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Strategic Plan 2021-2025

Institute for Biomedicine

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Many people have contributed to the development of this Strategic Plan. We thank all staff who participated in this collective effort. It represents a clear statement about who we are and what we are becoming. Also represents the future perspective we build on the growth and results presented in this document.

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Institute for Biomedicine
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Introduction

Over recent years, we at the Institute for Biomedicine (IFB) have built the foundation to allow sustainable biomedical research in South Tyrol, with the flexibility to respond to health crises as they emerge, such as the SARS-Cov2 pandemic. Our goal is to create an Internationally renowned research institute using a multidisciplinary approach to understand factors that can influence, and ultimately improve, human health. Our strategy is to have greater impact on society through our activities, while building on our achievements to become even more attractive to the best scientific minds and innovative companies to help us reach this goal.
By consolidating, expanding and better utilising our resources we will continue to generate new knowledge and seek potential ways to use this knowledge in a more translational way, where we impact health through innovative products, services and solutions. Under our guidance the CHRIS study has grown to the largest single-site, single centre genetic study in Italy. It is the cornerstone of continuing biomedical research efforts in the Province for both the near and longer term future, and supports the development of more predictive and preventative products and services. Ultimately it is hoped that these will drive more precision Medicine and Health (PMH) initiatives in the region. A PMH approach represents one of the most innovative new concepts in healthcare. It holds real promise for better monitoring health and disease progression, more accurate and early diagnosis and more effective and safer treatments for patients, for improved medical services to citizens, and for improving the overall health of the population.
Our immediate priorities are to successfully conduct the second phase of the CHRIS study, and improve the quality and passive clinical phenotype information through linking with the electronic health records of participants. This will give us much needed longitudinal data. We will also start to use more focused sub-studies within CHRIS, especially in the precision health field, where we can use the study as a testing ground of novel ideas. Our biobanked resources can be used to create more personalised cell models to investigate mechanisms of disease, and screen for possible ways to intervene in the disease process. We will combine our data with that from large-scale data efforts worldwide to develop appropriate tools to analyse, browse and mine these datasets in informative ways. We will engage in more systematic genetic epidemiological analysis, especially considering the unique strengths in CHRIS enhanced by studying extended pedigrees. Developing these ideas is the basis of our activities going forward.
Striving towards excellence, an emphasis on multi-disciplinary research, our focus on young and emerging talent from the region and beyond, and our continued and expanding partnerships, are just some of the factors necessary to help us achieve the goals we have set.
Coupled with the right strategic partnerships in academia, healthcare and industry, we hope to maximize the utility of our resources and knowledge generation, even to the point of identifying and validating novel therapeutic targets, through genetics and cell biology. Success in these efforts will place our Institute amongst the foremost precision health research centres in Italy and leave us well situated in relation to European efforts.
By working together, we have the opportunity to create a resource for biomedical discovery and its practical application into new treatments and technologies that benefit patients and the population. This strategic plan can help readers understand why we are doing what we do, and how we hope to advance towards achieving our vision for a healthier population.

Prof. Dr. Peter P. Pramstaller
Founding Director and Head of Institute for Biomedicine

Global challenges

Increase Years in Good Health
Increasing life expectancy in the population brings the major global challenge of increasing Healthy life years. Cancer, cardiovascular and circulatory disease, neurological problems, and metabolic imbalances exacerbated by obesity still account for significant poor health and deaths everywhere.

Increase Awareness and Empower Individuals
There is increasing importance of providing evidence to the population and healthcare professionals of the economic and societal benefits of a PMH approach. In parallel, models for individual responsibility, ownership and sharing of personal health data under the highest ethical guidelines need constant development, and patient participation in research and development programs should increase.

Increase Emphasis on Prevention
There is a paradigm shift in thinking away from disease and patient research to include more research on factors that preserve good health and which therefore might be used to delay or prevent disease onset. This paradigm shift is the main driver behind the global challenges necessary to create better Precision Medicine/Health (PMH) initiatives, which will lead to health solutions based on individual makeup that are tailored more precisely to the individual.

Integrate Big Data and ICT Solutions
High quality sustainable databases and solutions for the increasingly massive datasets of harmonised molecular information being gathered should be created. These can be merged with clinical, environmental, social, health and wellbeing information, collected through ongoing increasingly large PMH projects.

Design New Clinical Trial Structures
We need to integrate longitudinal and in-depth studies to characterise health and disease mechanisms. This molecular information needs integration into new innovative clinical trial designs and preclinical testing to test and improve the effectiveness of interventions tailored to the individual.

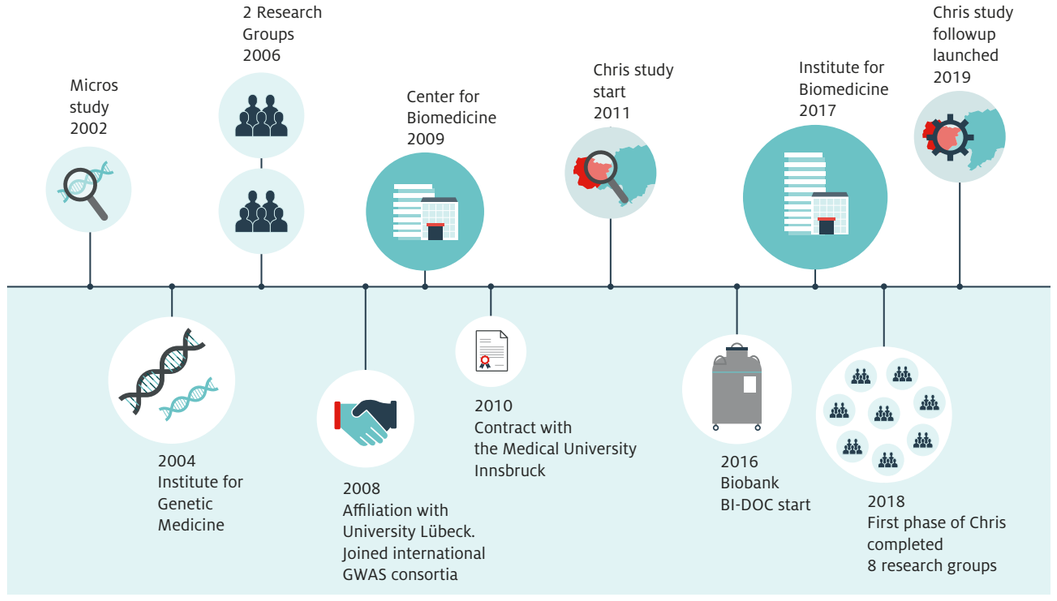
A Paradigm Shift towards PMH
PMH approaches for diagnosis and treatment of cancer, infectious and some rare diseases are slowly proving successful and becoming more common. The global challenge is to expand these approaches for other diseases. Many aspects of healthcare delivery will need to adapt to incorporate this new knowledge into such approaches, and this paradigm shift should directly impact citizens, researchers and national healthcare systems to allow people to live longer and healthier lives.

Increase Translation of Basic Research
There is increasing need to support translational research infrastructures, collect extensive and detailed longitudinal data characterising health trajectories, create and harness tools to analyse and interpret those massive datasets, and examine health related traits in the context of lifestyle and environment. The collected data will rely increasingly on high-throughput technologies, that allow genomic, epigenetic, transcriptomic, proteomic, metabolomic and microbiome analysis.

