The needs to be met change greatly depending on the situation and experience.Cogentech's workers are largely young, so a number of initiatives have been designed to benefit work-life balance and family management.

Social initiatives for the families of employees

One of the needs of Cogentech, is the constant increase in the quality of the service offered and competitiveness, to cope with new market contexts. At the same time, however, the management, is aware of the need to offer its professionals a favorable working environment, which allows them to better reconcile their social, family and cultural life with their work life.

For this reason, a series of actions have been put in place that have, as their goal, the care and well-being of both workers and their families.

Lab G

For the pregnant woman and while breastfeeding the child, the laboratory represents a "critical" workplace due to the presence of potentially hazardous agents.

At IFOM and Cogentech, "Lab G" was thus created: a safe, unique laboratory in which there are no dangerous substances, physical or biological agents or otherwise incompatible with the state of pregnancy. Lab G was therefore designed specifically with the aim of allowing "mothers" to continue their laboratory activities, in complete peace of mind for themselves and their baby, throughout the entire period of pregnancy and breastfeeding.

In 2021, no Cogentech employees took advantage of Lab G.

Corporate nursery

Children of Cogentech employees between the ages of 11 and 36 months can take advantage of a bilingual company crèche. The opportunity to learn two languages and the advanced pedagogical approach, including the use of music and guidance on proper nutrition, are a plus for the children's development.

The nursery location is within walking distance of Cogentech and is open during September-July with hours of 8:30 a.m.-6:30 p.m., so as to meet the diverse work needs of the staff, facilitating mothers and fathers during a rather complicated period of family life.

Cogentech also covers part of the monthly tuition, providing tangible economic support to families.

At the same time, the parents who took advantage of it were able to manage their work days, in attendance or remotely, with the peace of mind of those who know their children are in good hands.

Flexible Hours

Cogentech, in order to meet work-family balance needs, has long adopted a flexible schedule.

The scientific and administrative staff enjoy flexible schedules, inbound, outbound, and within the workday, in order to best manage both work commitments and those of personal and family life.

Smartworking

For Cogentech, it is important that employees attend the workplace on a daily basis: only in presence can that sense of belonging to a community be cultivated and proactive discussion among colleagues be facilitated.

During 2021, times when there was a worsening of the pandemic situation, workers were able to take advantage of smartworking, in the manner agreed upon with management as we went along.

Cogentech is always willing to assess the needs of its staff and grant smartworking when deemed necessary.

Solidarity Time Bank

Inspired by the implementation decree of the Jobs Act (Art. 24 Legislative Decree 151/2015) and as part of its Corporate Social Responsibility initiatives, IFOM and Cogentech have introduced a new Welfare measure that represents an opening towards an innovative conception of internal relations within the Institute, stimulating mechanisms of solidarity and mutual aid, to the benefit of workers who are facing a time of difficult management of the reconciliation of family-work commitments. This is the Solidarity Time Bank initiative: employees have the opportunity to donate days or hours of unused vacation and leave to colleagues in need, who are forced to be absent from work due to burdensome family needs, such as caring for a sick minor child or an elderly and needy parent, or other difficult household issues. In this way, those who donate hours to the solidarity time bank offer a colleague the opportunity to experience their own difficult family situation with greater peace of mind.

Life insurance

For the benefit of each employee, Cogentech has provided an important benefit, totally at its own expense, consisting of life insurance, which guarantees, for the duration of the employment contract, coverage in the event of death from any cause, for the benefit of legal or testamentary heirs.

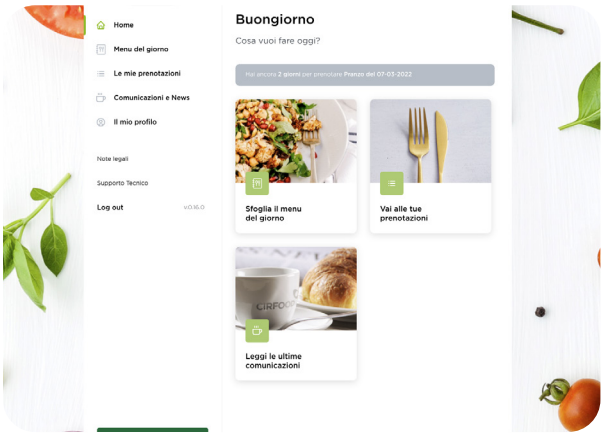
Internal CAF service

For the past few years, Cogentech has made available to all staff (direct employees and external contractors) a free in-house CAF service, which is also open to family members of employees and contractors upon payment of a subsidized fee.

Employee wellness initiatives

Healthy Nutrition

It is recognized that a healthy and varied diet rich in fresh, quality foods such as fruits and vegetables, grains and legumes can prevent the onset of cancer. "We are what we eat"-Cogentech knows this since it is involved in the diagnosis and development of therapeutic solutions for a disease such as cancer. Therefore, Cogentech offers in the company cafeteria areas to employees, co-workers, and guests the most varied, healthy, and open menu for different dietary needs.



As of March 2021, in an effort to make the lunch break more enjoyable and the offer more varied, two new options available in the bar area have been introduced: a light menu and the introduction of the Poke bowl, different for each day of the week.

