YENEPOYA
(DEEMED TO BE UNIVERSITY)
Recognized under Sec 3(A) of the UGC Act 1956
Accredited by NAAC with 'A' Grade

Details of the Collaborative Activity

2020-21

Name of the Collaborating Institute: Department of Medical Genetics, University of Siena, Italy

Name of the Collaborating Department with YDU: Yenepoya Research Center

Activity:

A Joint collaborative agreement was signed between Department of Medical Genetics, University of Siena, Italy and Yenepoya Research Center in the year 2021 for a research project on "Impact of Host Genome on Covid-19 clinical variability". The project has been initiated and the collaborating institute is sharing the data for deep bioinformatics analysis.

ATTESTED
Dr.Gangadhara Somayaji K.S.
Registrar
Yenepoya(Deemed to be University)
University Road, Deralakatte
Mangalore- 575 018, Karnataka

RESEARCH AGREEMENT
BETWEEN THE
YENEPOYA (DEEMED TO BE UNIVERSITY)
AND
UNIVERSITY OF SIENA

DATA SHARING

This RESEARCH AGREEMENT ("Agreement") is between the Yenepoya (Deemed to be University) represented by Dr. Gangadhara Somayaji, the Registrar (the "Recipient"), located at Mangalore, India and University of Siena (the "Sender"), Department of Medical Biotechnologies, an Italian Public Research Institution duly organized and validly existing under Italian laws, represented by Prof. Gianni Pozzi as Head of the Department, each of the aforementioned being referred to individually as the "Party" or collectively as the "Parties";

The Parties agree as follows:

1. STATEMENT OF WORK. The Recipient shall use its reasonable efforts to perform the Research entitled "Impact of Host Genome on COVID-19 clinical variability" (The "Research Program" as further described in the attached Appendix A) and as a part of the project led as PI by Prof. Alessandra Renieri, University of Siena. The statement of work shall not be changed except by written amendment to this Agreement signed by the Parties.

2. PRINCIPAL INVESTIGATOR. The Research will be supervised by Dr. Ranajit Das from the Recipient to serve as Principal Investigator. If, for any reason, he is unable to continue to serve as Principal Investigator(s) and a successor acceptable to Sender is not available, this Agreement shall be terminated for convenience as provided in Article 7.

3. PERIOD OF PERFORMANCE. The Research shall be conducted during the period commencing 10th October, 2021 (the "Effective Date") and, unless earlier terminated in accordance with this Agreement, ending 9th October, 2022 (the "Completion Date"). An extension of additional 5 years is related to data analysis only. The Completion Date may be modified or extended only by written agreement of the Parties.

4. DELIVERABLES. The Principal Investigator at Recipient shall furnish PI at Sender with deliverables and reports as specified in Appendix A.

5. TERMINATION.

   A. Performance under this Agreement may be terminated for convenience by either Party upon 30 days written notice.

   B. In addition to the termination right set forth above in 7A hereof, either Party may terminate this Agreement effective upon written notice to the other Party, if the other Party breaches

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any of the terms and conditions of this Agreement and fails to cure such breach within 30 days after receiving written notice thereof. In the event of an incurable breach, the non-breaching Party may terminate this Agreement effective immediately upon written notice to the breaching Party.

6. INTELLECTUAL PROPERTY.

A. "Foreground Intellectual Property" (below defined as "Project IP") means all intellectual property, including without limitation, electronic or otherwise, technical information, know-how, copyrights, patents and trade secrets, ideas, thoughts, concepts, processes, techniques, data, development tools, models, drawings, specifications, prototypes, inventions and software which are generated or conceived and reduced to practice in the performance of the Research and under the Statement of Work of this Agreement.

B. "Sideground Intellectual Property" means all intellectual property, including without limitation, electronic or otherwise, technical information, know-how, copyrights, patents and trade secrets, ideas, thoughts, concepts, processes, techniques, data, development tools, models, drawings, specifications, prototypes, inventions and software which are generated or produced outside the Research by any of the partners or independent of this Agreement during the project's tenure.