Contribute Knowledge to Improve Healthcare
New clinical decision support tools will need development, and more health economics studies performed to measure real benefits of PMH solutions. Systematic active dialogue between innovators, citizens and decision makers, throughout all steps of regulatory processes in providing healthcare, will need to occur.

Our history

In 2001 an agreement with the provincial government saw the launching of the GeNova project, which transformed to the MICROS study in the years 2002-2003. The MICROS study, a population-based survey on three small, isolated villages, characterized by settlement a long time ago, small number of founders and slow/ null population expansion, began the collection and biobanking of resources for local research into the use of small, isolated populations to find genes involved in the etiology of disease. This led to the founding of the Institute for Genetic Medicine in 2004, and the consolidation of research groups using the tools of molecular genetics, genetic epidemiology and biostatistics in 2006. In 2006 we joined our resources with those from four other European centres to create the EUROSPAN consortium (European Special Population Research Network). The success of the cooperative approach led to an active period from 2008 to the present in which MICROS data has been successfully incorporated into some of the largest international consortia currently operating (see appendix), generating scientific results published in the world's top scientific journals. Over approximately 15 years, GWAS consortia have created some of the largest current experiments in biology. As of 2020, online catalogues contain information from >4500 publications and >185,000 associations to thousands of health-related traits, which have led to new discoveries about genes and pathways involved in common diseases and other complex traits, provided a wealth of new biological insights, led to discoveries with direct clinical utility, and facilitated basic research in human genetics and genomics. In 2011 the follow up to MICROS (the CHRIS study) began, enrolling over 13,400 people by December 2018 when phase 1 completed. In 2016 we opened the largest biobank in the region and created our first joint doctoral program (BI-DOC) in cooperation with the Medical University of Innsbruck. The first follow up phase of CHRIS began in 2019, and is ongoing despite a disruption due to the SARS-Cov2 pandemic. Extending our dedicated groups to focus on computational genomics/ metabolomics, translational genomics, mitochondria in health and disease, molecular neurodegeneration and biology of cardiac health and disease, will help maximise the health insights from this precious resource.



Our achievements

1. GENERATING KNOWLEDGE

Using the resources gathered and data generated since the founding of the Institute for Biomedicine, we have had a steady scientific output in world-leading scientific journals (references in the Appendix).

BRAIN

— Parkin mutations and mitochondrial dysfunction are known to play a role in Parkinson's disease (PD), leading us to investigate the profile of binding partners of Parkin at the mitochondrial level[1]. Our work indicates that one of these binding partners rescues mitochondrial dysfunction in Parkin deficient cells, which might eventually be useful for potential therapy[2,3].

— Identifying possible modifiable risks is an important step in the prevention of Parkinson disease. Previous studies have shown a possible association between iron blood levels of iron and Parkinson disease. Our study indicates that increased iron levels are causally associated with a decreased risk of developing PD[4].

— We have investigated alpha-synuclein role in Parkinson's disease pathogenesis and pathology. Our results indicate that alpha-synuclein interferes with the normal calcium signaling, which is relevant for designing future treatment strategies in PD[5]. Additional genetic targets that alter calcium processing are being actively studied in nematode and human cellular models.

— We are validating *in vitro* and *in vivo* a novel gene, identified by GWAS, that modifies the cell processes that mediate degradation of pathologic alpha-synuclein. We are investigating an approach to increase the cellular production of this protein in the hope that this provides a novel potentially therapeutic approach.

— In a cell model system that reproduces some of the alpha-synuclein clustering observed in PD, we have identified compounds already in the clinic that may modulate this, and thus may be re-purposed to provide novel combinatorial therapeutic approaches.

— We performed the first reported Whole Exome Scan (WES) for time-to-LID onset in PD, where we observe association at OPRM1, and suggest variants in MAD2L2 and MAP7 genes[6]. The OPRM1 result suggests treatment with agonists of the mu opioid receptor might reduce dyskinesia induced by levodopa treatment, a major unmet clinical need in PD.

— We have identified potential causal variants in a family with epilepsy and intellectual disability[7]. We are now developing and testing cell models to better understand the biological processes underlying drug-resistant epilepsy, and these models will be used to develop novel therapeutic approaches.

CARDIOVASCULAR

— We have contributed to the clarification of cardiac cell function regulation in pathophysiological conditions[8], including diabetes[9,10].

— Induced pluripotent stem cells (iPSCs) represent an invaluable tool to derive human cardiomyocytes and to model human cardiac disease. We have demonstrated that the tissue of origin can have an impact on the cardiomyogenic ability of iPSCs[11]. We have also set up an efficient method to derive iPSCs from frozen buffy coats[12] and created iPSC lines from patients with caveolinopathies and arrhythmogenic cardiomyopathy (ACM)[13].

— The cellular and genetic basis of ACM are still partly unknown. We have contributed to the clarification of the role of cardiac stromal cells in ACM[14,15], and revealed new insights into the genetic mechanisms of this disease[16]. We are now exploring the mechanisms of fat accumulation in ACM primary adult cardiac stromal cells and investigating the molecular mechanisms of reduced penetrance in ACM using iPSC-derived cardiomyocytes.

— Atrial arrhythmias are extremely common in the general population. We have identified an association, mediated by BMI, between the P-Wave duration and the relative phosphatidylcholine 38:3 concentration in blood[17]. The apparent correlations between lipids and cardiac health indexes that we observe might simply reflect a double role of increased body mass, which alters both lipid metabolism and cardiac risk. We are now actively studying the genetic basis of atrial fibrillation.

— Dozens of genes have been successfully identified for complex electrical and structural heart traits, some of which have been shown to be involved in predisposing to heart disease[18,19,20].

METABOLIC

— We been actively involved in a major international effort to investigate genetic variants associated with type 2 diabetes where DNA-sequencing data was used to evaluate the contribution of rare and infrequent variants to disease risk[21].

— Through the Genetic Investigation of ANthropometric Traits (GIANT) Consortium, many genes related to obesity and body fat distribution have been discovered. Moreover, the genetic link between obesity and type 2 diabetes is becoming clearer. This new knowledge will support the development of precision disease prevention programs[22,23].

— By integrating genetic and biological data on thyroid function, we demonstrated the causal role of thyroid alterations on a number of health outcomes: variation in the normal range of thyroid function and Hashimoto's thyroiditis are causal risk factors for stroke and CAD, respectively[24].

NEPHROLOGY

— Chronic kidney disease (CKD) is a global health problem, affecting >10% adults worldwide. We co-lead the world's largest collaborative effort to identify genes associated with CKD[25], and recently uncovered hundreds of genes related to normal kidney function regulation[26,27,28,29], kidney damage[30], and urate metabolism[31]. In many cases, the implementation of innovative data analysis techniques, integrated with transcriptomic, proteomic, and methylomic data has allowed the causal gene to be identified, moving towards mechanistic understanding. These are important steps towards the development of target pharmaceutical intervention for a disease that, so far, was considered irreversible.

— The exploitation of genetic findings through causal inference models has additionally allowed the role of kidney function in human health to be elucidated: we established a protective effect of iron levels[32] and a negative effect of vitamin D[33] on kidney function. Careful examination of the bidirectional link between kidney function and blood pressure levels has established that a lower kidney function can be a cause for higher blood pressure, thus suggesting that prevention of a decline in kidney function can reduce the public health burden of hypertension[34].

AGEING

— Ageing is a complex phenomenon that involves multitude biological processes. We have used network models to analyze the relations between ageing and age-related diseases and provide a resource for exploring the genetic landscape of human ageing[35].