In addition, this year, again in order to make the lunch break, pleasant and smart, a new App has been prepared that allows you to check in advance what the menus will be for the next 7 days at the company restaurant and bar or book a take away meal.

From the App, it is also possible to see what the nutritional values of the chosen food are and the ingredients used in the recipe: with food allergies, an informed choice becomes a safe choice!

Fitness

Regular physical activity, along with proper nutrition, is a key ingredient for good health of the individual. In order to also meet the physical well-being of its workers, IFOM and Cogentech have therefore entered into an agreement with a number of gyms in order to allow each person to identify the most suitable activity, at the most convenient time.

Psychological counseling

The ongoing pandemic has generated a strong impact on people's mental and physical well-being. Quarantine and smartworking, disrupting everyday life and blurring the boundaries between work and private life, have brought out discomforts such as fear, anxiety, stress...In this context, it has therefore become essential for companies to support workers by providing them with tools to improve their psychophysical well-being. After all, Work represents a fundamental part of everyone's life, and the well-being or discomfort experienced in the work context has repercussions at the family level.

When the drill accident occurred in June 2021, the escaped danger made it even more necessary for some of us to have some form of psychological assistance.

To this end, to meet the possible needs of all staff, IFOM and Cogentech have entered into agreements with a psychologist's office and an online psychology start-up.

We're going Smoke-free!

he smoking, including passive smoking, is among the leading causes of diseases of the cardiovascular system and lung cancer.

Cogentech and IFOM, who are particularly sensitive to this issue of Social Responsibility, in order to protect even non-smokers from possible consequent harmful health effects, have decided to make all spaces smoke- free on the occasion of Word NO tobacco Day (June 3, 2019).

The project, kept on during 2020 and 2021, fits naturally with the research and care mission of IFOM and Cogentech, as well as promoting a participatory message to contribute to the improvement of air quality as well as to the health and well-being of all employees and the many guests who attend our Institute every day.

Medical Service

The company doctor, who throughout the emergency period related to the Covid-19 pandemic gave his invaluable support to all staff, is available to provide his assistance to anyone who requests support. This service is especially designed for off-site workers, who find it more difficult to reach their primary care physician, but all staff members can take advantage of it.

Vaccine Campaign

With the valuable support of the Corporate Physician, IFOM and Cogentech, promoted and supported the

Flu vaccine campaign, which, in 2021, 15 Cogenetech workers benefited from.

Security Service and NighTime Taxi

Cogentech offers all staff who leave the Institute between 7 p.m. and 10 p.m. the opportunitỳ to ask the security service, which is present at the Front Desk, to accompany them to the parking lot or to be monitored remotely through video surveillance equipment.

For those who have to leave morè late for exceptional reasons, the possibilitỳ of using a cab voucher is offered.

Our valuable relationships

Benefit Corporations, such as Cogentech, are powerfully innovative enterprises because in carrying out their activities, they pursue one or more purposes of common benefit by generating positive impacts and/or reducing possible negative impacts on people, communities, territories and the environment, cultural and social activities, bodies and associations and other stakeholders.

Cogentech, by its very nature, in addition to devoting itself with care and responsibility to the activity carried out within its laboratories, cultivates all its relationships with care and interest.

Beginning with building a valuable relationship with its customers, who are fundamental to the economic sustainability of the business, Cogentech seeks to go a step further and also reserve a special look at the community around it and the environment in which it operates.

Thus, several initiatives of common benefit have been carried out over the years, both in the scientific and socio-educational fields.

These initiatives, like others already mentioned, were inevitably affected by the ongoing pandemic. Therefore, Cogentech and IFOM had to forego direct contact with students and, more generally, with citizens and outside guests. No "live" events were organized because the persistence of the Covid-19 pandemic did not allow it, but when possible, alternative channels, such as the Web, were exploited.

In order to reduce its impact on the environment, Cogentech is constantly striving to effectively manage the disposal of special waste, as well as implement projects aimed at reducing plastic consumption.

Customers

Customers and their satisfaction are of paramount importance to Cogentech.

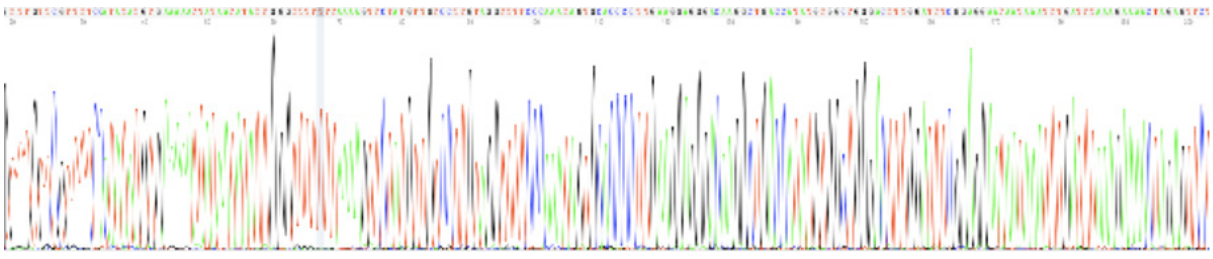
For all Cogentech staff there is a vivid awareness that every interaction can prove to be a useful opportunity for growth, which can lead to the creation of new opportunities. Therefore, cultivating a valuable relationship with customers, based on listening and discussion, is fundamental to strengthening the continuous improvement process that Cogentech wants to pursue.

