



**Call for proposals – 2021
Appel à projets vague 2
Excellence in all its forms (ExcellencES)**

SHAPE-Med@Lyon

Submission form

Acronyme du projet / Project acronym	SHAPE-Med@Lyon / SHAPE	
Project title (in English)	Structuring a one H ealth Approach for P ersonalized M edicine in L yon	
Titre du projet en français	Structuration d'une approche « une seule santé » pour la médecine personnalisée à Lyon	
Keywords / mots clés (min 5 – max 10)	One Health; Personalized medicine; Health research and innovation hub; Public health school; Transdisciplinary institute for health; Double graduation; Integrated CHU-university governance; Health data; Environmental health; 5P-medicine	
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Établissement coordinateur / Leading institution	Université Claude Bernard Lyon 1 (UCBL) EPSCP		
Partner institution(s) involved in the project / Institution(s) partenaire(s) impliqué(es)	Hospices Civils de Lyon (HCL) Université Lumière Lyon 2 (ULL) Institut d'enseignement supérieur et de recherche en alimentation, santé animale, sciences agronomiques et de l'environnement (VétAgro Sup) École supérieure de Chimie Physique Électronique de Lyon (CPE) Centre Léon Bérard (CLB) Centre Hospitalier Le Vinatier (CHLV) Institut National de la Santé et de la Recherche Médicale (Inserm) Centre National de la Recherche Scientifique (CNRS) Institut National de Recherche pour l'Agriculture, l'Alimentation et l'Environnement (INRAé) Institut National de Recherche en Informatique et Automatique (Inria) International Agency for Research on Cancer (IARC-WHO)		
Project duration / Durée du projet entre 72 mois et 120 mois	120 Months / Mois		
Requested funding / Aide demandée (minimum 5M€)	35 132 400 €	Full cost	492 646 222 €
Le cas échéant : Listes des projets PIA auxquels ce projet est éventuellement lié (notamment EUR, universités européennes, Equipex, Labex, Institut convergence, IDEFI, etc.) / Project links with existing PIA entities (e.g. EUR, Equipex, Labex, Institut convergence, IDEFI, etc.)	SFRI Graduate+ Cohorte OFSEP RHU MARVELOUS, PERFUSE, cirB-RNA, BETPSY, IdBioRiv, SMART, ICELAND DUNE SIDES 3.0 (partenaire) Equipex IVTV, PHARE, LILI, PHENOCAN Equipex+ InfectioTron, SpatialCell'ID EUR H2O'Lyon IDEFI SAMSEI IDEFIN OpenMiage IHU B CESAME et OPERA LabEx DevweCan, CORTEX, PRIMES, IMU, MILYON, CeLyA, ASLAN Institut Carnot CALYM Instituts Convergences PLASCAN, EUL IRT BIOASTER NCU CURSUS+, THEME CRB CryANim DEMOES INCLUDE SATT PULSALYS		



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Ce projet s'inscrit-il dans le cadre d'une Initiative d'excellence labellisée IdEx ou ISITE ?
Si oui, laquelle

Non



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List of partner institutions / Liste des institutions partenaires

Name of the research organisations / Nom des organismes de recherche	Legal status / Statut
Institut National de la Santé et de la Recherche Médicale (Inserm) Centre National de la Recherche Scientifique (CNRS) Institut National de Recherche pour l'Agriculture, l'Alimentation et l'Environnement (INRAé) International Agency for Research on Cancer (IARC-WHO) Institut National de Recherche en Informatique et Automatique (Inria)	EPST EPST EPST International Organization (WHO) EPST
Name of the institutions of higher education and research / Nom des établissements d'enseignement supérieur et de recherche	Legal status / Statut
Université Claude Bernard Lyon 1 (UCBL) Université Lumière Lyon 2 (ULL) Institut d'enseignement supérieur et de recherche en alimentation, santé animale, sciences agronomiques et de l'environnement (VétAgro Sup) École supérieure de Chimie Physique Électronique de Lyon (CPE)	EPSCP EPSCP EPSCP EESPIG
Name of the Clinical Entity / Nom des établissements hospitaliers (services, unités...)	Legal status / Statut
Hospices Civils de Lyon (HCL) Centre Léon Bérard (CLB) Centre Hospitalier Le Vinatier (CHLV)	Établissement public de santé Centre Régional de Lutte Contre le Cancer Établissement public de santé mentale
Name of secondary schools / Nom des établissements d'enseignement secondaire	Legal status / Statut
Other partners (Companies, Start-up, Associations, etc.) / Autres partenaires (Industries, Entreprises, Start-up, Associations, etc.)	Field(s) of activity / Secteur(s) d'activité



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RESUME / SUMMARY

Abstract - English version (max. 4000 characters)

SHAPE-Med@Lyon builds on the exceptional strengths of Lyon in all fields of health (human, environment, societies). In addition to its powerful HEI ecosystem, it is the top French industrial network for healthcare innovation and world-leading research in biomedical sciences, the 2nd academic hospital system in France with leading clinical research and simulation-based medical training, and the headquarter of IARC-WHO. Our ambition is to create a major Health Hub to better support and connect public and private actors in order to launch ambitious programs and develop one health approaches to tackle the challenges of predictive, preventive, personalized, participatory, and proof-based medicine. Our aim is to develop new solutions for care and to contribute to public decision making in health issues.

Lyon Health Hub 2030 has a joint governance model, bringing together all the relevant stakeholders in health research and innovation: HEIs, health institutions, NROs, industry, patient associations, local authorities. It relies on integrated research support services and an HR strategy involving all key partners. Governance and services are housed in a *Maison de la recherche en santé*, supported by HCL and UCBL, which will house a joint health research directorate, involving all partners, companies, and local players. This level of integration among HEIs and a university hospital is unique in France. The project will benefit from a unique partnership with the Ottawa Health Innovation Hub, with joint research funding and graduate training. It will also be embedded in a broader institutional transformation of the Lyon academic site, with UCBL, ULL, and CPE committed to creating a new research-intensive multidisciplinary university.

SHAPE-Med@Lyon will be a cornerstone and an accelerator for the Lyon Health Hub initiative and this institutional transformation. It will focus on the creation of the Lyon Transdisciplinary Institute for Health, bringing together all scientific communities with the goal of structuring a one health approach for personalized medicine. The Institute will support and coordinate four scientific programs, building on the differentiating scientific strengths of the Lyon site:

- Health and Territories: Innovative approaches to relate health to environmental and social characteristics of territories and predict spillover effects
- Adaptation and evolution in infectious diseases: from pathogens to societies
- Brain Disorders, Remediation, and Inclusive Society
- Transdisciplinary approaches to understanding, preventing & curing cancer.

To support these scientific programs, SHAPE will contribute to develop:

- A digital strategy and infrastructure to tackle the major challenges of data in health research which combine individual, environmental and social information and proxies which are necessary to develop personalized medicine
- An interdisciplinary teaching offer bringing together all health-related disciplines such as medical sciences, basic and data sciences, HSS and engineering, to train future leaders in health research, care, and innovation
- Health innovation by bringing together academics, hospital practitioners, businesses and decision makers through public-private mobility and joint learning expeditions with the support of the Ottawa Health hub which shares similar objectives.

SHAPE is also linked to a Swafs project that will promote knowledge dissemination to society and participatory approaches in research.



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The SHAPE-Med@Lyon project bring together all major partners of the health field in Lyon, with a simple and agile governance. Clear milestones and deliverables have been defined to monitor the implementation of the SHAPE programs and the overall strategy. An International Scientific Advisory Board will conduct in-depth external evaluations of the strategy and governance of SHAPE and the Health Hub as a whole every two years. The funding request for SHAPE-Med@Lyon is ~35 M€.



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Résumé en français (max. 4000 caractères)

SHAPE-Med@Lyon s'appuie sur les forces de Lyon dans tous les domaines de la santé (humaine, environnementale, sociale). Dotée d'un écosystème ESRI puissant, Lyon constitue le premier tissu industriel français de l'innovation en santé, est un leader en recherche biomédicale, abrite le deuxième centre hospitalier, avec une recherche clinique de pointe et des formations intégrant la simulation en santé, et le siège du CIRC-OMS. Notre ambition est de constituer un Hub Santé reconnu, connectant acteurs publics et privés, afin de porter des programmes ambitieux et de développer les approches « santé unique » pour relever les défis de la médecine prédictive, préventive, personnalisée, participative et basée sur les preuves. Notre objectif est de développer de nouvelles solutions pour les soins et de contribuer à l'élaboration des politiques de santé publique.

Lyon Hub Santé 2030 sera doté d'une gouvernance impliquant tous les acteurs de la recherche et de l'innovation : établissements ESRI, institutions de santé, organismes de recherche, entreprises, associations de patients, collectivités. Il s'appuie sur une gouvernance intégrée de la recherche et une stratégie RH qui engagent tous les partenaires clés. La gouvernance et les fonctions supports seront localisées dans une maison de la recherche en santé, qui hébergera une direction conjointe de la recherche impliquant tous les acteurs locaux, publics et privés. Cette intégration des stratégies entre universités et hôpitaux sera unique en France. Le projet bénéficiera d'un partenariat avec le Hub d'Innovation en Santé d'Ottawa, avec des actions de recherche et de formation financées conjointement. Il sera aussi imbriqué dans une transformation plus large du site académique lyonnais, l'UCBL, Lyon 2 et CPE s'engageant dans la création d'une université pluridisciplinaire de recherche intensive.