EPIDEMIOLOGY

— An innovative causal inference method, called Mendelian randomization (MR), has become widely used as it allows blind randomization of study participants by their genetic exposure in the same way a randomized clinical trial would do. MR has become a popular tool to test causal effects of human behavior and biological alterations on health and diseases as well as a tool for drug repurposing and testing. By exploiting available data from genome-wide association studies, MR has proven to be as efficient as randomized clinical trials, and much more cost effective. Our Institute is involved in methodological studies in the field of MR, contributing to provide insights into disease pathogenesis and supporting development of new strategies for disease prevention and therapy[36,37,38,39,40,41,42,43,44].

— Our Institute is always concerned about rigorous methodology across all fields. In epidemiology, in particular, careful analysis of a pain sensitivity questionnaire has identified underlying data structure, allowing more efficient data collection[45]. Similarly, implementation of non-linear interaction models for exposures and outcomes analyses has enabled us to quantify the detrimental effects of current smoking on both the sympathetic and parasympathetic nervous system, and the beneficial effect of smoking cessation[46].

— In response to the COVID-19 pandemic we have set up the CHRIS COVID-19 study for monitoring the immune response of infected individuals and which aims to investigate the determinants of COVID-19 infection and severity[47]. With this new study we joined the COVID-19 Host Genetics Initiative (www.covid19hg.org) as contributing partners. This initiative has successfully set up a global research network to elucidate the role of host genetic factors in COVID-19, leading to the identification of 13 genome-wide significant loci associated with SARS-CoV-2 infection or disease severity[48]. These findings help shed light on the underlying biological and molecular mechanisms of COVID-19 and of potential therapeutic relevance.

ELSI

— In the past years the ELSI group developed the ethical and legal framework for running the population based study CHRIS based on comprehensive research in the field[49,50]. We developed informed guidelines, rules and documents to ensure that data and samples were collected, stored and used within high standards of Privacy protection. In accordance with national and EU legislation and individual rights, we developed a comprehensive access policy foreseeing oversight and governance mechanisms for data and samples that informs our biobanking procedures[51].

— This research and expertise led us to be recognized at international level as experts, setting standards for others and impacting directly policy making at international level. We were invited to present to the OECD expert consultation on "OECD Recommendation of the Council concerning Access to Research Data from Public Funding"[52], and members of the group led the development of the WHO ACT-Accelerator Data Governance Framework[53], are involved in an international position paper on big data led by the NIH, were involved in the Go-FAIR Task Force by ELIXIR (the leading consortium on big DATA) and data stewardship[54,55], are actively contributing to BBMRI-ERIC's Code of Conduct for Research, were invited to contribute to series on Pandemic Law Making, and have contributed to public outreach as in an investigation by investigative journalist group Noteworthy on "Selling our genes"[56].

— The dynamic consent model developed by the ELSI group was the first Dynamic consent model developed[57,58] and has been key both for the CHRIS main study success story as well as for other studies such as the CHRIS COVID-19 study during the current pandemic. The group is internationally recognized for the dynamic consent work[59], continues to publish on this topic[60,61] and counts itself as a world leader in this field.

— The attention to participants' rights lead to important international collaborations that is generating impactful research[62,63,64] that also involves participants' voices[65].

Our achievements

2. BUILDING RESOURCES

We have been building up the resources necessary to place biomedical research in South Tyrol on a solid foundation for future decades.

SCIENTIFIC RESOURCES

— We developed a cohort study (Cooperative Health Research in South Tyrol - CHRIS) in close partnership with the local healthcare provider, establishing a resource for future biomedical research.

— We have recruited the human expertise required to implement as well as maintain these resources, and to perform these research activities, and we are actively further training local young scientists.

INFRASTRUCTRE

— We successfully established the physical infrastructure needed for collecting, processing and storing biosamples.

— We established the laboratory infrastructure required to perform wide range of research activities, from analysing biosamples through to characterisation of molecular mechanisms of disease processes

PARTERNSHIPS

— We have built up academic ties to many renowned institutions both in Italy, and internationally (see Appendix)

— We have built up collaborative efforts with hundreds of research institutions globally through defined Consortia, leading to landmark studies on the characterisation of the genetic determinants of health-related traits

RESEARCH SOLUTIONS

— We have established the IT solutions necessary for the collection, management and retrieval of data and biosamples.

— We have developed cutting edge ethical and legal frameworks for our research resources to allow for dynamic consent, recall by genotype, data sharing and deposition in databases, return of research results and secondary findings.

— We have worked at the highest level of EU ELSI networks and committees to oversee international planning for adoption of GDPR.

RESEARCH TECHNOLOGIES

— We have established many of the technologies to generate experimental cell models and support experiments on any tissue of interest.

— We established a dynamic imaging suite with technologies necessary to image cellular processes at high resolution, and contributed to the development of new sensor technologies through strategic partnerships with private sector and academia.

— We established and use technologies within the new Mass Spectrometry (MS) facility capable of performing very sensitive metabolic profiling.

— We successfully set-up two electrophysiology systems to functionally investigate living cells.

— Through our ongoing program of methodological research, we have established and developed statistical and bioinformatics tools to analyse our data. and we have made the tools available (see Appendix).

Our strengths

— A comprehensive set of complementary resources and infrastructure to conduct research now and in future years.

— Biobanks and data repositories comprised of individual health data, extended pedigree information, biosamples and high resolution molecular and genetic profiles.

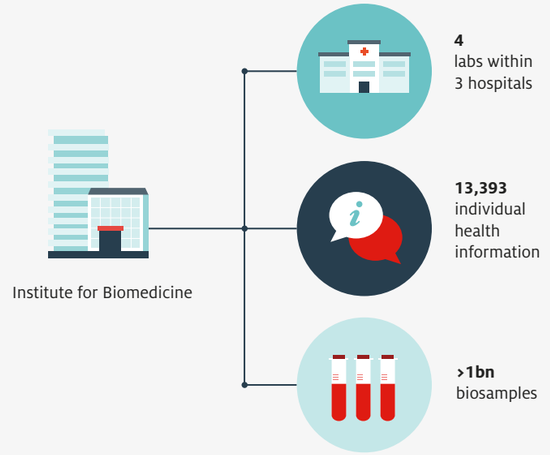
— The right human and technical experts to use these data and biosamples effectively.