Cogentech considers it a priority to establish a partnership based on trust with all its clients, not least because of the sensitive nature of the services offered.

For this reason, Cogentech is committed on a daily basis to putting customers and their needs at the center, in order to understand them and find the best possible response, always in accordance with the highest quality standards, the values that guide us as well as the company's Mission.

Cogentech's staff proves to be present, helpful and collaborative. When suggestions or remarks emerge from customers, Cogentech welcomes them and considers them as an additional boost in resolutely pursuing a path of continuous research and innovation.

In the field of scientific research, Cogentech, over the years, has established fruitful cooperation with research centers and universities, resulting in innovations and contextual publications.



*(*elettroferogramma ottenuto tramite sequenziamento col metodo di Sanger di una porzione di DNA- Sequencing Facility)*

In the diagnostic field, on the other hand, Cogentech has established fruitful relationships with hospitals, large and small, in the public and private sectors.

Cogentech, thanks to the expertise of the staff employed and thus the high level of quality of the services offered, working side by side with its clients, is committed to the development of a new clinical offering, compatible with the diagnostic needs that may arise from time to time.

Therefore, in the year 2021 we developed the following areas of projects and collaborations: revisiting the "OncoPan" panel, a multigenic diagnostic panel that allows for the extension of analysis, in addition to proven susceptibility genes, to genes more rarely involved in hereditary-familial cancers; development of liquid biopsy for the clinical management of hereditary breast and/or ovarian cancers; molecular study of "weakly positive" Covid-19 swabs; metabolomic analysis of biological samples (For any further details, please see the section Objectives Achieved in 2021).

The professional relationships that Cogentech has established with its clients over the years can be analyzed from different perspectives.

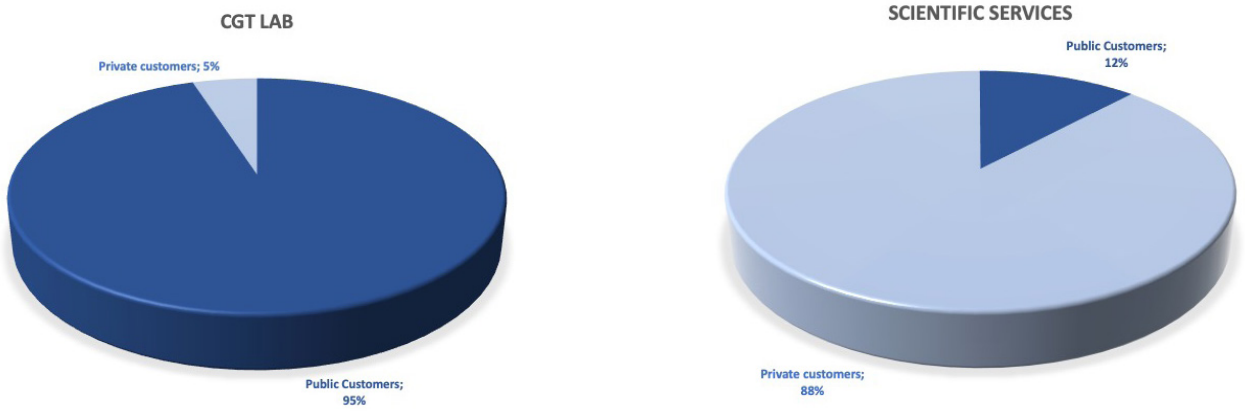
There are basically four categories of stakeholders to whom Cogentech offers its contribution:

- Clinical Institutes
- Intramural academic clients,
- External academic clients
- Business clients.

Customers can then be divided between public and private and based on the service they require.

In 2021, in particular, private customers covered more than 53.5 percent of Cogentech's revenue, compared to 68 percent in 2020.

Looking instead at the breakdown based on the type of service requested, Scientific Services are mainly requested by Private Clients (88 percent) while the demand for CGT Lab Genetic Testing comes mainly from public sector operators (95 percent).



Cogentech's management identifies the degree of customer satisfaction, a key component of its performance measurement.

The evaluation of satisfaction with the services offered is monitored annually by sending "evaluation questionnaires" to clients. The result, which emerges from the analysis of the feedback received, is a valuable tool as from here it is possible to identify possible areas for improvement and then take the necessary actions to create a virtuous path, aimed at improving stakeholdes' satisfaction.

The constant work of updating and searching for new opportunities to implement its portfolio of offerings, which occurs both at the level of scientific services and at the level of the CGT Lab genetic testing laboratory, sees feedback from the client as one of the main components of evaluation of its work and thus a valuable opportunity to proactively outline, our best offer.