C. "Background Intellectual Property" means any information, data, materials, inventions, processes, methods, methodologies, techniques, technologies, software, know-how, patents, patent applications or any other intellectual property owned or controlled by a Party before the Effective Date of this Agreement.

D. It is agreed that: the Recipient will retain all right, title and interest in and to Recipient's Background and Sideground Intellectual Property. Sender will retain all right, title and interest in and to Sender's Background and Sideground Intellectual Property.

E. Ownership of Project IP shall be as follows:

Title to any Project IP made or conceived solely by employees of Sender and that is not based on Recipient's Background or Sideground IP, vests in Sender (below defined as Sender Project IP).

Title to any Project IP made or conceived jointly by employees of both Recipient and Sender (hereinafter called "Joint IP") vests jointly in Recipient and Sender.
Sender and Recipient shall promptly disclose in sufficient detail ("Invention Disclosure") any Joint IP or discoveries resulting from the Research to their Technology Transfer Offices. Any such Invention Disclosure shall be considered Confidential Information. The Parties shall regulate the protection of any Joint IP with Joint Ownership Agreements.

7. CONFIDENTIAL INFORMATION.

A. Confidential Information. It is contemplated that the disclosing Party ("Disclosing Party") may be disclosing certain confidential and/or proprietary information to the receiving Party

("Receiving Party") unknown to the general public (hereinafter referred to as "Confidential Information"). The Parties agree the terms of this Article shall apply to any confidential and/or proprietary information that may be disclosed under this Agreement, and that such Confidential Information shall be used solely for the benefit of the Disclosing Party. Receiving Party acknowledges the above-described Confidential Information is confidential and/or proprietary to the Disclosing Party and is claimed to be a valuable, special, and unique asset of the Disclosing Party.

B. Subject to the limitations set forth in D below, all non-public information exchanged between the Parties shall be deemed to be Confidential Information. In order for the Parties to appreciate when non-public information is being conveyed, to the reasonable extent possible, information disclosed in tangible form shall be clearly identified at the time of disclosure as being Confidential Information by an appropriate and conspicuous marking. Similarly, to the reasonable extent possible, information disclosed in intangible form (e.g., oral or visual) shall be identified as being Confidential Information at the time of disclosure, and shall be confirmed as such in writing to the Receiving Party within 30 days after such disclosure.

C. Confidential Information shall include by way of example, without any limitation:

All information of a Disclosing Party which has been maintained as confidential, including draft publications, technical reports, research plans and results, processes, techniques, know-how, biological materials, computer source code, diagrams, electronic files, financial information, customer lists, trade secrets, invention disclosures, patent applications or test data; all existing and future plans of the Disclosing Party, which have been maintained as confidential, including plans relating to existing and planned products, research, development, engineering, manufacturing, marketing, servicing, or financing; all past, present and future business or commercial relationships of the Disclosing Party, which have been maintained as confidential, including suppliers, service providers, clients, customers, employees, or investors; or information that has generally been considered and treated by the Disclosing Party as confidential prior to the time of disclosure and is clearly identified as "Confidential" or "Proprietary" when disclosed to the other Party.

D. Exclusions from Confidential Information: Confidential Information shall not be deemed to include information that the Receiving Party can demonstrate by competent written proof:

(i) is now, or hereafter becomes, publicly known or available through no act or failure to act on the part of the Receiving Party;

(ii) was known by the Receiving Party at the time of receipt of such information as evidenced by its records;

(iii) is hereafter furnished to the Receiving Party by a third party as a matter of right and without violating any confidentiality obligation to the Disclosing Party; or

(iv) was independently developed by employees of the Receiving Party without use or knowledge of the Confidential Information of the Disclosing Party.