SHAPE sera la pierre angulaire et un accélérateur du Lyon Hub santé et de ce processus de transformation. Un institut de recherche transdisciplinaire en santé rassemblera les communautés scientifiques afin de structurer une approche de santé unique pour une médecine personnalisée. Cet institut soutiendra et coordonnera quatre programmes construits sur la base de nos forces scientifiques :

- Santé et territoires : une approche innovante pour relier santé, environnement et société
- Adaptation et évolution des maladies infectieuses : des pathogènes aux sociétés
- Troubles cérébraux, remédiation et société inclusive
- Approches transdisciplinaires pour comprendre, prévenir et soigner les cancers

Pour porter ces programmes, qui identifieront chacun des pilotes, SHAPE développera :

- Une stratégie et des infrastructures numériques pour l'analyse des données de santé qui combinent informations individuelles, environnementales et sociales en vue d'une médecine personnalisée
- Des formations transdisciplinaires qui impliquent sciences médicales, sciences dures et des données, SHS et ingénierie pour former les futurs leaders de la recherche, de l'innovation et des activités cliniques
- L'innovation en santé en rassemblant académiques, praticiens hospitaliers, entrepreneurs et décideurs à travers des mobilités publique-privée et des apprentissages en lien avec le hub santé d'Ottawa.

SHAPE est articulé à un projet SAPS qui contribuera à la diffusion des savoirs et soutiendra la recherche participative.



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Le projet rassemble les acteurs majeurs de la santé dans une gouvernance simple et agile. Des jalons et des livrables ont été définis pour suivre sa mise en œuvre et celle de la stratégie globale du site. Un comité international fera une évaluation de la stratégie et de la gouvernance de SHAPE ainsi que celle du Hub Santé 2030 tous les deux ans. Le financement demandé est de ~35 M€.



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PREAMBLE AND ANSWERS TO THE JURY'S COMMENTS

Higher education and research institutions in Lyon have developed a longstanding collaboration to strengthen the excellence and visibility of scientific research and training, including transdisciplinary approaches with a major socioeconomic impact. The recently selected SFRI Graduate+ strategy is one of the many examples of ambitious collaborations covering a wide variety of scientific fields. Based on this pragmatic approach, HEIs in Lyon have decided to focus on an academic development that addresses upcoming challenges and benefits students and society. Through shared and coordinated efforts, we have identified two core priorities, which result in two complementary proposals to the PIA4 ExcellencES call, reflecting the acknowledged strengths of the Lyon site: SHAPE-Med@Lyon, aiming at reinforcing Lyon as a major hub of health research and innovation; and TOOLS+, aiming at opening training programs to more diversity, opening research towards more multidisciplinary. These proposals are supported collegially by all the HEI in Lyon, many contributing to both, in relation to their area of expertise. They are supported by all NRO, as well as local authorities and major economic partners.

SHAPE-Med@Lyon is a radically revised proposal building on the jury's comments on the LYNX project submitted in round 1. The jury's assessment in round 1 recognized our scientific strengths, especially in the health field. However, the jury considered the program to be too wide-ranging and too costly. The project of a new university was not considered to be sufficiently transformational for the site. The jury also stressed the importance of developing a more significant strategy to support talent development and international attractiveness.

Following the jury's comments, we radically revised our approach by focusing on health issues. Health and more specifically medicine is a longstanding field of excellence in Lyon, shared by academics, hospitals, pharma industries, and local authorities. SHAPE-Med@Lyon comes with:

- A clear scientific focus on building the Lyon Transdisciplinary Institute for Health
- A clear institutional focus on a few key partners, with a lean governance scheme and a strategic integration of a university and a university hospital that is unique in France
- A radical revision of the funding request
- A strategy to train and support top talents
- An international strategy including an ambitious partnership with uOttawa, with the IARC-WHO, and potentially in the future with the Lyon based WHO Academy.

SHAPE-Med@Lyon is a part of a deeper transformation of Health research and innovation strategy and organization (Lyon Health Hub) which constitute a cornerstone and a pilot of an overall project aiming to transform the Lyon academic ecosystem and build a new multidisciplinary university including the universities Claude Bernard Lyon 1 (UCBL), Lumière Lyon 2 (ULL), and the engineering school CPE.



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1. CONTEXT AND SCOPE OF THE PROJECT

1.1 LYON, AN EXCEPTIONAL 360° HEALTH ENVIRONMENT: RESEARCH, INNOVATION, INDUSTRY, AND TRAINING

The leading industrial ecosystem for health innovation in France. Auvergne-Rhône-Alpes region is one of the most industrialized areas in the country, ranking first nationally for the total number of industrial jobs. In Lyon, health represents a major economic engine, with Sanofi the largest private employer, HCL the largest employer, and health representing 35,000 private jobs (72,500 jobs, including healthcare). Lyon is the second site of pharmaceutical industries in France, with 260 pharma and biotech enterprises, 800 life science companies, and 150 health companies. Two other key players are the biocluster Lyonbiopôle, the regional gateway to healthcare innovation, and the Technology Transfer Office Pulsalys, with more than 40 start-ups created and a portfolio of 100 IP families in health innovation, mostly originating from HEIs.

<p>HEIs and NROs covering all health-related disciplines</p>	<p>The 2nd academic hospital system in France</p>	<p>The first industrial ecosystem for health innovation in France</p>	<p>Key facts and figures</p> <ul style="list-style-type: none"> • 1st national site of pharma industry • 2nd academic hospital in France • 2nd psychiatric hospital in France • 1st national hub for medical interns (« internat ») • Top level research in oncology, neurology and immunology • 2nd French university site in terms of patents • National leader in simulation-based medical training • 2nd HSS university in France • One of two collaborating centers in Europe of the World Organisation for Animal Health (OIE)
<p>Associate partners</p>			

A strong transdisciplinary research and innovation record. UCBL and ULL together have 75,000 students and cover the fields of medicine, science, technology, and human and social sciences (HSS). Associated with NROs, they undertake research of the highest excellence in health, contribute to major national and international programs in this field and carry out, with numerous companies, major valorization, and innovation initiatives. This dynamic is shared by the **CPE** engineering school and **VétAgro Sup** in the field of veterinary science and veterinary public health. The associate partners also contribute, in their respective skills, to enriching this high potential in health (see annexes). Together, our institutions have successfully implemented a number of transdisciplinary research and training programs such as LabEx (4 in health), Equipex and Equipex + (6), the forthcoming SFRI Graduate+..., and interface chairs with major partners: veterinary health (Boehringer-Ingelheim), cancer prevention (Institut national du cancer), and a forthcoming chair on respiratory pathogens surveillance (Sanofi Pasteur). They have also coordinated 33 H2020 health projects (including 4 ERC), and represent 16 % of the RHU’s nationwide, 15 % of national scientific production and 5 HiCi researchers in cancerology.

The 2nd academic hospital system in France. HCL, CLB, and CHLV form, with more than 6,000 beds, the second largest academic hospital system in France, the **first national hub for medical interns**, the second for the number of competitive clinical research grants, rare disease reference centers, and cancer expert centers, and a **national leader in simulation-based medical training** (SimuLyon).



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An exceptional scientific environment, and strong research incentives. The partners have set up >10 top level health research platforms, such as the iconic CERMEP (preclinical and clinical in vivo biomedical imaging platform) and the genome sequencing platform AURAGEN (> 7,000 sequenced genomes), part of the 2025 France Genomic Medicine plan. The institutions are also committed to provide strong support for researchers: internal calls for proposals of 4.5 M€/yr for UCBL, 2.5 M€/yr for HCL, research grants for CHLV.

Lyon hosts the **IARC-WHO** (> 250 researchers) and the WHO Lyon Office, recognized as a Center of Excellence for public and global health. In 2024, the opening of the WHO Academy in Lyon will offer the world’s largest and innovative lifelong learning platform in global health.

SHAPE also benefits from strong support from local authorities.

1.2 SHAPE-MED@LYON AND THE LYON HEALTH RESEARCH AND INNOVATION HUB 2030

Based on academic, hospital, and industrial strengths, our ambition is to create Lyon Health Hub 2030, relying on a new way of working with stakeholders, public and private local partners, which improves synergies among all institutions. Our aim is to transform organizations in order to enhance our ability to tackle major societal issues and thus better contribute to the French national priorities of Health Innovation 2030. We have identified **4 key challenges at the Health Hub level:**

- Deepening strategic integration by joint governance to strengthen the hospital-university research continuum in terms of steering, policy, support services, and integrated HR strategy
- Developing transdisciplinary approaches for health research and training
- Boosting the health innovation ecosystem by building a hub infrastructure connecting Lyon-based health researchers and innovators in academia, industry research, and health institutions
- Enhancing international visibility and attractiveness for high potential students and researchers.

SHAPE-Med@Lyon is a part and a first step of ‘Lyon Health Hub 2030’ plan with the objective to enhance our scientific and societal impact through a One Health approach for personalized medicine. The project will enable research forces to investigate, in an innovative way, the close links between the environment, social groups, and the health of individuals (genotype - individual phenotype - territories - society - environment relationship). It will also foster the development of causal and global approaches to health, including environmental health, and thus make relevant deductions and projections leading to the management of both populations and individuals, in terms of prevention, diagnosis, and treatment.



Figure: SHAPE-Med@Lyon within the Lyon Health research and innovation hub

To achieve these objectives, SHAPE-Med@Lyon will rely on several innovative structures, which will be set up as part of the overall Lyon Health Hub:

- The Health Hub has a joint governance and support services, and an integrated HR strategy, based on its members’ shared resources, and partly funded by SHAPE. Governance and services



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are hosted in a ‘Maison de la recherche en santé à Lyon’, which will ensure a concerted research management on the site in the field of health

- The Lyon Public Health School, which will train future and current health professionals, and provide foundations in life sciences, health, and health data science to a general audience
- The Health Innovation Factory, supporting start-ups and pedagogical innovation in health, and strengthening the continuum between fundamental research, innovation, and commercialization
- A Data Center, hosting a meso-center certified for processing and storing health data. This will facilitate cross-referencing of heterogeneous and large quantities of patient and public health data with environmental and socio-economic data, in particular relying on AI.