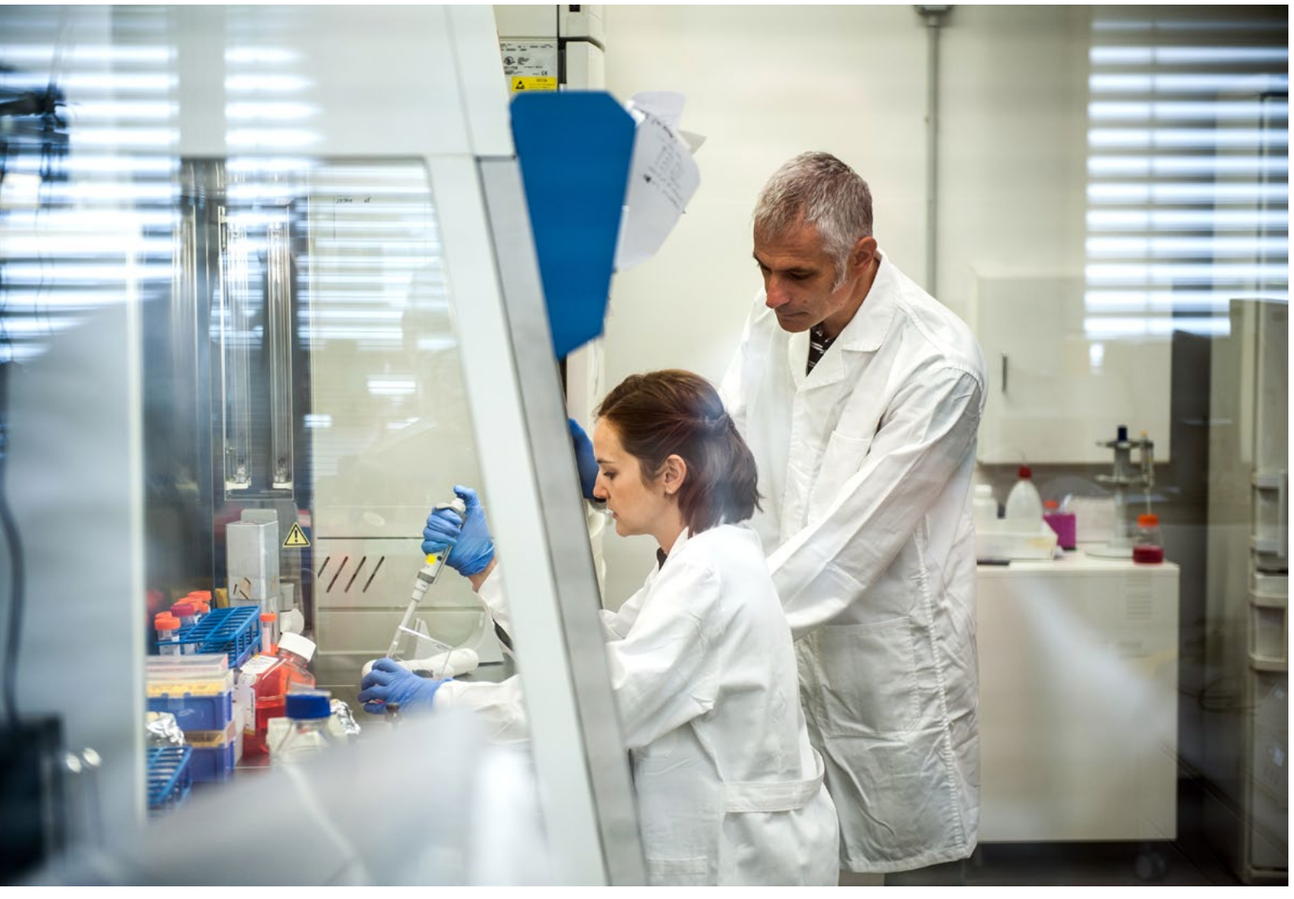
— A strong and active partnership with the local healthcare system, vital to create more precision health and medicine projects.

— An engaged and participative study population.

— Independence to creatively set the direction and focus of our research programs, with the flexibility to take advantage of opportunities as they arise, such as the COVID-19 pandemic in 2020.

— Novel areas of health data that distinguish CHRIS amongst similar studies elsewhere and allow us to create relatively unique and therefore highly competitive research projects.

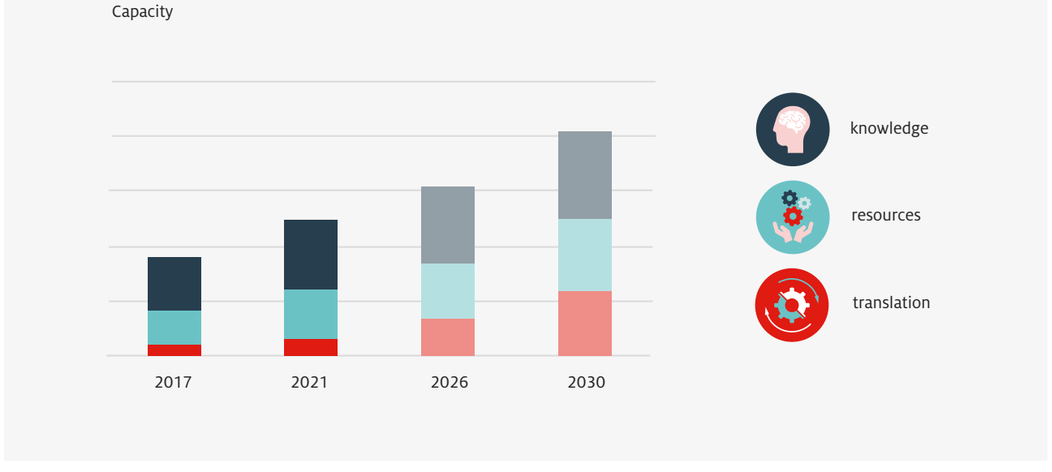




Strategic context

We envision the growth of the Institute in three stages. The initial strategic plan covered the **first stage (concept and startup)** focused on **building our resources**, including human expertise, research technologies and capabilities, data and biobanks derived from our study participants (including CHRIS). In this phase we created the core research groups that are using the above resources to drive high quality scientific outputs using local, national and international collaborations and partnerships where necessary. This current strategic plan covers the **second stage**, with a focus on **consolidating all our current resources and activities**. Here we intend to **maximize the scientific output** based on the completed CHRIS baseline collection, and set up the foundations for future translational opportunities for healthcare impact. We will **promote research activities, especially more innovative ones, that are of potential value for healthcare**, including the development of predictive approaches for precision health and prevention, development of model systems of value for development of therapeutics, and we will continue and expand on partnerships with healthcare providers and industries active in precision medicine and health (PMH) sector. We will continue to engage the best minds from across the biological, clinical, chemical, engineering and data sciences. We will encourage multidisciplinary work together with our counterparts in the healthcare system, local and regional industries and other research partners from the wider EUREGIO region and beyond. We are building on an established basic research foundation, that we will extend and improve by incorporating access to healthcare records, and supplement with personalised healthcare data gathered through mobile devices and tools to allow dynamic capturing of continuous data.

We will expand our data storage and data access interfaces to **support both researchers and clinicians** in the development of such PMH approaches. We will also continue developing the ethical, legal, societal and informatics frameworks that allow people to securely share their individual data to allow better interpretation, something vital as research moves forward. All of these measures can enable us to make use of the CHRIS study to **prototype and develop new approaches for precision medicine and healthcare**. The consolidation and development of data and capabilities generated in the second phase will create an even stronger foundation for a successful future **third stage**, where we will make use of the experience acquired and opportunities established in PMH to **increase our scientific impact and to contribute to the development of healthcare solutions for the benefit of the population**.



Our commitments

1. We will continue to expand the Institute resources for biomedical research and for development of PMH research and potential solutions.
2. We will ensure a strong and sustainable Institute that promotes biomedical research excellence.
3. We will build in the flexibility that allows us to respond to emergent crises such as the COVID-19 pandemic of 2020.
4. We will continue to actively explore translational opportunities, including activities such as drug repurposing and screening, that may arise from our research activities and resources.

Our mission

To foster biomedical research in the region and through this improve individual and population health both locally and beyond.

Our vision

To make the Institute for Biomedicine into a state of the art internationally renowned R&D centre that will be a driver for innovative biomedical and translational health research.