The performance of Cogentech's system and individual processes is constantly monitored by means of various indicators, system and process, developed within the Quality Management System. The analysis of the results thus obtained is discussed by the Management of the scope of the Annual Review, which, in fact, is the time when the management from the perspective of "Quality" evaluates what has been done and what can be implemented in order to provide an even more precise, timely and reliable service that is the basis of the relationship with each individual customer.

Below is a brief example of the indicators analyzed:

- Response time;
- Complaints received;
- Outcome of evaluation questionnaires;

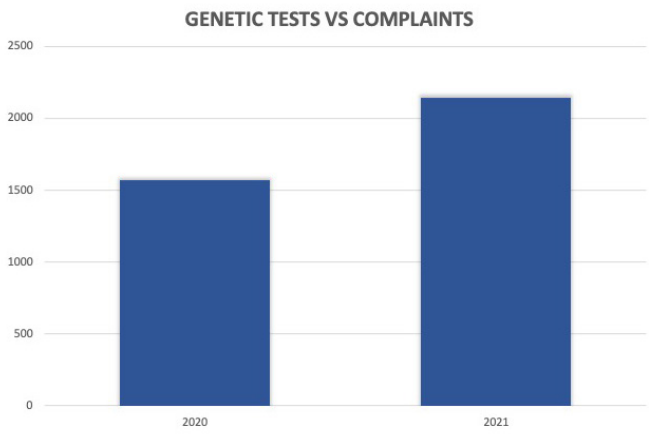
Given the peculiarities of Cogentech's different facilities and the different services respectively offered, customer response times vary widely. Despite the different timelines related to the specific testing activities to be performed, it is possible to say that on average, during 2021, more than 90 percent of the tests performed and services delivered were completed on time.

The average value of the customer satisfaction index, obtained as a result of the administration of Survey 2021, regarding the services offered by Cogentech, was 9.13 out of a maximum score of 10, continuously improving since 2019. This is an average score, obtained by reworking the scores for facilities that are certified and have a Quality Management System.

	2019	2020	2021
CGT Lab	9.09	9.20	9.27
Microarray/NGS	8.10	9.20	9.03
Hystopathology	8.90	9.10	9.29
Mouse Facility	8.26	8.80	8.54
QPCR	8.89	9.20	9.74
DNA Sequencing	8.81	8.70	8.88
Media	**8.70**	**9.03**	**9.13**

Customers of the scientific services participated in the analysis by accessing an online Survey, via a special link, while CGT Lab customers received the Customer Satisfaction Questionnaire via e-mail. In both cases, customers were asked to express their opinions with absolute impartialitỳ and objectivity since the answers provided were received anonymously and their analysis was done only in aggregate. The results obtained are shared with all operators so that the culture of Quality is spread at all levels and can be constantly nurtured.

In CGT Lab's service charter, it is again emphasized that the complaints received are the starting point for encouraging actions to improve the services offered, involving all operators. Therefore, a complaint procedure has been set up involving the Service Managers, who are called to report about the event encountered, thus enabling the implementation of effective corrective actions (and to study further preventive actions, in order to avoid the recurrence of the critical issue encountered) and to then provide a clarifying response to solve the problem, in the shortest possible time.



Out of a total of 2183 genetic tests analyzed in 2021, no reports of Non-Compliance or Complaints were received. Similarly, no complaints had been observed in 2020 and 2019. It is proudly reported that during 2021 there was a 39% increase in the number of genetic tests performed (2138 tests performed in 2021 versus 1571 tests in 2020).

The community in which we operate

Contribution to proper disclosure regarding Covid-19 and UNASMI award.

Cogentech's commitment to disseminating correct scientific information has been nationally recognized: the president as well as director of the CGT Lab, Prof. Marco Alessandro Pierotti, was honored in December 2021, along with other distinguished scientists, by UNAMSI (National Union of Medical Scientific Information).

In fact, during 2021, Prof. Pierotti-in collaboration with the other awardees-participated in a series of meetings organized online, on a weekly basis, in which UNAMSI journalists asked questions, expounded their doubts and uncertainties about the recent findings of science and research on the Sars-Cov-2 virus. By answering the various questions, Prof. Pierotti contributed, in a precise and constant manner, to shed light on the role played by vaccines and drugs in the fight against COVID-19.

These meetings enabled journalists to better understand such a complex topic and thus, indirectly, to convey correct and complete information to readers.

The official ceremony honored Italian excellence, which has contributed so much to spreading correct and rigorous information about Covid-19.

Extension of BRCA testing to all healthy women of at-risk age

Prof. Pierotti's working group focused on another goal with immediate benefits for the community.

In fact, an important paper, "Towards population-based genetic screenings for breast and ovarian cancer: A comprehensive review from economic evaluations to patient perspectives," was published in the journal The Breast in 2021, the contents of which have been taken up by industry associations (e.g., Mutagens Foundation, https://mutagens.it/fondazione/) and national newspapers.

Cogentech's ongoing efforts to promote the extension of genetic testing to an increasing number of subjects and to validate it as the most appropriate prevention method to reduce the risk of developing breast and ovarian cancers, finds in this paper the rationale and scientific reasons supporting the strategy. In fact, the review analyzes several studies carried out in different countries with different health care systems showing how the cost-benefit ratio is decidedly in favor of the "Test" strategy over the "No test" option. The "Test" strategy also allows the extension of testing to healthy family members, consequently reducing mortality, social impact, and the costs associated with the clinical management of these diseases. So, from an ethical point of view, it seems clear that the call for intervention to improve the management and ultimately the survival of these people is in response to the call not to add to a "genetic injustice" a "social injustice."