Within this overall strategy, SHAPE-Med@Lyon will focus on creating the **Lyon Transdisciplinary Institute for Health** dedicated to high level research and supporting a **teaching offer** to train future leaders of health research and innovation. This initiative is inspired by international models such as UC Davis, Utrecht University, or Karolinska Institute.

An ecosystem that promotes dissemination of knowledge. The project will be linked to a ‘Sciences with and for Society’ project (SwafS label), led by ULL, associating all SHAPE partners. Scientific mediation and participatory research in the field of health, in particular in relation to 5P Medicine, will be supported and funded in the framework of this SwafS project. We will also support good research practices and a culture of openness (e.g., author identifiers), to comply with Open Science norms.

SHAPE-Med@Lyon as a part of a new research-intensive multidisciplinary university in Lyon

SHAPE-Med@Lyon is embedded in a broader and simultaneous institutional transformation which will be submitted for State support beyond the ExcellencES call. Following the end of the Idex, a new organization of the Lyon site is necessary. UCBL, ULL and CPE are committed to creating a new research-intensive multidisciplinary university. This new university will capitalize on the strengths, diversity and complementarity of our institutions, our unique partnership with HCL, and strong links with NROs and other HEI partners in Lyon. The new university will cover all major scientific fields. The focused institutional scope of the project, with 3 institutions at its core, will enable us to advance quickly in structuring the new organization. Intensive consultations among the governance teams of UCBL, ULL, and CPE began at the end of 2021, will carry on in 2022, and the new university could be effectively created on 1 January 2024. Building on our fields of expertise, the new university will develop an ambitious academic strategy to tackle, in addition to Health, societal challenges such as environmental and planetary changes, sustainable economy and manufacturing, and social transformations. These topics could be organized and steered in a similar way as what it is planned for Health. Thus, while SHAPE-Med@Lyon is an ambitious and focused transformation strategy in itself, it also constitutes the first building block of the target university.



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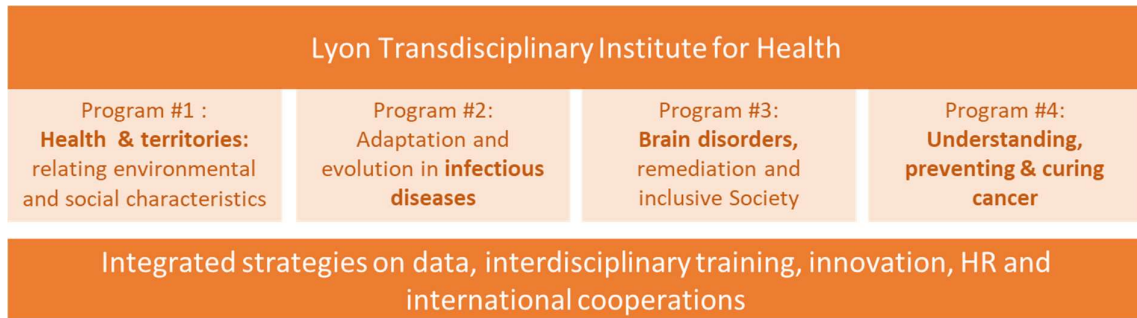
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2. PROJECT DESCRIPTION

2.1 LYON TRANSDISCIPLINARY INSTITUTE OF HEALTH

Health faces the challenge of the transition from a more curative to a more global medicine, from a 4P (personalized, preventive, predictive, and participatory) to a 5P medicine (addition of proof-based medicine), with the rapid implementation of new technologies in imaging, nucleic acid sequencing, and individual monitoring. The quality and quantity of patient information is on the increase, opening new opportunities to better understand individual specificities. The One Health approach stresses the need for considering human beings in their environment: human, animal and environmental health must be considered conjointly, to promote well-being and prevent disease emergence. Converging 5P medicine and One Health depends on the development of a holistic approach, from personalized medicine to the environmental and social sciences, to put individuals in their context.



The objective of the Institute is to build a research ecosystem addressing health questions through this vision. With a strong University-hospital continuum, a unique diversity of disciplines on health-related issues, a solid engineering and numerical science interface, and a structured private sector, Lyon is an ideal place to meet this challenge. We will rely on 4 programs built on scientific strengths in Lyon, with seed funding for pilot studies to develop this transdisciplinary approach. The pilot programs of this call will be implemented with SHAPE support, building foundations for the broader program granted by additional funding. The partners are committed to the Lyon 2030 project, allocating necessary resources, and leveraging SHAPE to obtain European & national funding and private partnerships...

Our research strategy is built upon a transversal program that will tackle the question of ‘territories of health’ and serve as an umbrella for three other programs focused on transdisciplinary issues developing personalized medicine, in oncology, neuroscience, and infectiology. By analyzing how the environment (ecosystem, social, cultural aspects) affects well-being and health, we will understand the articulation between individuals and their context as well as key factors that favor, synergize, or antagonize health issues.

Bringing together expertise on socio-environments, public health, veterinary and human health, quality of life, care and treatments, the programs will enable the co-construction of closer links between environment, social groups, and individual health (genotype, molecular, cellular, and individual phenotypes, territories...). They will enable the development of comprehensive approaches to make relevant deductions and projections leading to innovations in the management of populations and individuals in prevention, diagnosis and treatment for humans, animals, and all living organisms.



The Institute will use data from the social sciences such as geographical monitoring of pathologies, data relating to beliefs, health behaviors, health of ecosystems interacting with individuals, analyses of risk factors from the standpoint of all stakeholders, studies of the impact of public policies, with a study of the mechanisms of pathologies in order to develop innovative data driven preventive and curative methods. We will build on a variety of disciplines, e.g., medicine, veterinary science, biology, ecology, environmental sciences, and the humanities, together with supporting disciplines engineering and numerical sciences, and on our ability to transform the way researchers work together across disciplines and institutional boundaries. With this objective of transdisciplinarity, the SHAPE program and the commitment of the partners will unlock barriers to acculturation in a secured long-term environment, building on experiences of transdisciplinarity with the Labex. To foster transdisciplinarity, SHAPE will implement:

- 1) Pilot programs with transdisciplinary objectives, methodology, and research teams
- 2) A transdisciplinary scientific coordination, serving as the link between the transversal and other programs to facilitate information and data sharing, to organize the animation of the Institute, as well as to evaluate programs
- 3) Theses for doctoral students with a double degree, with development of co-supervision for PhDs from different disciplines
- 4) A network of PhDs and post-docs involved in transdisciplinary research on health and environmental issues

Acquisition, availability, quality, and analysis of data are all associated with important methodological challenges. Regarding acquisition, building on local engineering experts with health and environmental data, we will develop sensors, smartphone applications, involve citizens and patients. Handling of big, heterogeneous, spatially structured, and multi-scale data will require mathematical, statistical, and computer science developments, with computer scientists for artificial intelligence and machine learning, data analytics, modelling and simulation, and imaging. The Institute will be accompanied by an epistemological and ethical reflection on the context of knowledge production and on the scientific knowledge produced, together with the consequences for the people concerned. The four programs are detailed as follows.

Program#1: Health and territories: innovative approaches to relate health to environmental and social characteristics of territories and predict spillover effects

This program is based on the paradigm that territorial inequalities (geographical, environmental, socio-cultural, and socio-economic) generate heterogeneous landscapes for exposure to chemical contaminants, living organisms, access to food, information, education, health care..., and that this influences well-being and disease emergence. The objective is to understand how some territories enable (or not) the maintenance of a good health; and conversely, how health crises affect the functioning and quality of territories.



This systemic territorial approach will be central to this program and will provide all SHAPE programs a description and analysis of the social and environmental determinants of health.

Lyon is uniquely positioned to develop this program. 1,000 researchers within the Research Federation ‘Biodiversity, Water, Environment, Cities and Health’, 1 Labex, 1 Convergences Institute, 1 EUR, and a partnership in the PEPR ‘One Water’, show Lyon’s impact on the study of urbanization and socio-ecosystemic health. The hospital, veterinary services, and our partners (IARC-WHO) have the expertise on collection, access, and use of health data, including cohorts, public health, and veterinary public health.

Objectives and ambition for the 10-year program. Public health interventions should be implemented locally and adapted to the heterogeneity of territories and health determinants. We thus aim at exploring three topics.

1) Analyze the relationships between social, environmental, and health variables, through integration of health data (incidence, mortality, quality of life), socio-economic (beliefs, acceptance of public policies, poverty, nutrition) and ecological characteristics (pollutants, biodiversity, pathogens and disease hosts/vectors, access to nature, education, **and information**). **We will analyze and describe the major socio-environmental determinants of health.**

2) Evaluate the processes underlying unequal capacity of territories to produce the conditions for improved health: impacts of land planning and management on socio-ecological systems relevant for health; impact of the socio-economic dynamics and local policies on social determinants of health. The territorial characteristics revealed by this approach could be very different from the classical typology and lead to new hypotheses regarding the dynamics of health inequalities.

3) Enlarge and tackle the concept of spillover used in health research, widening its scope by extending the concept to non-infectious diseases (NIDs), with the objective to explore possible links of diseases to socio-ecological factors. We will concomitantly study infectious diseases and NIDs, assuming that factors participating in the spillover landscape can be shared between diseases and that diseases themselves are part of the landscape. This integration is an innovative and transforming approach.