E. Use of Confidential Information: Each Party agrees it will use the Confidential Information of the other solely for the Purpose and for no other purpose whatsoever. In particular, the Receiving Party shall not file any patent application containing any claim to subject matter derived in whole or in part from the Disclosing Party's Confidential Information. The Confidential Information, including any documents, drawings, sketches, designs, materials or samples supplied hereunder, shall remain the property of the Party disclosing the same and no rights or licenses are granted to the other Party in the same, whether patented or not, except the limited right to use the Confidential Information as set forth above.

F. Confidential Obligations: For a period of 3 years from the date any such Confidential Information is disclosed, the Parties agrees to exert reasonable efforts to maintain each other's Confidential Information in confidence and to take all necessary and reasonable precautions to prevent its unauthorized disclosure and to ensure it does not fall into the public domain or the possession of unauthorized third parties. Each Party shall restrict access to the Confidential Information of the other Party to those officers, employees, consultants, agents, and students of the Receiving Party having a need to know the Confidential Information to fulfill the Purpose, provided that, each Party shall ensure that any individual having access to the Confidential Information is made expressly aware of the obligation of confidence according to the terms hereof prior to gaining access to the Confidential Information. To the extent that a Party perceives a need for disclosure of the Confidential Information it receives from the other Party to any third party, such third party shall be prospectively identified and written permission to disclose shall be obtained from Disclosing Party. A written non-disclosure agreement shall be obtained from the third party contractor and a copy shall be promptly provided to the Party whose Confidential Information is being disclosed.

G. Required Disclosure: If a Receiving Party is legally required by court order, law, or other governmental regulation or authority to disclose certain Confidential Information received from a Disclosing Party, such disclosure may be made only after giving written notice to the Disclosing Party and providing a reasonable opportunity for pursuit of appropriate process to prevent or limit such disclosure. In any event, required disclosure shall be limited to only that portion of the Confidential Information which is legally required to be disclosed. The Receiving Party is not however, required to pursue any claim, defense, cause of action, or legal process or proceeding on the Disclosing Party's behalf.

H. Return of Documents: It is understood that the Confidential Information disclosed by each Party shall remain the property of the Disclosing Party. All material or documents furnished by the Disclosing Party, including all copies, shall upon request of the Disclosing Party, or in any event at the termination of this Agreement, be promptly returned to the Disclosing Party or destroyed, except the Receiving Party may securely retain one copy in its files solely for record purposes of its obligations under this Agreement.

8. PUBLICATIONS. Recipient may publish the results of the Research, either jointly with Sender or provided Sender is cited as the source of the data, except for Sender's Confidential Information, after providing the Sender with a 30 day period in which to review each publication to identify patentable subject matter and to identify any inadvertent disclosure of Confidential Information. If necessary to permit the preparation and filing of U.S. patent applications, the Recipient may agree to an additional review period not to exceed 60 days. Such delay shall not, however, be

imposed on the filing or publication of any student thesis or dissertation. Failure to respond within 30 days shall constitute de facto agreement of SPONSOR that no delay in publication is necessary. Any further extension will require agreement between Sender and Recipient.

9. DATA PROTECTION. In executing the contractual activities, the Parties shall treat all the personal data they receive for any reason in relation to the Research Program in accordance with the objectives of the foregoing articles and in conformity with the provisions of Regulation (EU) 2016/679 of the European Parliament and Council of 27 April 2016, and with the related provisions of law and orders of national administrations, including any subsequent amendments (collectively the "Data Protection Laws").

The Sender and the Recipient are independent data controllers for the purposes of article 4 paragraph 17 of the GDPR.

The Parties warrant that the persons authorized by them to process personal data for the purposes of the Research Program will comply with the principles in place to safeguard data protection and the right to confidentiality and that any persons having access to the personal data will be obligated to process the data in accordance with the instructions given, in accordance with this article, by the data controller.

The Principal Investigator has been identified by the Entity as a person authorized for the data processing for the purposes of Article 29 GDPR and as a designated party for the purposes of Article 2 of the Code.