Genuine population screening would also allow for the identification of a higher number of individuals with BRCA variants, their early introduction into targeted care pathways, the saving of costly diagnostic investigations when they follow a failure to detect the disease early, and lower costs of genetic testing, which can be summed up as a huge benefit to health care systems.

The environment around us

For Cogentech, the environment is a primary asset: the Company is committed to safeguarding it, not only in compliance with current regulations, but also taking into account the development of scientific research and the best experiences in the field. To this end, Cogentech seeks to direct its choices and manage its activities so as to ensure a balance between economic initiatives and environmental needs.

Thus, Cogentech cares about the environment and is increasingly manifesting its intention to adopt environmental sustainability measures in line with its institutional mission and the goals of the 2030 Agenda for Sustainable Development.

This commitment has always translated into virtuous waste management practices: Glass, Plastic and Paper are constantly sorted and disposed of with AMSA.

Special attention is then paid to the management of Special Waste, most of which comes from laboratories.

During 2021, of the approximately 32 tons of special waste generated, almost all of it belongs to the "hazardous" category.

Compared to the previous year, there has been a 25% reduction in waste generation: this is mainly due to the temporary outsourcing of the operation of an enclosure.

The management of Cogentech was faced with this decision as a result of the start of several construction sites in the vicinity of the enclosure, resulting in loud noise and vibration. This would certainly have had negative impacts on animal welfare and colony productivity. Hence the decision to outsource the operation, temporarily transferring the animals to a specialized, globally recognized breeder.

In dealing with these wastes, which are characteristic of the scientific work carried out by Cogentech, it is essential to adopt careful management methods and to respect the proper disposal of them.

Hazardous wastes produced are delivered to licensed transporters, who take care of hazardous waste pickup, in compliance with specific legal regulations and with total respect for the environment.

Hazardous waste, if not properly handled, could produce environmental damage or damage to people's health. For this reason, the rules prescribed by ADR (Accord européen relatif au transport international des marchandises Dangereuses par Route) are scrupulously followed, with the use of approved containers and proper labeling, in order to prevent possible risks for the entire logistics chain. To this end, waste handlers receive appropriate refresher training each year during which specific topics are covered in depth.

With the aim of facilitating the proper packaging of waste by laboratory operators, Cogentech and IFOM have devised a special classification system, which involves the use of colored labels containing specific information and symbols that enable researchers to properly recognize and handle each waste.

The waste is then delivered to companies registered with the Register of Environmental Managers for the transportation of hazardous waste. The company that primarily collects, transports, and disposes of special waste, possessing all relevant permits, has obtained several ISO certifications (ISO 9001, ISO 14001, and ISO 45001), available on the contractor's website

Special waste generated	UoM	2021	2020
Non-Hazardous Waste	**ton**	**0,467**	**0,288**
of which sent for energy recovery	ton	0,454	0,286
of which sent for disposal	ton	0,013	0,002
Hazardous waste	**ton**	**31,08**	**43,50**
of which sent for energy recovery	ton	15,11	33,11
of which sent for disposal	ton	16,04	10,38
Total Waste Produced	**ton**	**31,63**	**43,79**

Plastic Free Project

Unfortunately, the Plastic Free project, which began enthusiastically in 2019, has been temporarily suspended due to the Covid-19 emergency during 2020.

However, as early as February 2021, CONTACTLESS dispensers for beverages to be consumed in washable and reusable cups have been installed in collective catering spaces. This has avoided the distribution of plastic bottles, safeguarding both the environment and the health protection of our employees.

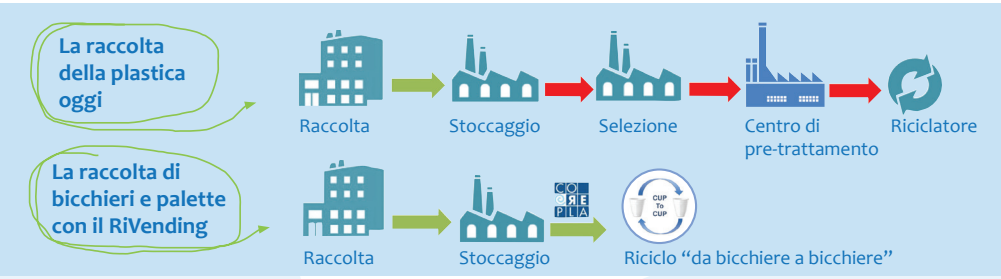
For much of 2021, the dispensing of hot drinks in break areas continued to be done using paper cups instead of plastic cups.

RiVending project: "glass-to-glass" recycling

With a view to continuous improvement, towards the end of 2021, IFOM joined the RiVending Project (www.rivending.eu) which is still being implemented.