This program will generate major breakthroughs towards understanding and predicting the role of land planning, ecosystem management and social organizations, and their dynamics, on various facets of territories of health along a continuum of anthropization.

Methodology. Understanding of spillover landscapes will help develop better, targeted prevention and health policies. Identification of early ecological and social markers will allow spillovers detection at an early stage, enabling actions for reducing risk.

This will be done in three sub-programs:

Sub-program 1 (year 1-2): Analyze the quality of geographic, social, ecological, and health data from different holders; evaluate their availability at a fine geographic scale; build databases and analyze gaps in data. The interoperability of these different data is a challenge.



Analyses will first help to target new data acquisition, with technological development (e.g., sensors) through collaboration with engineering. Participatory science will enable to study the relationships between environment and health and produce educational tools. *Deliverable 1: Quality, availability, and consistency of heterogeneous data (M18).*

Sub-program 2 (year 2-6): **Tackle the methodological challenges** of processing massive data with their characteristics (spatial, temporal, multi-level information). Spatially homogeneous ‘contexts’ will be identified based e.g., on regionalizing coefficients of a Geographically Weighted Regression model or Bayesian inferences. *Deliverable 2: Modeling resulting in an innovative territorial typology summarizing territorial contextual effects, and health outcomes (M30).* *Deliverable 3: Analyses on health inequalities, disease emergence, and spillover landscapes (M72).*

Sub-program 3 (year 5-10): **Develop models and scenarios.** Using data acquired by sub-programs 1 and 2, we will develop models to simulate how future dynamics of territorial contexts can amplify or dampen emergence of multiple diseases and pathologies. *Deliverable 4: Scenarios and simulated trajectories of health across territories (M96).*

Within this global program, we will implement a few focused pilots. We here give two examples.

Pilot A- From green to healthy city to assess the effect of revegetation in cities.

- Biodiversity mapping (vegetation including allergenic species, animal hosts & vectors of diseases, water and soil potentially acting as reservoirs of pathogens) is ongoing in the Lyon Metropole across urban territories, in parallel to a coherent mapping of social and health data.
- Analysis of the balance between greening benefits vs costs due to harmful species; quantification of territorial inequalities e.g., access to vegetated areas, exposure to disease reservoirs and vectors.
- Modelling different scenarios of urban greening to guide e.g., tree planting and watering methods that influence emergence of harmful species or the contamination of soils and vegetables, etc.

Pilot B: Farm type consequences on human and animal health

- Within Lyon Metropole, different types of farms will be defined based on existing results on pesticide exposure.
- We will quantify (i) well-being and health status of farmers, (ii) as well as of livestock, using existing data from our Veterinary partners. We will develop innovative methods for quantifying metabolic and immune status of livestock as proxies of health.
- Farm description will be completed by social (behavior, access to information, education...) and environmental data. This will include the development of new approaches on water analysis, used as a sentinel for pollutions and contacts between livestock, wild animals, and arthropods through environmental DNA and metabarcoding approaches.
- Finally, we will model the different dimensions of health, well-being, and their determinants, allowing integrated risk analyses across different farm types.



Program #2: Adaptation and evolution in infectious diseases: from pathogens to societies

The COVID-19 pandemic shows the burden of infectious diseases on human societies, public health, the nation's economy, social life, politics. This comes in addition to recent outbreaks in humans and animals and growing antibiotic resistance, coinciding with unprecedented environmental changes. This epidemic of epidemics relate to the extraordinary capacity of pathogens to evolve and adapt. In return, human, animals, and other living organisms continuously develop strategies (genetic, behavioural, or political) to avoid, tolerate or resist pathogens. The current pandemic highlights the difficulty societies face in implementing strategies to anticipate these continuous cycles of adaptation and evolution.

This program expands the management of emerging infectious diseases to social, animal, and environmental health, bringing together ecological, biological, clinical, epidemiological, psychosocial, socio-economic, or political perspectives. By exploring pathogen and host variability, and the **evolutionary and social feedbacks**, we prepare the response and management of infectious risks.

Lyon is uniquely positioned to develop this program, based on a unique academic ecosystem in microbiology, immunology, ecology of infectious diseases, as well as in social sciences (e.g., decision-making), linked with hospital facilities (e.g., rooms for patients infected by level 3 and 4 agents), high security platforms (e.g., the Jean Mérieux Inserm BSL4), sequencing facilities for surveillance (GENEPI), and a strong connection with industrials (LYON BIPOLE and IRT BIOASTER). The One Health approach is facilitated by two epidemiosurveillance national platforms, 9 National Reference Centres, and the Equipex+ InfectioTron.

Objectives and ambition for the 10-year program. What are the biological, clinical, and psychosocial indicators required to develop a global management of infectious diseases? We address these issues through five aims:

- 1) Assess pathogen and host adaptations, at biological, ecological, psychosocial levels.
- 2) Investigate the impact of individual and collective beliefs related to health and disease control on epidemiological dynamics.
- 3) Understand the impact of these adaptations on host-pathogen relationships, antimicrobial resistance, and severity of infections.
- 4) Propose preventive and curative solutions integrating adaptation to control the emergence, spread, public health management in a sustainable way.
- 5) Evaluate the retroactive impact of preventive and curative solutions on pathogens, societies, and ecosystems.

Methodology. To build transdisciplinarity, and to remain open to any new infectious threats, we build our strategies on two sub-programs phased in time:

Sub-program 1: We will build first on initiated projects where the contribution of new disciplines appears necessary to integrate biological, clinical, and socio-behavioral data to follow infections. We will rely on our local network to develop integrative modelling and inference of the complex dynamics of spatially and socially structured hosts-pathogens-reservoirs communities.



Sub-program 2: In 5-10 years, we will construct common projects aiming to apply the integrated approach developed. The precise object could be a new emergence representing a threat to societies.

The first, short term, 3-to-5-year scale, sub-program will be conducted on 3 pilots that illustrate 3 challenges at different timeframes in managing the emergence of infectious diseases:

Pilot A. Phagotherapy is an innovative **management of antibiotic resistance** through the use of viral particles targeting the pathogen. We will capitalize on the Phage-One project that aims to develop phagotherapy to:

- 1) Assess of the phage/pathogen genomic/transcriptomic/phenotypic variability to determine the risk for resistance evolution.
- 2) Perform multiparametric monitoring of host immune responses to phages, depending on age, gender, immune senescence, microbiota, nutrition, in the frame of personalized medicine.
- 3) Evaluate the acceptability of this solution for patients, general population, physicians.
- 4) Assess patient-provider relationship, care organization, health and drugs beliefs, self-medication, and alternative medicine.

Deliverables: Method to co-develop innovative therapy integrating molecular, evolutionary, and patient behavioural response. Phages with defined bacteria-spectrum. Guidelines for medical policies. Tools for information, education, and communication strategies.

Pilot B. Crimean-Congo hemorrhagic fever (CCHF). CCHF, a tick-borne disease due to CCHF virus (BSL4), overlaps with *Hyalomma* tick, its main vector. Its presence outside the endemic areas was evidenced in different animals. Within project RESPOND, studies explore how specific host, vector and microbial factors influence the transmission of CCHFV, from structural and molecular aspects up to populations and ecosystems. In the frame of this pilot, we will complement these studies through the collection of data about risk perception (economy, psychology, sociology) in various populations of nature users to understand interaction between environmental, societal, and individual risks perception regarding health and nature. These elements will be used to develop projection models to evaluate the risk of emergence.

Deliverables: Method to co-develop prevention strategies integrating molecular, ecological data and behavioural response of nature users. Risk assessment of CCHFV emergence.

Pilot C. Research on immunocompromised and long COVID cases. Immunocompromised individuals represent a specific evolutionary niche for SARS-Cov2. Longitudinal data allows regular sequencing of the viral population (and of the rest of the metagenome), to assess intra-individual viral variation/evolution, and the interaction with other microorganisms. This will permit to determine how the absence of inter-host transmission impacts the evolution of the virus, identify populations at risk, and anticipate emergence of new variants. To better understand long COVID, we will collect, in community-based research, biological, clinical data and patient-reported outcomes on COVID impact (psychological, psychiatric characteristics, side effect...) to characterize individual determinants of susceptibility to this syndrome.



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Deliverable: Methodology to co-construct longitudinal patient's study with multiple interconnected objectives: guidelines to care, to improved patient's quality of life, and patient-provider relationship.

Program#3: Brain disorders, remediation, and inclusive society

Brain and mental disorders affect 30% of EU citizens, with a large spectrum of disabilities impacting quality of life and social inclusion, and a major economic burden. Despite the complexity of the brain and the uniqueness of individual injury, emerging strategies relying on transdisciplinary approaches can now be developed to remediate brain dysfunctions and to propose personalized treatment strategies.

The objective of the program is to build an innovative transdisciplinary resource oriented towards the remediation of neuro-psychiatric disabilities. This initiative will:

- 1) Characterize and understand neuro-psychiatric disabilities at the individual level.
- 2) Identify the impact of lifestyle and societal factors on personal disabilities and social interactions.
- 3) Develop personalized remediation strategies, to improve quality of life as well as acceptability and social inclusion.

Lyon is uniquely positioned to develop this program, with expertise in basic and clinical research in neurology and psychiatry, with **~1,100 researchers and clinicians**, leading several national Reference Centers, national (Parkinson, Multiple Sclerosis, schizophrenia...) and European (epilepsy) expert networks and unique patient cohorts (MS, stroke, epilepsy, Alzheimer, DYS, autism, head trauma, ...). **Over 200+ trials/year are conducted onsite with 4 Labex, 1 EQUIPEX, 6 RHU, an Excellence Center.** Lyon hosts **research-dedicated technological platforms** in genetics (AURAGEN), multimodal life-neuroimaging (CERMEP), advanced behavioral testing, intracranial EEG (epilepsy), biobanks, stem-cell expertise in primates, blood-brain interface models, and animal housing for rodents and non-human primates.