Our principles

In pursuing our mission and vision, the fundamental principles and standards that consistently shape our thinking and approach are:

1. Consideration and respect for our stakeholders, who represent the purpose of our work, and enable us to do it.
2. Determination to produce knowledge that can be translated and applied, using the highest ethical standards.
3. Commitment to a culture of trust, communication, cooperation, and achievement.

Our goals

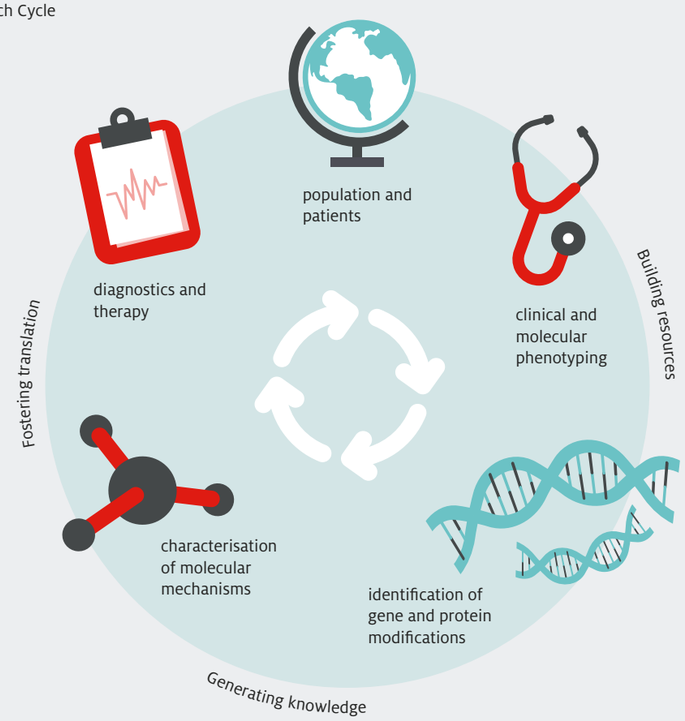
During the next five years, as we build our activities towards our growth and expansion phase, and consolidate ongoing activities, we will continue to focus on three main strategic goals in order to achieve our vision and fulfil our mission.

Building Resources
Consolidate, expand, and continuously develop our resources to enable innovative biomedical and translational health research in the region for future decades.

Generating Knowledge
Investigate the basis of health and disease, focusing on molecular and genetic determinants, biomarkers and mechanisms, and use the knowledge generated to holistically explore precision medicine and health opportunities.

Fostering Translation
Promote translation of scientific discoveries into new solutions, products and services.

Biomedical Research Cycle



1. BUILDING RESOURCES

We will continue to build up CHRIS resources to sustain biomedical research in the region for many decades. We will continue enriching the study data, and increase the utility and value of the resource by including more objective, continuous and digital phenotyping, especially of clinical relevance. We will develop our biobanks and data storage and analysis platforms and reinforce our tools and reagents and expertise to create cellular models of disease which can then be used to characterise molecular pathways of health and disease, and be useful for screening approaches to discover or repurpose drugs for novel therapeutic applications. We will expand our observational studies and start to design more interventional PMH studies, build up our ICT and bioanalytical infrastructure and begin to create banks of cells for the cell modelling. To support all our activities, we will develop concrete ethical and legal frameworks based on existing or emerging guidelines.

1.1 Increase our Population Resources

We will perform the first follow-up phase of our long-term CHRIS population study in approximately 10,000 people and integrate data from electronic medical records (EMR) and other health databases.

We will expand and continuously evolve our research resources, our available infrastructure and technologies, and our human capital. We will reinforce the CHRIS study by successfully launching and executing the first longitudinal follow up stage (CHRIS phase II). Phase II will collect deeper and more quantitative phenotype data directly related to clinical outcomes of relevance for the local population. We will link this data to other population health databases including electronic medical records (EMR) to allow regular updates of the clinical information of the CHRIS participants at no extra cost.

1.2 Reinforce our Study Capacity

Improve our capacity to implement specific precision medicine and health (PMH) studies in parallel with the CHRIS phase II.

We will also start to conduct more focused sub-studies to investigate specific health and disease focus areas, and through these accelerate possible translational use of the data and resources collected. To boost specific molecular studies, we will also begin building up a bank of disease specific cells based on individual genetic backgrounds and will expand and refine these cellular models to encompass more complex 3D tissue models that reflect better mature tissues of interest to the research questions to be answered

1.3 Strengthen our Databases and ICT Tools

Create bioinformatic platforms and tools for faster and more efficient browsing and interpreting data and analytical results.

Integrated "big data", bioinformatic and statistical analysis solutions and adequate ICT frameworks are necessary to warehouse large amounts of individual level data and use it more effectively. Remote phenotyping technologies will increase and need adequate solutions for data collection and storage. Sustainability will be important so data can be preserved and used for future purposes, especially as new analytical methods and modelling approaches emerge. Ultimately, these data can help create a foundation for novel clinical decision support tools.

1.4 Develop Ethics and Legal Guidelines

Establish a comprehensive ELSI operational framework that allows the best translational use of our data and biological resources.

Development of ethics guidelines that enhance individual responsibility, ownership and sharing of personal health data, and protecting patient participation in research under the highest standards, need development if PMH initiatives are to be successful. By converging empirical and theoretical approaches, we will develop and apply ethically conscious methods that incorporate all regulatory requirements, to inform planning, development and realisation of research strategies that move towards more translational use of the knowledge generated.

2. GENERATING KNOWLEDGE

We will continue to use our resources, and the focused expertise of our complementary research groups, to promote excellent research. Methodological and applied research in biostatistics and epidemiology will help in unravelling the complex mechanisms underlying human health. Our genomics work will build on the achievements so far and orient towards developing models for predictive health at the population and individual level, in order to convert knowledge into scientific and health impact. Novel targets will be identified for functional follow-up using our cellular and molecular biology expertise, alongside technical capacities in advanced cell culture, imaging and electrophysiology, all established over the last few years, to drive more molecular phenotyping and disease mechanism programs. We will continue to focus on metabolic diseases, including obesity and diabetes, as well as kidney disease, alongside cellular and molecular cardiology and neurobiology, initially prioritising arrhythmic heart disease, neurodegeneration, sleep and pain. We will also maintain a focus on mitochondrial function and its cellular consequences to ageing and health.

2.1 Maximise Scientific Productivity

Maximize our research outputs by systematically generating and harnessing new data and knowledge.

We will perform systematic analysis of our genomic and metabolomic datasets to determine variants, genes and pathways involved in health and disease and use these to drive more functional in-house biology programs. We will use the advantage of extensive pedigree structure in CHRIS to better determine the genetic contributors to human health. Increased clinically relevant data will be analysed systematically with latest epidemiological tools. Molecular epidemiological research and bioinformatic capabilities will integrate different datasets, that currently include genomics data and novel un-targeted metabolomics data. Joined with data on life-style and environmental factors, we can derive better predictive models or identify disease causal pathways.

2.2 Develop New Experimental Models

Produce appropriate and optimised experimental models to investigate the basis of health and disease mechanisms within our focus areas.

We will use our expanded bank of optimised human cell models based on iPS cell technology, and the latest genome editing techniques, and use these to generate specific resources for target compound screening and secondary validation of any identified compounds. Improved 3D cellular models to capture the properties of more mature tissue will be created and used for research in our areas of expertise. We will compliment human cell models with *C. elegans* models.