This is a virtuous cycle of recovering and recycling plastic cups and scoops by separating and collecting them separately at the source. Next to each vending machine, in the break areas also used by Cogentech employees, a special container has been placed that allows the glasses to be stacked, one inside the other. This results in a reduction of the occupied volume,

In the future, when fully implemented, the program will enable the transformation of used tumbler into new tumbler, thus creating an efficient circular economy in the industry. RiVending is a "zero-waste" program because the plastic used (polystyrene) is washed and fully recycled and reintroduced into the production cycle of new products, avoiding the costly and wasteful steps of separation from other plastics and impactful, pushy industrial washing



Publications

Opti-nQL: An Optimized, Versatile and Sensitive Nano-LC Method for MS-Based Lipidomics Analysis

Cattaneo A, Martano G, Restuccia U, Tronci L, Bianchi M, Bachi A, Matafora

Metabolites -- 2021 Oct 21;11(11):720. doi: 10.3390/metabo11110720.

This work proposes a sensitive and reproducible LC method for lipidomics analysis, called Opti-nQL (nanoLC-optimized quantitative lipidomics), which can be used for the analysis of a variety of biological systems. Opti-nQL was validated by analyzing cellular lipid extracts of human and murine origin obtained by different lipid extraction methods. 700+ lipid species comprising 16 lipid subclasses were identified, while 400 lipids were identified by MS/MS analysis. The results shown were obtained from the analysis of 40ng proteins, making this method suitable even for the analysis of low abundant samples. Analysis by mass spectrometry thus showed that this method allow more lipids to be identified, as demonstrated by injecting 20 times less material than conventional chromatographic analysis by microflow, making this lipidomic analysis much more reproducible, accurate and robust.

Endosomal trafficking and DNA damage checkpoint kinases dictate survival to replication stress by regulating amino acid uptake and protein synthesis.

Ajazi A, Bruhn C, Shubassi G, Lucca C, Ferrari E, Cattaneo A, Bachi A, Manfrini N, Biffo S, Martini E, Minucci S, Vernieri C, Foiani M

Dev Cell. 2021 Sep 27;56(18):2607-2622.e6. doi: 10.1016/j.devcel.2021.08.019. Epub 2021 Sep 16. PMID: 34534458

The influence of Atg6 on replicative stress has been studied by different analytical approaches such as: genetics, genomics, metabolomics, and proteomics.

We performed Label Free proteomic analysis of ymr1Δ inp53Δ cells treated with culture medium (YPD) with different aromatic amino acid content (+/- Tryptophan) with the aim of looking for which proteins were altered by aromatic amino acid imbalance and replicative stress. It was observed that the addition of tryptophan to the culture medium of ymr1Δ inp53Δ cells caused obvious changes in the cell proteome.

Human iPSC-based neurodevelopmental models of globoid cell leukodystrophy uncover patient- and cell type-specific disease phenotypes.

Mangiameli E, Cecchele A, Morena F, Sanvito F, Matafora V, Cattaneo A, Della Volpe L, Gnani D, Paulis M, Susani L, Martino S, Di Micco R, Bachi A, Gritti A

Stem Cell Reports. 2021 Jun 8;16(6):1478-1495. doi: 10.1016/j.stemcr.2021.04.011. Epub 2021 May 13. PMID: 33989519

LGloboid cell leukodystrophy (GLD) is a neurogenerative lysosomal storage disease caused by hereditary β-galactocerebrosidase (GALC) deficiency.

This work created patient-specific iPSC cell lines with GLD, used as a human model to study the pathogenesis of GLS and to test the efficacy of gene therapy in relevant neural cell types. GLD neural progeny showed progressive psychosin accumulation, oligodendroglial and neuronal defects, and altered lipid composition.

We performed a comprehensive lipidomics analysis using the Opti-nQL method developed in our laboratory (doi: 10.3390/metabo11110720.PMID: 34822378) with the aim of studying the effect of the absence of GALC or its increased expression on the lipidome of iPSCs cells and neural progeny.

PA28γ-20S proteasome is a proteolytic complex committed to degrade unfolded proteins.

Frayssinhes JA, Cerruti F, Laulin J, Cattaneo A, Bachi A, Apcher S, Coux O, Cascio P.

Cell Mol Life Sci. 2021 Dec 16. doi: 10.1007/s00018-021-04045-9. PMID: 34913092

Online ahead of print.

PA28γ is a nuclear activator of the 20S proteosome that stimulates the hydrolysis of numerous substrates through an ATP- and ubiquitin-independent mechanism.

We performed quantitative proteomics analysis by mass spectrometry of products generated by proteosomal degradation by 20S of IGF-1 and MBP proteins.

We have shown that PA28γ decreases the variability of peptides that are potentially suitable for MHC class I antigen

presentation.

MITO-Luc/GFP zebrafish model to assess spatial and temporal evolution of cell proliferation in vivo.

Latouliere L, Manni I, Ferrari L, Pisati F, Totaro MG, Gurtner A, Marra E, Pacello L, Pozzoli O, Aurisicchio L, Capogrossi MC, Deflorian G, Piaggio G.

Sci Rep. 2021 Jan 12;11(1):671. doi: 10.1038/s41598-020-79530-5.