Objectives and ambition for the 10-year program. Create an unprecedented transdisciplinary program for holistic and personalized remediation of brain and mental disabilities. This will involve synergistic interactions between the neuroscience community, genetics, psychology, social and education sciences, engineering, AI, epidemiology, biostatistics, patients, and associations.

Methodology. This program relies on three sub-programs: i) Characterizing the diversity singularity and dynamics of neurological and psychiatric disabilities, through the development of a multimodal precision phenotyping platform; ii) Understanding the impact of lifestyle and territorial factors on disability using large patients' cohorts combined with population analyses iii) Developing new concepts/technologies to improve personalized care and tailored remediation strategies with a holistic approach, articulated with a more inclusive society.

Sub-program 1. Characterizing neuro-psychiatric disabilities via multimodal phenotyping

Create a collaborative computational modelling platform integrating multilevel/multimodal data to extract relevant biomarkers for diagnosis/prognosis, elaborate and test models of brain dysfunctions and



their causal relationship with behavioral measures. **Multimodal life-neuroimaging** provides state-of-the-art instruments to explore the structural, functional, and metabolic aspects of brain function, all in humans or animal models. **This unique resource gives us the convergence of complementary disciplines** to decipher the complexity and dynamics of multimodal imaging data. *Deliverable 3 years: A collaborative computational modelling platform for integration and sharing of multimodal data. Deliverables 5-10 years: An open platform to clinicians and companies. Pilot projects: Epilepsy, Post-stroke patients.*

Sub-program 2. Understanding populational diversities and neuro-psychiatric disabilities

Lyon developed many databases on patients with brain disabilities (multiple sclerosis, stroke, rare diseases...). Collecting and analyzing this information (including parameters of social environment and day-to-day life) is essential to understand quality of life, populational diversities of neuro-psychiatric disabilities and their evolution. We will address medical research issues with innovative personalized strategies integrating the environment of patient to boost the effectiveness of their societal inclusion. This platform will aggregate and analyze multimodal and heterogeneous data, i.e., brain, clinical disability data, and Medico Administrative data from nationwide health data system. This will be developed in connection with the transversal program 'Territories of Health'. *Deliverable at 3 years: A pilot project on multiple sclerosis patients. Deliverables at 5-10 years: Translate to stroke, autism, epilepsy, aging, psychiatry, and rare neurological brain diseases.*

Sub-program 3. Developing personalized and holistic remediation strategies

Effective remediation of brain and mental disorders relies on a precise behavioral and neuropsychological assessment, combined with structural/functional imaging and neurophysiological evaluation. Interactions between clinicians and researchers are still intermittent, and integration of lifestyle or patient's individual trajectory data is rare. **The aim is to implement a transdisciplinary collaborative platform** to develop a holistic evaluation, and validation of innovative personalized remediation strategies.

Objectives are:

- 1) To integrate the knowledge on brain plasticity from sub-program 1, to identify individual remediation procedure targeting deficits and capitalizing on the preserved brain capacities
- 2) To integrate real-life individual data of sub-program 2, including the patient's health trajectory
- 3) To develop innovative remediation approaches, based on digital technologies and by implementing therapeutical strategies at home
- 4) To support clinical trial methodology for evidence-based evaluations

This collaborative platform will gather various clinical specialties, neuroscience, psychology, education, social sciences... to strengthen synergies for personalized remediation, **with a view to a more inclusive society**, by **promoting participatory research** involving patients, peer helpers, teachers...

Deliverable 3-5 years: A collaborative platform for innovation in personalized and holistic remediation.



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Pilot project on neurodevelopmental disorders, with a focus on the remediation of learning disorders. Deliverable at 5-10 years: Translate to other disabilities related to stroke, epilepsy, psychiatry, Alzheimer's disease... with openings toward the private sector.

Program#4: Understanding, preventing & curing cancer

Cancer is a large and complex group of frequent (400K in France, 4 M in EU) diseases whose nosological fragmentation rapidly evolves with molecular and immunological classifications. Many cancers remain incurable despite the advent of precision medicine. Paradigmatic changes are thus needed for most cancers, requiring more advanced understanding of biological drivers of progression, refined strategies for prevention, better understanding of exogenous risk factors. Treatment now requires comprehensive molecular & immunological analyses of the cells, in their spatial and time dependent evolutions. All these are challenges facing patients, caregivers, and researchers in the coming years. **The connection of these components are the objectives of the SHAPE oncology program.**

Lyon is uniquely positioned to develop this program, hosting a large set of cutting-edge expertise, scientific production, and education programs in oncology, (>1,300 yearly high-level publications, 15% of France), the unique Cancer Research Center in France (CRCL), the IARC/WHO, VetAgro Sup, CLB and HCL. With leadership in basic, epidemiology, clinical, human, and social sciences, Lyon's excellence track-record also includes the AURAGEN platform for WGS sequencing, led by the project leader, the SIRIC LYRICAN, 1 Labex, 1 Convergences Institute, the European Reference networks (ERN) EURACAN, and Cancer Prevention Europe (CPE).

Methodology. We will create an oncology research program embedded in the local ecosystem, with a transdisciplinary approach. We will connect existing tools (databases, EHR, tumor banks) from different institutions, generating novel platforms, databases, resources for local researchers and EU and international partners, enabling a unique synergy. We will set an operational interface around specific objects to build the conditions for transdisciplinarity to share data, theories and indicators inviting citizens and patients for community-based research.

Sub-program 1. Explore the unknown causes of cancers, using transdisciplinary approaches, from exogenous causes (nutrition, beliefs, behaviors...) to genetic predispositions.

Epidemiological, psychosocial, clinical, biological data of patients and relatives will be connected, linking electronic patients records of the different hospitals and from veterinary school, bringing together the tumor banks and data sets of human and veterinary medicine. **At a larger EU scale, we will focus on the 20% of cancers which are rare, including children, adolescents, and young adults,** building on the leading role of Lyon on rare cancers, at the national and international level, and on ERNs, EURACAN and PAEDCAN (pediatric cancers), the former being led by CLB.

In collaboration with international companies and the expert academic research teams in bioinformatics



and biostatistics on the site, **we will develop artificial intelligence programs for pathology, molecular pathology, and radiological diagnostic**, connected to the electronic patient records.

Milestones and deliverables: 1) Implement a shared histopathology platform and tumor bank for CLB & IARC-WHO, giving access to researchers and students in the new headquarters of IARC-WHO (Milestone 4 years). 2) A high-resolution European Rare Cancer Registry including childhood cancers and rare adult cancers, in partnership with the 2 ERNs.

Milestone 3 years: a federated database merging clinical, socio-behavioral, molecular, and immune characteristics linked with geographical distribution and exposure at a regional level). 3) Address childhood & rare adult cancers etiology exploring genetic and epigenetic biomarkers of early-life factors associated with risk of childhood cancer, to guide evidence-based prevention strategies. (Deliverable at 3 years: publication). 4) Implement artificial intelligence programs for molecular pathology, and radiological diagnostic with start-up partners.

Sub-program 2. Connected European and national cancer plans, **we will develop innovative strategies of primary prevention based on the identification of exogenous and endogenous risk factors.** Prevention work will focus on at-risk populations, identified by IARC/WHO, as well as on community-based populations. For example, we will explore key nutritional risk factors and deliver new research data on understudied nutritional concepts to support policymakers for evidence-informed policies for a health. **We will deploy an innovative program dedicated to the connection between environment, exposome, and cancers** focus on multi-exposure and cocktail effects of environmental exposures and identify proven risks according to geographical locations and life trajectories.

Milestones and deliverables: 1) Launching of the first (randomized) clinical trial aiming at preventing the emergence of secondary cancers for patients at high risk. (Milestone 1 year.) Study report (Deliverable 4 years). 2) A first publication on food biodiversity with recommendations for policy makers. (Deliverable at 3 years). 3) The European Code against Cancer coordinated by IARC-WHO will be updated to include the latest scientific evidence to improve health literacy (Deliverable at 4 years.)

Sub-program 3. **We will develop innovative precision medicine strategies for local treatments of neoplastic diseases,** involving the research teams and engineering schools. These will involve in particular high intensity focal ultrasounds, innovative interventional radiology programs, and a worldwide unique developments for radiotherapy. **The development of precision medicine in oncology,** using targeted treatments, and anti-immune checkpoint immunotherapies will build on the database of somatic molecular alterations developed on site in the last decade expanding to the exhaustive population of cancer patients on the site.

Milestones and deliverables: 1) Implement an integrative research program between HSS, clinical, and biological data to a) develop community-based approach to cancer treatment considering the social,



ethical, organizational challenges b) address the issue of accessibility of innovations in cancerology for patients, relatives, physicians. (Deliverables at 4 years: first two publications). 2) A novel strategy to deliver photon and proton beam therapy with treatment in upright position: solving the gap with next generation material, relevant to give access to radiotherapy to unserved territories (Milestone 2 years).

SHAPE will thus establish a unique consortium establishing Lyon as a leading place for the development of paradigm changing oncology research and teaching worldwide.

2.2 TACKLING THE MAJOR CHALLENGES OF MASSIVE DATA

Data, IT, and methods represent the three major cornerstones, on which to launch a digital strategy for transformation of the whole landscape ranging from 5P medicine to One health. The challenges faced by this transformation are, however, significant, owing to the mass and heterogeneity of the data, the dispersion of the digital resources, and the disconnect that can exist between the scientific disciplines, the training programs, and the professional networks.