2.3 Develop Strategies to Protect Health

Explore and develop predictive and preventive health strategies based on our research outputs.

Polygenic risk models for risk and outcome prediction in common diseases can now be generated based on genomic data collected within the baseline of CHRIS, integrating clinical information and family health history. The development of such models will provide a first step in the creation of enhanced screening and disease prevention strategies for PMH. Longitudinal CHRIS phase II data will open new possibilities to derive models assessing risk of transition from pre-clinic to the clinical chronic disease.

2.4 Enhance Strategic Partnerships

Enhance further knowledge generation through the right strategic partnerships within academia, the clinics or industry.

We will be actively establishing strategic partnerships that benefit our scientific productivity and impact. We will select academic, clinical and industrial partners that share common research interests and focus areas. Strengthening university ties will increase funding opportunities and guarantee a mutually beneficial exchange of students and other scientists, as well as access to additional technological platforms and expertise. Our outreach will include complimentary technology platforms, drug target prioritization, compound screening and experimental models.

3. FOSTERING TRANSLATION

We will build pioneering partnerships that bring the necessary clinicians, scientists and companies together to foster the development and practical application of biomedical and health research knowledge and resources. Through such partnerships we will explore opportunities to develop innovative and effective products, strategies, interventions or services. Translating scientific concepts into clinical applications is a major contemporary challenge in medicine and healthcare, and a process that might take decades rather than single years. Given the potential to effect both individual and societal change through biomedical research, it's important to design programs, such as those that incorporate family history for risk assessment, and specific pharmacogenomics projects, to start to lay the foundation for such change.

3.1 Developing Precision Health Solutions

We will develop opportunities to use the CHRIS study as a testing ground for precision medicine and health programs.

We will start to perform pilot projects, with external partners when necessary, that let us use CHRIS as a testing ground for new promising solutions with precision health implications. Successful pilot projects will facilitate translation by supporting the eventual deployment of these solutions on a wider scale, with the help of local healthcare providers and the appropriate resources to manage and implement such solutions. We will further engage the local community in helping pilot novel health-related technologies and solutions such as target interventional studies, as this can help facilitate a transition from disease risk prediction to strategies for disease prevention or promotion of health. These pilot

studies will support the development of novel products and solutions for wider use.

3.2 **Identify and Validate Novel Targets**

Expand on the knowledge generated from our resources to specifically identify and validate new targets through genetics and basic cell biology.

We will continue to generate and use model systems, including cell types of interest derived from individuals with specific phenotypic and genetic backgrounds, to investigate molecular mechanisms of disease with respect to particular variants of interest in candidate genes identified through our genetic screening programs. Such individualized models can be used directly as a testing ground for identification and validation of new targets for potential diagnostic or therapeutic use. We will therefore use validated targets and models to screen for new compounds or opportunities to re-purpose drugs.

3.3 **Acquire Business Acumen**

Encourage an entrepreneurial research culture by exposing our scientists to projects with industry, technology transfer and business developers.

To move from basic research to developing and implementing specific products and solutions we will need to expand our expertise in business orientation, expose scientists to interfaces with industry and business development experts and increase awareness for the translation and monetization of research findings. To achieve these goals we will be increasing our dialogue with experts in relevant fields.

3.4 **Develop Strategic PMH Partnerships**

Establish strategic alliances and partnering with industrial and clinical partners with an established track record in pioneering.

PMH solutions Bringing innovative PMH solutions to the market presents new challenges and opportunities that will require dialogue with all stakeholders, including regulators, funders and innovators and companies. We will choose partners with a track record in pioneering PMH products and solutions, such as remote digital phenotyping and dynamic health monitoring, and through such activities lay the foundations for future development and implementation of PMH solutions.

Our objectives in short

1. BUILDING RESOURCES

1.1 **Increase our Population Resources**

1.2 **Reinforce our Study Capacity**

1.3 **Strengthen our Databases and ICT Tools**

1.4 **Develop Ethics and Legal Guidelines**

2. GENERATING KNOWLEDGE

2.1 **Maximise Scientific Productivity**

2.2 **Develop New Experimental Models**

2.3 **Develop Strategies to Protect Health**

2.4 **Enhance Strategic Partnerships**

3. FOSTERING TRANSLATION

3.1 **Developing Precision Health Solutions**

3.2 **Identify and Validate Novel Targets**

3.3 **Acquire Business Acumen**

3.4 **Develop Strategic PMH Partnerships**

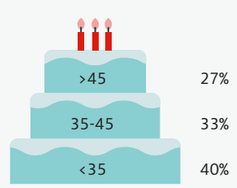
Our people mean the world to us

HR growth and development

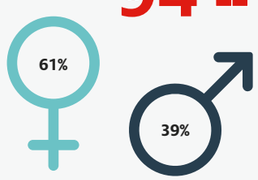
Over the past five years, we have undergone a significant growth in personnel, hiring researchers (mostly at the PhD and post-doc level) and research support staff from all over the world, to increase our expertise in all areas. We guarantee equality (i.e. gender) and a motivating, stable and secure working environment. To support the professional growth of our staff and careers of young students, we developed diversified career paths and individual training possibilities.

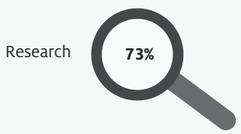
Personnel by nationality

Personnel by age

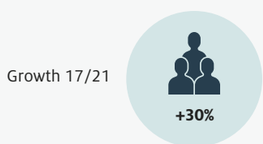


Personnel by gender





86 FTE

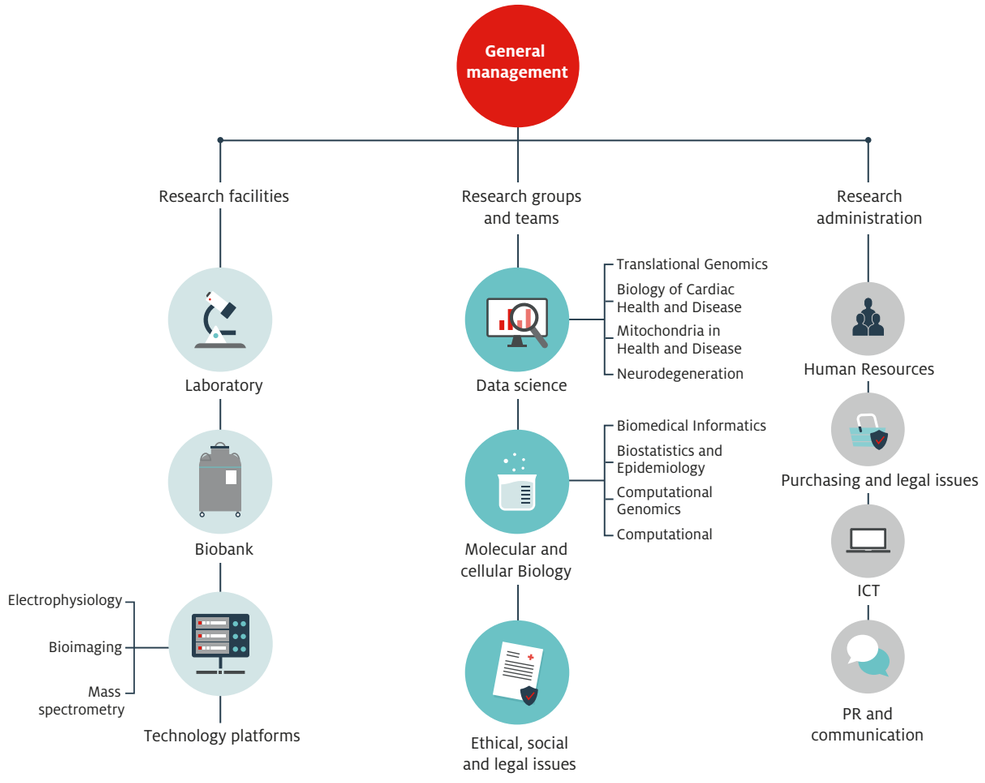


Our structure & composition

Leadership, Management and Structure
Building up the Institute over the last 5 years meant not only doubling in size, but also developing and integrating new research initiatives, acquiring new technologies and developing new labs. In doing so, it was clear that increased flexibility was necessary to allow execution of our new strategy with the needed velocity and adaptability to face today's fast changing environment. Therefore, we are transforming our management and leadership structure in order to speed up decision making, to keep communication targeted and improve our operational effectiveness.