Tuning gut microbiota through a probiotic blend in gemcitabine-treated pancreatic cancer xenografted mice.

Panebianco C, Pisati F, Ulaszewska M, Andolfo A, Villani A, Federici F, Laura M, Rizzi E, Potenza A, Latiano TP, Perri F, Tripodo C, Pazienza V.

Clin Transl Med. 2021 Nov;11(11): e580. doi: 10.1002/ctm2.580.

Epigenomic landscape of human colorectal cancer unveils an aberrant core of pan-cancer enhancers orchestrated by YAP/TAZ.

Della Chiara G, Gervasoni F, Fakiola M, Godano C, D'Oria C, Azzolin L, Bonnal RJP, Moreni G, Drufuca L, Rossetti G, Ranzani V, Bason R, De Simone M, Panariello F, Ferrari I, Fabbris T, Zanconato F, Forcato M, Romano O, Caroli J, Gruarin P, Sarnicola ML, Cordenonsi M, Bardelli A, Zucchini N, Ceretti AP, Mariani NM, Cassingena A, Sartore-Bianchi A, Testa G, Gianotti L, Opocher E, Pisati F, Tripodo C, Macino G, Siena S, Bicciato S, Piccolo S, Pagani

Nat Commun. 2021 Apr 20;12(1):2340. doi: 10.1038/s41467-021-22544-y.

Towards population-based genetic screenings for breast and ovarian cancer: A comprehensive review from economic evaluations to patient perspectives

Ficarazzi F, Vecchi M, Ferrari M, Pierotti M.A.

Breast 2021 Aug; 58:121-129. doi: 10.1016/j.breast.2021.04.011. Epub 2021 May 12.

Analysis of Italian BRCA1/2 Pathogenic Variants Identifies a Private Spectrum in the Population from the Bergamo Province in Northern Italy.

Figlioli G, De Nicolo A, Catucci I, Manoukian S, Peissel B, Azzollini J, Beltrami B, Bonanni B, Calvello M, Bondavalli D, Pasini B, Vignolo Lutati F, Ogliara P, Zuradelli M, Pensotti V, De Vecchi G, Volorio S, Verderio P, Pizzamiglio S, Matullo G, Aneli S, Birolo G, Zanardi F, Tondini C, Zambelli A, Livraghi L, Franchi M, Radice P, Peterlongo P.

Cancers (Basel) 2021 Jan 30;13(3):532. doi:10.3390/cancers13030532. PMID: 33573335

Definition and management of colorectal polyposis not associated with APC/MUTYH germline pathogenic variants: AIFEG consensus statement

Urso EDL, Ponz de Leon M, Vitellaro M, Piozzi GN, Bao QR, Martayan A, Remo A, Stigliano V, Oliani C, Lucci Cordisco E, Pucciarelli S, Ranzani GN, Viel A, AIFEG group*

* Pensotti V. e De Vecchi G. (membri AIFEG al momento della pubblicazione)

Dig Liver Dis 2021 Apr;53(4): 409-417.doi: 10.1016/j.dld.2020.11.018. PMID: 33504457

Mixed Neuroendocrine/Non-neuroendocrine Neoplasm (MiNEN) of the Ovary Arising from Endometriosis: Molecular Pathology Analysis in Support of a Pathogenetic Paradigm.

Maragliano R, Libera L, Carnevali I, Pensotti V, De Vecchi G, Testa M, Amaglio C, Leoni E, Formenti G, Sessa F, Furlan D, Uccella S.

Endocr Pathol 2021 Aug 3. doi: 10.1007/s12022-021-09689-8. Online ahead of print. PMID: 34342838

Clinical heterogeneity and reduced penetrance in DICER1 syndrome: a report of three families.

Azzollini J, Ferrari A, Stracuzzi A, Chiaravalli S, Terenziani M, Spreafico F, Grasso M, Collini P, Pensotti V, Massimino M, Arbustini E, Manoukian S.

Tumori 2021 Dec;107(6):NP144-NP148. doi: 10.1177/03008916211058788. PMID: 34761719

A ligand-insensitive UNC5B splicing isoform regulates angiogenesis by promoting apoptosis

Pradella D, Deflorian G, Pezzotta A, Di Matteo A, Belloni E, Campolungo D, Paradisi, BugattiM,Vermi W, Campioni M, Chiapparino A, Scietti L, Forneris F, Giampietro C, Volf N, Rehman M, Zacchigna S, Paronetto MP, Pistocchi A, Eichmann A, Mehlen P, Ghigna C

Nat Commun. 2021 Aug 11;12(1):4872. doi: 10.1038/s41467-021-24998-6.

TAp63 regulates bone remodeling by modulating the expression of TNFRSF11B/Osteoprotegerin

Lena AM, Foffi E, Agostini M, Mancini M, Annicchiarico-Petruzzelli M, Aberdam D, Velletri T, Shi Y, Melino G, Wang Y, Candi E

Cell Cycle 2021 Nov;20(22):2428-2441. doi: 10.1080/15384101.2021.1985772. Epub 2021 Nov 11.