To meet these challenges, SHAPE aims to establish a complete scientific value chain, from data collection to knowledge production and implementation, by creating a **data warehouse** based on an **integrated digital infrastructure** and **LyonTech datacenter**. These will represent a strategic resource, around which to attract, structure, and integrate an entire community: research/engineering/hospital and socio-economic actors/training programs. At all levels, the digital transformation will make transdisciplinarity a key strategy, promoting feedbacks and cross-fertilization between fundamental research and translational output.

A comprehensive data hub. Cutting-edge science will be built on a fully integrated data collection and management programs, connecting quantitative/qualitative/historical/prospective/multiscale data, to strengthen the links between academic research, health institutions, and policy makers. Electronic patient records/imaging/biological/sequencing/environmental/social science data are examples of the data involved. We will capitalize on the outstanding landscape offered by Lyon on digital health and engineering expertise (telemedicine/connected devices/population and environmental sensors...) in a One Health perspective. The data hub will enable networked environmental and human/animal health agencies to share and exchange medical data based on FAIR principles and will ensure the interoperability of data from different disciplines.

A mixed brainstorming committee will gather experts from disciplinary fields, health institutions, lawyers, and socio-economic actors. It will consider the diversity of ethical and regulatory issues raised by the collection, processing, and aspects relating to the restitution of data. This will create a framework to go beyond the silo treatment of the questions posed by the implementation of transdisciplinarity as much as to their ethical, epistemological, and regulatory scope. The committee will provide a reflexive and operational framework regarding the implementation issues raised by transdisciplinary projects and



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will find interface levers allowing actors to exchange and co-analyze. It will also link with the strategies around SwafS or Open science.

Integrated digital infrastructure and environment through the MesoLys support unit. The MesoLys unit (founded by UCBL/HCL/Centrale Lyon/INSA Lyon) will provide services and high-level digital infrastructures, hosted in the LyonTech data center (see annex), to support research activities, and thus meet the resource and digital support needs of programs.

A scientific consortium in computational sciences. SHAPE will build on the current impetus toward multi-disciplinary integration that is emerging locally, to create a network bringing together a broad range of cross-fertilizing expertise. The task force will associate engineers, researchers, physicians, veterinarians..., with expertise in digital approaches to serve applications in human/social/animal/environmental topics. Regarding their complementary expertise, they will address major issues in a bottom-up strategy working in direct coordination with the programs in order to undertake joint analysis of human and animal health and well-being. Further implementation will then be considered in all aspects of global health. The task force will focus on the needs of the regional stakeholders involved in scientific health and territories issues and notably the provision of data, models, and methods. Hackathons will be organized, especially targeting the students in the training curricula, to trigger a transdisciplinary catalysis and speed-up resolutions of challenges. The network will develop machine learning, AI, stochastic approaches for quantitative inference and decision-making to decipher the main analytical locks across the respective domains. Special emphasis will be put on experimental design, sampling issues, non-random missing data, specific correlation related to spatial-temporal or multiscale data...

The new Inria research center, created in Lyon in 2021, will support SHAPE. Its role will be complementary to that of the Institute, offering digital leverage at the service of the programs: modeling, software development, support for scientific computing and AI with the AI development pole.

2.3 BUILDING A TRANSDISCIPLINARY TEACHING OFFER TO TRAIN FUTURE LEADERS IN HEALTH RESEARCH AND INNOVATION

Our ambition is to create a leading transdisciplinary training offer in Lyon to meet current and future challenges of **global health, public health, and personalized medicine**. These teaching programs will also enable students to learn about transdisciplinarity, from an epistemological and methodological point of view. SHAPE represents an opportunity to federate HEI and strengthening the links with HCL to achieve these objectives. It will also strengthen Lyon as an exceptional site for students and health practitioners.

2.3.1. Develop excellency curricula for high level interdisciplinary training between medical sciences and basic, engineering, or human and social sciences

Meeting the challenges of global health in the next decades will require individuals able to lead scientific, technical, and organizational breakthroughs into medical practice and health structures.



UCBL is engaged in the development of ambitious MD-PhD programs, through the École de l'Inserm - L. Bettencourt national program (~ 6 students/year), a 4-year joint program between Health Schools/ENS Lyon/HCL (5 students/year), and an internal program (~25 students/year). UCBL has also created a unique partnership between the Med Schools and the École Centrale Lyon (ECL), allowing ECL students to join the medical track to get a double Engineering/MD degree. A symmetrical cursus is available to MD students who eventually get the same double degree. Our ambition is to increase and to substantially renew this training capacity:

- **Extend interdisciplinary training programs in health-related sciences.** The ECL-UCBL dual program will be extended to other engineering schools. Furthermore, new partnerships between UCBL health schools and the institute of rehabilitation, and ULL education, psychology, sociology, linguistics, economy, and management departments, and Université Lyon 3 philosophy and law departments will be developed to propose ambitious MD-PhD programs (~15 students/discipline/year).
- **Develop high-level health-related PhD programs.** In order to improve health students' research training, we will open pre-doctoral training programs and complementary grants for two-year support programs (Inserm, FRM). Furthermore, we will encourage students in basic, engineering, and HSS to undertake health-centered interdisciplinary PhDs by means of specific fellowship grants (up to 8/year). As completing a high-level interdisciplinary PhD within three years is very challenging, a fourth PhD year will be granted. The creation of a 'Health and society PhD' will allow the implementation of transdisciplinary training and better national and international visibility for this specialty.

2.3.2. Bridge gaps between health and engineering in order to accelerate the development and dissemination of innovative technologies for health

Technological and digital applications in the field of health are experiencing unprecedented progress. In this context, engineers with expertise in the field of health are key players in fulfilling the needs of organizations and healthcare professionals and valuable in academic and applied research. Conversely, the appropriation of these technologies and their applications by healthcare professionals is a major challenge to accelerate their dissemination and stimulate research. We propose two original actions for future healthcare professionals and engineers:

- **Develop intensive joint-curricula for health students to accelerate the development and dissemination of new technologies** through the delivery of an engineering degree in addition to their health degree. There are currently a few joint-training programs in Lyon, most of them involving the pharmacy curriculum (ISPB) and Polytech Lyon, CPE, and École des Mines de Saint-Étienne (~15-20 students/year). Our ambition is to significantly increase the number of trainees by involving new partners among Lyon engineering schools, and to propose new curricula for dentistry and med students.
- **Propose original training programs for engineers to fulfill the needs of companies, HCL and**



health research programs. Trainees will be made aware of challenges linked to global health and personalized medicine and obtain academic knowledge and technical skills in health issues. They will also receive field experience through an internship. Three programs will be proposed: specialty engineer (one additional year to the engineering diploma), one-year academic program leading to a certificate in health sciences, or a gap year carried out within a health structure. These one-year training programs will involve not only biomedical as is so often the case, but also HCL members, health teachers, and HSS teachers involved in health and remediation issues.

2.3.3. Transdisciplinary courses on the intertwined challenges of health

The Lyon Public Health School (for this Lyon 2030 initiative, see also the annex) will offer innovative courses at the intersection of territorial health, environment, society, and biodiversity aspects on the one hand, and medical disciplines on the other hand, for a continuum of target audiences, both in initial and continuing education. The courses will take different forms (academic courses, summer schools, workshops, online open courses...) and benefit from the pedagogical innovation and simulation facilities from the INCLUDE and SimuLYON projects. The courses will lead to the delivery of academic certificates and/or could be integrated into existing bachelor, master, or PhD training programs. They will be made widely available to students and healthcare professionals, as well as stakeholders in Health-in-all-policies, to have a scientific and socio-territorial understanding of health and well-being and ensure coherence with the principles of 5P medicine within a 'One Health' and 'Public Health' perspective.

The courses will be led by academics from different disciplines (health, biological and veterinary sciences, environmental sciences, epidemiology and infectiology, public health, data and numerical sciences, economy, history, geography, (neuro)psychology, sociology, anthropology, philosophy...), professionals and civil society players.

They are important levers to develop a common acculturation and the acquisition of new, decompartmentalized and cross-disciplinary skills, a prerequisite to develop sound and innovative personalized and predictive medicine and orientate public decisions. This will also be the bedrock of lifelong training and curricula. **This kind of training will**, to our knowledge, **be unique in France**, and is a direct response to the insufficient transdisciplinarity in training programs highlighted in the 'Stratégie nationale d'accélération Maladies Infectieuses Emergentes et Menaces NRBC (MIE-NRBC).

2.3.4. Make Lyon one of the national leaders in the field of simulation-based training

With the IDEFI SAMSEI, we have acquired a strong expertise in simulation-based training in health and developed more than nine dedicated technical platforms. We are currently involved in many national partnerships and projects. With the SimuLYON project, we want to go further and make Lyon one of the largest simulation centers in health. The objective is to create new synergies, in order to: i) promote



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and massify learning through simulation in health, basic science, engineering, training of trainers, and human and social sciences curricula, and ii) promote original health training and research programs in the field of simulation through the creation of an international interdisciplinary Master's program and dedicated PhD grants. Beyond academic interests, the students will present profiles of great interest for private and education companies.

2.4 CONNECTING ACADEMICS, HOSPITAL PRACTITIONERS, AND BUSINESSES TO FOSTER HEALTH INNOVATION

SHAPE aims to position the Lyon site as a major hub of health research and innovation, building on the strength of several health institutions, the presence of the entire development chain from TRL1 to TRL9, from basic research to market launch, and capitalizing on the valorization subsidiaries, Pulsalys, LyonBiopôle, and a strong partnership with Ottawa. SHAPE will also rely on the significant involvement of socio-economic players in the governance (see Section 3.1), which will allow mutual knowledge and understanding of mutual expectations, thus facilitating the establishment of partnerships, and boosting innovation possibilities. To accelerate innovation in chosen priorities of the project, we will mobilize resources to support the following actions.