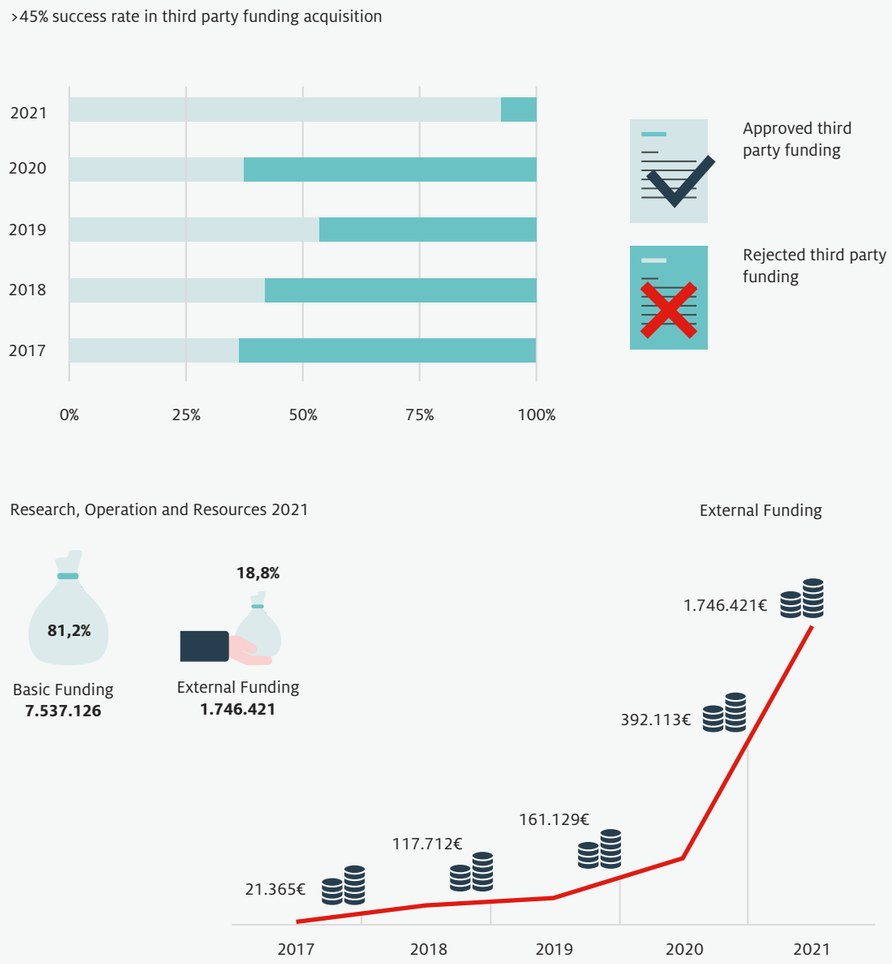
Above all, to allow for all members of IFB to grow professionally and act responsibly within their own area of expertise. The building blocks of our new management and leadership are:

- to serve a common purpose
- to foster a shared consciousness
- to empower execution



Finances

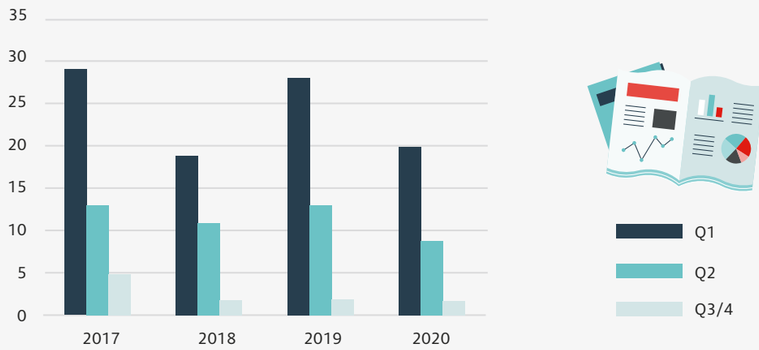
Basic public financing and third-party funding
Our Institute receives core funding through the Autonomous Province of Bolzano, via a performance agreement between the government and Eurac Research. The yearly available budget is approximately 6,5 Million Euro. Additional funding is generated through grants and other 3rd party funding schemes. To allow further growth in the future, we need to generate additional income in the form of increased public basic funding and third-party funding but also by investigating new avenues such services arising from our research and infrastructure.



Research output

Scientific publications and impact factor
One of our principal goals is to generate knowledge and to make this knowledge accessible to the global scientific community. Over the last 5 years we have disseminated > 150 science related papers.

> 65% of scientific papers are published in journals ranked in the top quartile within their field



Ø 2017-2020: 40 publication, 255,378 IF, 4.029 citations per year

2020

Scientific publications **32**

IF **202,811**

Citations **3.631**

Appendix

LIST OF MAIN CONSORTIA

CHARGE Consortium. The Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium was formed to facilitate genome-wide association study meta-analyses and replication opportunities among multiple large and well-phenotyped longitudinal cohort studies. There are a wide range of cardiovascular, neurological and other traits being studied in a large number of cohorts in addition to the founding cohorts.

QTSCD and **QRS** Consortia are offshoots of the CHARGE Consortium dealing with electrical and structural heart traits.

ENGAGE (European Network for Genetic and Genomic Epidemiology) is a research project funded with 12 million euros by the European Commission under the 7th Framework Programme-Health Theme. The ENGAGE Consortium has brought together 24 leading research organizations and two biotechnology and pharmaceutical companies across Europe and in Canada and Australia with the goal of identifying large numbers of novel susceptibility genes that influence metabolic, behavioral and cardiovascular traits, and to study the interactions between genes and life style factors.

GEFOS and **GENOMOS**. GEFOS stands for the GEnetic Factors for OSteoporosis Consortium. It is a large international collaboration involving various prominent research groups. It grew out of a EU FP5 funded project, named GENOMOS, by bringing together over 20 of Europe's largest collections of osteoporosic study populations with DNA available. The GEFOS project is using GWA analysis with high density SNP arrays, to identify common risk gene variants for osteoporosis.

GIANT: Genetic Investigation of ANthropometric Traits. The GIANT consortium is an international collaboration that seeks to identify genetic loci that modulate human body size and shape, including height and measures of obesity. The GIANT consortium is a collaboration between investigators from many different groups, institutions, countries, and studies, and the results represent their combined efforts. The primary approach has been meta-analysis of genome-wide association data and other large-scale genetic data sets. Anthropometric traits that have been studied by GIANT include body mass index (BMI), height, and traits related to waist circumference (such as waist-hip ratio adjusted for BMI, or WHRadjBMI). Thus far, the GIANT consortium has identified common genetic variants at hundreds of loci that are associated with anthropometric traits.