Exploring the association with disease recurrence of miRNAs predictive of colorectal cancer

Zanutto S, Ciniselli CM, Belfiore A, Dall'Olio V, Tizzoni L, Varinelli L, Pierotti MA, Battaglia L, Verderio P, Guaglio M, Gariboldi M.

Int J Biol Markers. 2021 Dec 21:17246008211064915. doi: 10.1177/17246008211064915. Online ahead of print.

GRI "Referenced" Table of Contents

Indicator	Indicator description	Disclosure	Chapter reference	Notes
General Disclosure				
102-1	Name of organization	Full Disclosure	Our history and mission statement	
102-2	Activities, brands, products and services	Full Disclosure	The services we offer	
102-3	Location of the main office	Full Disclosure	Our history and mission statement	
102-4	Location of activities	Full Disclosure	Our history and mission statement	
102-5	Ownership and legal form	Full Disclosure	Our history and mission statement - Our commitment	
102-6	Markets served	Full Disclosure	The services we offer - Clients	
102-8	Information about employees and other workers	Full Disclosure	People at the center	
102-14	Statement from the highest governing body	Full Disclosure	Letter to Stakeholders	
102-40	List of stakeholder groups	Full Disclosure	Methodological note	
102-41	Collective bargaining agreements	Full Disclosure	People at the center	
102-46	Report content definition and topic perimeters	Full Disclosure	Methodological note	
102-47	List of material topics	Full Disclosure	Methodological note	
102-50	Reporting period	Full Disclosure	Methodological note	
102-51	Date of the most recent report	Full Disclosure	Methodological note	
102-52	Periodicity of reporting	Full Disclosure	Methodological note	
102-53	Contacts to request information regarding the report	Full Disclosure	Methodological note	
102-55	GRI Table of Contents	Full Disclosure	GRI "Referenced" Table of Contents	
Employee training and professional development				
103-1	Explanation of the material theme and its perimeter	Disclosure related to item a	The development of human capital	
103-2	The management mode and its components	Full Disclosure	The development of human capital	
103-3	Assessment of management arrangements	Full Disclosure	The development of human capital	
404-1	Average annual training hours per employee	Full Disclosure	The development of human capital	

Staff welfare				
103-1	Explanation of the material theme and its perimeter	Disclosure related to item a	People at the center	
103-2	The management mode and its components	Full Disclosure	People at the center	
103-3	Assessment of management arrangements	Full Disclosure	People at the center	
405-1	Diversity in governing bodies and among employees	Full Disclosure	The composition of corporate governance - People at the center	
Occupational health and safety				
103-1	Explanation of the material theme and its perimeter	Disclosure related to item a	People at the center	
103-2	The management mode and its components	Full Disclosure	People at the center	
103-3	Assessment of management arrangements	Full Disclosure	People at the center	
403-2	Hazard identification, risk assessment, and accident investigation	Full Disclosure	The protection of occupational health and safety	
403-5	Occupational health and safety training for workers	Full Disclosure	The protection of health and safety at work - The development of human capital	
403-6	Promotion of workers' health	Full Disclosure	People at the center- Occupational health and safety protection- Health and safety beyond the laboratory- Wellfare: beyond the laboratory	
403-9	Occupational accidents	Disclosure related to item a	The protection of occupational health and safety	
Relationship with the community				
103-1	Explanation of the material theme and its perimeter	Disclosure related to item a	Our valuable relationships - The community in which we operate	
103-2	The management mode and its components	Full Disclosure	Our valuable relationships - The community in which we operate	
103-3	Assessment of management arrangements	Full Disclosure	Our valuable relationships - The community in which we operate	
No GRI	Projects carried out for the benefit of the community	n.a.	The community in which we operate	

Customer satisfaction and service quality				
103-1	Explanation of the material theme and its perimeter	Disclosure related to item a	Quality service - Customers	
103-2	The management mode and its components	Full Disclosure	Quality service - Customers	
103-3	Assessment of management arrangements	Full Disclosure	Quality service - Customers	
No GRI	Customer satisfaction index	n.a.	Customers	
No GRI	Response provided to customers on time	n.a.	Customers	
No GRI	Complaints received	n.a.	Customers	
Research and innovation				
103-1	Explanation of the material theme and its perimeter	Disclosure related to item a	Scientific research and innovation	
103-2	The management mode and its components	Full Disclosure	Scientific research and innovation	
103-3	Assessment of management arrangements	Full Disclosure	Scientific research and innovation	
No GRI	Accomplished publications	n.a.	Publications	
No GRI	Investment in research and development	n.a.	Scientific Research and Innovation - Targets achieved in 2021	
Environmental Sustainability				
103-1	Explanation of the material theme and its perimeter	Disclosure related to item a	The environment around us	
103-2	The management mode and its components	Full Disclosure	The environment around us	
103-3	Assessment of management arrangements	Full Disclosure	The environment around us	
306-1	Waste generation and significant waste-related impacts	Full Disclosure	The environment around us	
306-2	Management of significant waste-related impacts	Full Disclosure	The environment around us	
306-4	Waste not intended for disposal	Full Disclosure	The environment around us	Note
306-5	Waste for disposal	Full Disclosure	The environment around us	

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