Public-private mobility initiative, designed for entrepreneurs, researchers, or clinicians willing to set up collaborative innovation programs. It will allow up to 5 new laureates each year to spend one day per week away from their initial workplace, embedded in either a hospital team, a research team, or a startup. The grant given by the program could be used to compensate for their time at their initial workplace or to give them an extra bonus for the added workload (cost: 12 k€ net per year per laureate). This new collaborative innovation program is expected to promote better mutual understanding and, in the long term, to fuel new collaborative projects through cross-fertilization.

Learning expedition. Pulsalys and the Pôle d'innovation en santé d'Ottawa will establish an exchange program for health start-ups. Selected start-ups will visit partner's sites, meeting labs, enterprises, clusters, fund venturers, and seeking for mutual initiatives.

Beyond these initiatives, other already implemented policies will boost innovation and valorization:

- Support for researchers engaged in innovative projects that lead to new markets or have an impact on public policy.
- Awareness raising, training and support in entrepreneurship for graduate students, doctoral students, researchers.
- Enhanced interactions between the academic and socio-economic worlds through shared technological platforms, and skills and services portal.
- **SHAPE partners are committed to supporting new joint labs via dedicated resources.**

The Health Innovation Factory is a key element of the Lyon 2030 plan and UCBL's 1st priority for the future State-Region plan (CPER). Its construction is planned to start in 2028; in the heart of the Faculty of Medicine, next to CLB and HCL. Inspired by the soon-to-be-unveiled Public Factory, it will host co-working and innovative learning spaces, start-ups, and platforms.



2.5 STRENGTHENING TRANSDISCIPLINARY APPROACHES AND THE HOSPITAL-UNIVERSITY-RESEARCH CONTINUUM THROUGH AN INTEGRATED HR STRATEGY

Attracting and retaining top talent is the cornerstone of our academic strategy; this is particularly challenging in the field of health research, where academic physicians need to reconcile their role as clinicians, researchers, and scholars. The SHAPE partners will implement an integrated HR strategy strengthening the hospital-university-research continuum, by jointly defining job profiles for academic and research support staff, and through joint mechanisms to attract top talent and support promising academics and physicians in the development of a research-intensive career. Partners will also coordinate hiring to improve transdisciplinary approaches with top talent recruitment in sciences, HSS, numerical and health sciences. To reach these objectives several guidelines were considered.

2.5.1 Attracting top talents in health-related research

Junior Chairs (CPJ). This international tenure track program will be implemented as part of a long-term recruitment strategy jointly developed by universities, HCL, and other partner institutions, in particular Inserm. CPJ proposals will be assessed by the Science and Innovation Committee (see Section 3.1). All partners are committed to supporting CPJ focused on SHAPE pilot programs. Calls for applications will be advertised internationally in line with HRS4R standards. The assessment of candidates by independent recruitment committees will consider their international visibility, the excellence of their project, its significant contribution to the SHAPE pilot programs, risk-taking, and the potential for spin-offs. The SHAPE partners commit to a matching fund system providing additional resources such as PhD and postdoc contracts, research engineers, and equipment. This will enable chairholders to set up their research teams within highly renowned labs.

Beyond the CPJ program, SHAPE will rely on major commitments of the partners to focus existing attractiveness policies on the themes of the Institute (industry chairs, senior welcome packages, PhD and postdoc grants, research calls, UCBL associate professors' welcome packages and research calls; see the annex).

2.5.2 Supporting highly talented academic physicians, biologists, and pharmacists in the development of a research-intensive career

Attractiveness with special support package for highly talented academic physicians and pharmacists (PU-PH university professors). This initiative will provide an exceptional 360° support package for high potential PU-PH shortly after their recruitment. 1-2 candidates/year will be selected by the Science and Innovation Committee. Priority will be given to research projects within the SHAPE programs. The selected candidates will benefit from a 50% reduction of their clinical workload for 3 years, will be granted financial support for recruiting PhD students and postdocs, purchase equipment, research visits, as well as technical support from research engineers and a dedicated project manager. They will also benefit from peer mentoring by highly experienced researchers (e.g., ERC grant holders),



who will support them in career development by providing international networking opportunities and advice on funding opportunities.

Funding secured research time for young ‘chefs de Clinique’. Because the clinical workload is heavy for a junior hospital practitioner, UCBL and HCL, in partnership with Inserm and the Bettencourt Schueller Foundation, have set up an initiative that allows highly talented physicians to devote 50% of their time to research for at least 2 years, by funding compensatory clinician time. This program encourages outstanding MD-PhDs to develop independent projects at the interface between fundamental and clinical research. However, its impact remains limited, with an average of only 0.2 beneficiaries per year at UCBL/HCL at this stage. SHAPE will enable us to build on this experience by selecting 1 additional beneficiary every year. They will benefit from seed funding for their projects (45 k€) and a third year of preserved research time to help them set up a research team that will contribute to the Institute’s pilot programs.

Beyond the above measures, SHAPE partners have decided to launch a joint bonus policy to reward the investment of their staff in high level research, care, and teaching.

2.6 ENHANCING THE LYON HEALTH HUB’S INTERNATIONAL ATTRACTIVENESS AND VISIBILITY: STRONG PARTNERSHIPS WITH UOTTAWA AND THE WHO

A unique partnership with Ottawa health hub. Building on their longstanding partnerships in the field of health, SHAPE partners and uOttawa will launch, this fall, a 4P Health Partnership (Precision, Personalized, Public health, and Prevention). Combining the complementary strengths of their outstanding ecosystems, the partnership will focus on research, training, innovation, and valorization in the healthcare sector. A two-step approach will be pursued to provide seed and boost funding for joint scientific projects, bringing together researchers from the two hubs: a discovery phase for 1.5 years (scientific investigation, co-creation of academic or training output, selection of promising teams); an expansion phase of 3.5 years (launch of projects). Significant efforts will be devoted to promoting partnerships, including entrepreneurial and labcoms, to attract extramural funding (see also Section 2.4), and to implement an ambitious co-tutelle PhD program. A joint steering committee will monitor the implementation of the partnership.

Multiple joint programs with IARC-WHO. IARC-WHO is a full scientific partner of SHAPE, and a scientific contributor to two pilot programs. In addition, the Lyon Public Health School will build on IARC-WHO’s experience and international network to design, in collaboration with the US National Cancer Institute, and the German Cancer Research Center, new courses and webinars targeting an international audience of researchers and health professionals. This will lay the groundwork for future collaborations with the WHO Academy (see below). HCL, IARC-WHO, uOttawa, and the Jiaotong University will pursue high-level international courses in management and leadership for future key opinion leaders.



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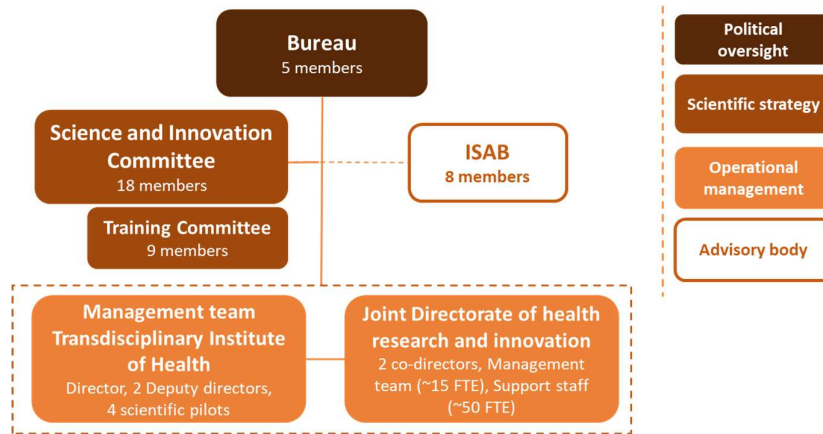
Submission form

Potential collaborations with WHO Academy. SHAPE partners are committed to establishing a fruitful collaboration with the WHO Academy, which will set up in Lyon starting 2024. Preliminary discussions with head of the program, A. Buzyn, have led us to identify potential collaborations on Mass Casualties Management programs, immersive simulation pedagogies (SimuLyon), and a future Global Health training program (the first one in France, to be implemented using the know-how of Canadian partner universities). A second round of discussions, in March 2022, will identify the pilot collaborations to be implemented in 2024.

3. MANAGEMENT FRAMEWORK

3.1 AN INTEGRATED GOVERNANCE OF HEALTH-RELATED RESEARCH, INNOVATION, AND TRAINING IN LYON

The SHAPE governance will be embedded into the Lyon Health Hub, relying on an unprecedented partnership between academic and health institutions. UCBL and HCL set up an integrated governance and a joint directorate of health research. This strategic integration between a university and a university hospital is unique in France. It will enable a simple and efficient framework for the SHAPE governance, while overcoming long standing institutional barriers which impede on health-related research, teaching, and innovation in France. We are committed to ensuring gender balance in the SHAPE governance, which remains particularly challenging in the field of biomedical sciences.



Governance of the Lyon Health Hub and the SHAPE-Med@Lyon project

Bureau of Heads of Institutions. The Bureau is composed of the presidents and general directors of UCBL, HCL, ULL, Inserm, and the SHAPE Scientific Director. It validates major strategic decisions, submitted to the governing boards of all SHAPE partners, when necessary, as well as SHAPE’s budget and annual report. The Bureau meets every two weeks. It invites the institutional leaders of other key partners including HEI, NRO, industry, and local authorities, at least once per trimester.