The **MAGIC** Consortium: Meta-Analyses of Glucose and Insulin-related traits. MAGIC represents a collaborative effort to combine data from multiple GWAS to identify additional loci that impact on glycemic and metabolic traits. MAGIC investigators have initially studied fasting glucose, fasting insulin, 2h glucose and HBA1c, as well as performed meta-analysis of more sophisticated measures of insulin secretion and sensitivity. Through these efforts, dozens of loci influencing these traits have been identified, a subset of which also influence risk of type 2 diabetes.

DIAGRAM. The DIAGRAM (DIAbetes Genetics Replication And Meta-analysis) consortium is a grouping of researchers with shared interests in performing large-scale studies to characterise the genetic basis of type 2 diabetes, and a principal focus on samples of European descent. The membership and scope of DIAGRAM has developed as the scale of collaboration in the field has increased. DIAGRAMv3 is comprised of 12,171 cases and 56,862 controls. In addition to these large discovery projects, DIAGRAM data have supported over 200 internal and external research projects. DIAGRAM has strong links and substantial overlap of membership with the GoT2D and T2D-GENES consortia that are leading sequence-based discovery efforts for T2D. GWA, metabochip and exome chip data from existing and new DIAGRAM partners will provide valuable extension, replication and validation of findings arising from those studies. There are also strong links with equivalent efforts in other major ancestral groups (e.g. AGEN, MEDIA) that will enable further rounds of GWA integration that support locus discovery and causal variant fine mapping.

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OUR ACHIEVEMENTS: PARTNERSHIPS

University of Milano

University of Parma

Centro Cardiologico Monzino Milano

Ospedale Careggi Firenze

Ospedale San Donato Milano

Humanitas Ospedale Milano

Innsbruck Medical University

University of Bologna

University of Brescia

University of Munich

University of Udine

University of Udine

ICGEB Trieste

University of Trento

University of Verona

Institute of Molecular Biotechnology (IMBA) in Vienna

Academic ties were made with the University of Lübeck

OUR ACHIEVEMENTS: STATISTICAL AND BIOINFORMATICS TOOLS

Software (year)	Description	Authors, publications, website
xcms (2019)	A package for preprocessing of LC-MS metabolomics data.	Rainer J https://github.com/sneumann/xcms
Spectra (2019)	A package providing flexible and scalable infrastructure for Mass spectrometry data.	Rainer J https://github.com/RforMassSpectrometry/Spectra
ensembldb (2019)	A package to retrieve and store Ensembl annotations and positional information.	Rainer J, Gatto L, Weichenberger CX (2019) ensembldb: an R package to create and use Ensembl-based annotation resources. Bioinformatics; 35:3151-3 https://bioconductor.org/packages/release/bioc/html/ense mbldb.html
emerald (2019)	A software tool for fast linkage disequilibrium estimation with massive datasets.	Quick C, Fuchsberger C, Taliun D, Abecasis G, Boehnke M, Kang HM. emeraLD: rapid linkage disequilibrium estimation with massive datasets. Bioinformatics. 2019 Jan 1;35(1):164-166. http://github.com/statgen/emeraLD
RescueOMR (2017)	A set of tools to perform batch OMR (Optical Mark Recognition) on paper questionnaires.	D'Elia Y https://github.com/EuracBiomedicalResearch/RescueOMR
LIDPD (2017)	Web resource for Levodopa-induced diskynesia in Parkinson's disease.	Blankenburg H, Falla M, Schwienbacher C, Fabbrini G, Berardelli A, Pramstaller PP, Domingues FS (2017) A Web Resource for Levodopa-Induced Dyskinesia Genetics in Parkinson's Disease. Neuroinformatics 15:297-300 - http://lidpd.eurac.edu/
Frela (2017)	A high-throughput web server for protein functional similarity calculation and interpretation.	Weichenberger CX, Palermo A, Pramstaller PP, Domingues FS (2017) Exploring Approaches for Detecting Protein Functional Similarity within an Orthology-based Framework. Sci Rep 7:381. https://frela.eurac.edu/

Genetic Imputation Server (2016)	A cloud computing solution for genotype imputation.	Das S, Forer L, ... Fuchsberger C (2016). Next-generation genotype imputation service and methods. Nat Genet 48:1284- 7 https://imputationserver.sph.umich.edu/index.html
FamAgg (2016)	A package to evaluate familial aggregation of traits in large pedigrees.	Rainer J, Taliun D, D'Elia Y, Pattaro C, Domingues FS, Weichenberger CX (2016). FamAgg: an R package to evaluate familial aggregation of traits in large pedigrees. Bioinformatics 32:1583-5. https://bioconductor.org/packages/release/bioc/html/Fam Agg.html
clickmaster-2000 (2016)	A program to count objects inside an image.	D'Elia Y https://github.com/EuracBiomedicalResearch/clickmaster20 00

Software (year)	Description	Authors, publications, website
Dintor (2015)	A data integration framework providing a set of tools for exploring omics datasets.	Weichenberger CX, Blankenburg H, Palermo A, D'Elia Y, König E, Bernstein E, Domingues FS (2015) Dintor: functional annotation of genomic and proteomic data. BMC Genomics 16:1081.
Bond (2015)	A tool for remote/recursive evaluation between Python and another interpreter.	D'Elia Y https://www.thregr.org/~wavexx/software/python-bond/
LDExplorer (2014)	A scalable implementation of a memory efficient algorithm for whole-genome LD-based haplotype block recognition.	Taliun D, Gamper J, Leser U, Pattaro C (2016). Fast Sampling-Based Whole-Genome Haplotype Block Recognition. IEEE/ACM Trans Comput Biol Bioinform 13:315-25. Taliun D, Gamper J, Pattaro C (2014). Efficient haplotype block recognition of very long and dense genetic sequences. BMC Bioinformatics 15:10. http://www.eurac.edu/en/research/health/biomed/services /Pages/LDExplorer.aspx

nephro (2013)	A software package providing a set of functions to estimate renal function based on common biomarkers.	Pattaro C, Riegler P, Stifter G, Modenese M, Minelli C, Pramstaller PP (2013) Estimating the Glomerular Filtration Rate in the General Population Using Different Equations: Effects on Classification and Association. Nephron Clin Pract 123:102-11 https://cran.r-project.org/web/packages/nephro/index.html
Twilight (2013)	A tool for analysis and visualization of ligands in electron density maps of protein structures.	Weichenberger CX, Pozharski E, Rupp B (2013). Visualizing ligand molecules in Twilight electron density. Acta Crystallogr Sect F Struct Biol Cryst Commun 69:195-200. http://www.ruppweb.org/twilight/
GWAtoolbox (2012)	A software package for fast quality control of genome-wide association data and used by major GWAS consortia.	Fuchsberger C, Taliun D, Pramstaller PP, Pattaro C, CKDGen consortium (2012). GWAtoolbox: an R package for fast quality control and handling of genome-wide association studies meta-analysis data. Bioinformatics 28:444-5 - http://www.eurac.edu/en/research/health/biomed/services /Pages/GWAtoolbox.aspx
Download Ticket Service (2010)	A file-sharing utility.	D'Elia Y - https://www.thregr.org/~wavexx/software/dl/
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