Scientific and Innovation Committee (SIC). It is composed of representatives of major partners of health research and innovation: UCBL, HCL, Inserm, ULL, CNRS, Inria, VétAgro Sup, CLB, IARC-WHO, industry (see annex). Representatives of patient associations, local authorities, and other partners will be invited. The SIC is the main decision-making body on scientific strategy, under the supervision of the Bureau. It evaluates projects submitted for funding, makes recommendations on scientific



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priorities and HR needs. It meets at least once per trimester. It will launch thematic working groups to support the joint steering of key scientific areas of health research and innovation in Lyon.

Training Committee. It will be composed of the VPs for training of UCBL, ULL, CPE, and VétAgro Sup, the Dean of medicine, 1 representative of engineering schools, 1 student representative, the directors of SimuLyon and the Public Health School. Other partners will be invited. It will work in collaboration with the SIC to coordinate the transdisciplinary training programs and make recommendations on the strategy for health-related training.

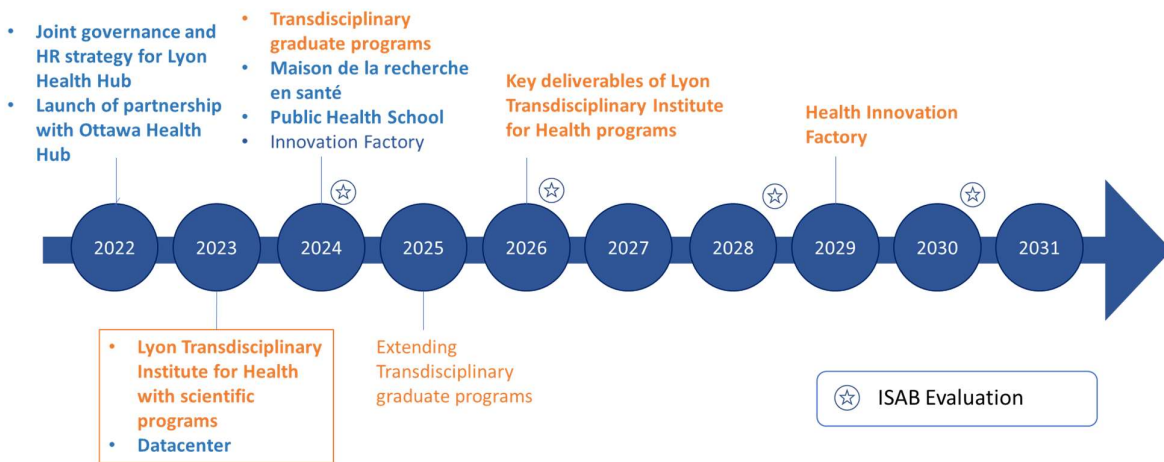
Joint Directorate of Health Research and Innovation. The Joint Directorate is co-chaired by the UCBL VP for health research and the HCL director of research. VPs of ULL and VétAgro Sup are invited when relevant. The Joint Directorate integrates research management staff of UCBL and HCL, which is a unique initiative in the French university hospital system. It is responsible for the strategic management of all major issues relevant for SHAPE. It prepares decisions of the Bureau and the SIC.

International Scientific Advisory Board (ISAB). The ISAB is composed of 8 foreign scientists with an outstanding track record in health-related research and innovation (see the annex for details on its composition). The ISAB makes recommendations on our strategic priorities and supervises the evaluation and selection of projects of >1M€. The ISAB meets once per year to provide feedback on the implementation of the projects and conducts an in-depth external evaluation of the strategy and governance of the Lyon Health Hub every two years.

Management team of the Lyon Transdisciplinary Institute for Health. It will be composed of its director, 2 deputy directors, and the leaders of the scientific programs. The directors will be appointed by the Bureau on the proposition of the SIC. The management team is responsible to design and implement the Institute's action plan, under the aegis of the SIC. It will be supported by a project manager embedded in the Joint Directorate.

3.2 ROADMAP, MONITORING AND EVALUATION OF THE SHAPE-MED@LYON PROJECT

Key milestones of the Lyon Health Hub and the SHAPE-Med@Lyon project





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The implementation of SHAPE will be monitored by the Joint Directorate, under the supervision of the SIC. The SHAPE project team will draw up an annual project report to be validated by the Bureau. Financial management will be ensured by the Joint Directorate.

SHAPE scientific programs. Their implementation will build on the experience of transdisciplinary programs which have already been implemented in Lyon (see 1.1). Clear milestones and deliverables have been defined to monitor the implementation of the scientific programs (see 2.1). We will also monitor research output (see annex) and conduct reputation surveys to evaluate the Institute’s visibility, internationally (with similar leading institutes worldwide) and locally (with socio-economic partners and public authorities).

Quality assurance for training. SHAPE training programs will be evaluated by the students and the results will be shared with the Training Committee and submitted to the Bureau. Teaching teams will consider this feedback and propose concrete measures to improve training quality when necessary. Building on Idefi SAMSEI and other PIA projects, we have defined key indicators to measure the impact of the training programs (see table below).

An **in-depth evaluation by the ISAB** will be carried out every two years, providing a global review of the SHAPE project and its impact on the Lyon 2030 overall transformation. The ISAB will rely on all available project documents and indicators, on-site visits, and interviews with all relevant stakeholders. The evaluations will be presented to the Bureau and the Scientific and Innovation Committee and communicated to the ANR. The SHAPE governance will propose concrete measures to consider the ISAB’s recommendations.

See the annex for a comprehensive table of monitoring indicators.

4. FUNDING JUSTIFICATION

The budget requested (see administrative file) represents a total of 35 M€ for 10 years (incl. 2.6 M€ overheads) divided into 27.5 M€ for the research institute, 7 M€ for interdisciplinary health-related graduate training and 0.5 M€ for other costs.

The ~20 M€ (excl. overheads) for the Institute will be divided in ~5 M€ for each program:

- 2 M€ for 1 senior (1M€) and 2 junior (500k€ each) chairs
- 1 M€ for post-doctoral fellowships
- 100 k€/year for running costs
- 540 k€ for meetings fees and collaboration development

	ANR GRANT Request (k€)			Partner Contributions* (k€)
	Research	Training	Innovation	
Lyon Transdisciplinary Institute for Health				
Equipment	1920			12500
Lyon Transdisciplinary Institute for Health (480k€/ Pilot prog.) Call for innovative equipments (internal to UCBL): 2,5M€/year				
Contract staff				
PhD (4 pilots x 6 PhD) - Pilot prog.	2640			
Post-doctorant (10 x 24 months / Pilot)	4000			
IE (Lyon Transdisc. Institute for Health)	1520			
IR (Lyon Transdisc. Institute for Health)	2520			
Research manager (72k€/year) + training manager (66k€/year)	720	660		



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Operational costs				
Conferences, workshops and congress for scientific programs	960			
Functioning costs and small materials (200k€/program/year)	6400			
Tackling the major challenges of massive data				
Contract staff				
IR (data management and AI - SimuLyon)	840			
Operational costs				
Infrastructure software development for data management (SimuLyon)	200			
Building a Transdisciplinary teaching offer to train future leaders in health research and innovation				
Equipment - SimuLyon - IT infrastructure	200			
Contract staff				
ENS-UCBL programs (theses)				220
Transdisciplinary theses (easing access to thesis (4th year of thesis)				880
Post-doc and PhD for welcoming highly cited researchers (2 packages)	1000			
Interdisciplinary professionalization, for non-medical students and engineers		1100		
MD-PhD programs in health and SHS (theses)		330		
Operational costs				
Training in public health for public bodies, managers, companies / Seminars		200		
Training for health professionals/doctors/engineer		200		
UCBL-ECL degree (32k€/year)		320		
Expenses for training for public bodies, managers, companies		200		
Life-long training workshops for health professionals, doctors and engineers		200		
Implementation of cases studies in the field (1500€ x 20 students x 10 years)		300		
ENS-UCBL programs (MD PhD programs model)				1056
MD-PhD programs in health and SHS (Master gratifications and functioning costs)		390		
Adaptable "Kits" of field cases for distance training courses (5 kits x 16 k€)		80		
Connecting academics, hospital practitioners, and businesses to foster health innovation				
Contract staff				
Public-private mobility initiative (12k€/y x 5 fundings x 1 year)		600		
Strengthening multidisciplinary approaches and the hospital-university-research continuum through an integrated HR strategy				
Contract staff				
Project manager (specializing in project development) - Support for PUPH				420
Functioning costs for junior professorships – 1M€/year funded by UCBL				5000
Functioning costs for senior professorships - 1M€/year funded by UCBL				5000
Chief of clinic assistant (clinical discharge for MCUPH or PUPH) - 4 fundings	960			
Operational costs				
Call for innovative projects (internal call, funded by HCL – 2,5M€/year)				12500
Welcoming highly cited researchers (package of 750 k€ x 2)	500			
Costs for Medical Head Assistant for PUPH support packages	1080			
Full-time year of research for young health professionals: environment costs			540000	480
Enhancing the Lyon Health Hub's international attractiveness and visibility: strong partnerships with uOttawa and the WHO				
Operational costs				
Ottawa : summer school (20k€/year)		200		
Travels and exchange programs with Ottawa / Canada (50k€/year)		500		
International network: 1 symposium (20k€) and 1 summer school (40 k€) / 2 years		300		
Calls for international mobility program during PhD		450		
Contract staff				
Permanent staff				210352
Health hub Project manager				780
Sub-total (k€)	25460	6530	540	249188
Overheads (k€) : 8%	2036,8	522,4	43,2	
TOTAL ANR GRANT REQUEST for 10 YEARS (€)		35,132,400		