The Principal Investigator shall provide clear, complete information to all patients before the Research Program starts to all patients, regarding the nature, purpose, results, consequences, risks and methods of the processing of personal data; in particular, all patients must be informed that the national and international authorities and the Ethics Committee may, in connection with the monitoring, checking and control of the Research Program, have access to the related documentation and also to the original healthcare records of the patient, and that the data may also be accessed by the monitors and auditors in connection with their respective duties.

After the patient has been duly informed the Principal Investigator shall obtain the consent form for participation in the Research Program and also the consent to the processing of personal data.

The Sender is responsible for keeping the consent forms.
If either Party discovers a data protection breach, the other Party shall be informed within 48 hours from the breach having been verified, without affecting the Party's independent assessment of the existence of the conditions and fulfilment of the obligations contained in Articles 33 and 34 GDPR.

10. NOTICES/COMMUNICATIONS. All notices to Parties under this Agreement shall be in writing and sent to the names and addresses stated below under NOTICES. Either Party to the Agreement may change such name and address by notice to the other in accordance herewith, and any such change shall take effect immediately upon receipt of such notice. Other communications between the Parties can be addressed as stated below under COMMUNICATIONS.

COMMUNICATIONS to Yenepoya (Deemed to be University):

ATTESTED
Dr.Gangadhara Somayaji K.S.
Registrar
Yenepoya(Deemed to be University)
University Road, Deralakatte
Mangalore- 575 018, Karnataka

ADMINISTRATION:

Yenepoya (Deemed to be University)
University Road, Deralakatte
Mangalore, Karnataka 575018, India
Telephone: +918242203943
Email: registrar@yenepoya.edu.in

TECHNICAL:

Yenepoya Research Centre
Yenepoya (Deemed to be University)
University Road, Deralakatte
Mangalore, Karnataka 575018, India
Attn: Dr. Ranajit Das
Telephone: +918582802871
Email: das.ranajit@gmail.com

COMMUNICATIONS to SENDER:

ADMINISTRATION:

University of Siena
Via Banchi di Sotto 55
53100 Siena (SI), Italy
Telephone: 0577 233326
Email: amministrazione.dbm@unisi.it
PEC: pec.dbm@pec.unisipec.it

TECHNICAL:

University of Siena
Department of Medical Biotechnologies
Viale Bracci 2
53100 Siena (SI), Italy
Attn: Prof. Alessandra Renieri
Telephone: +39 0577 233303
Email: alessandra.renieri@unisi.it

10. INDEPENDENT CONTRACTOR. For the purposes of this Agreement and all services to be provided hereunder, the Parties shall be, and shall be deemed to be, independent contractors and not agents or employees of the other Party. Neither Party may make any statements, representations, or commitments of any kind, or to take any action which are binding on the other Party, except as may be explicitly provided for herein or authorized in writing.

11. SEVERABILITY. If any of the provisions of this Agreement is rendered or declared illegal for any reason, or shall be invalid or unenforceable, the remainder of this Agreement shall remain in full force and effect if the essential terms of this Agreement remain, valid, legal, and enforceable.

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12. ASSIGNMENT. This Agreement may not be assigned in whole or in part by any of the Parties without prior written consent of the other Party, except to a successor to all or substantially all of its business and assets.

13. PUBLICITY. Neither Party may use the names of the other Party, nor of any of its employees or members, nor any adaptation thereof, in any advertising, promotional or sales literature or news release without the prior written consent obtained from the other Party, as applicable in each case.

14. HEADINGS. The headings used herein are for reference and convenience only and shall not enter into the interpretation hereof.

15. DISPUTE RESOLUTION. The Parties shall use the dispute resolution process provided in mediation. SENDER must submit written notice of a claim of breach of contract under this chapter to Director of the Recipient.

16. ORDER OF PRECEDENCE. In the event of an inconsistency between the provisions of this Agreement, the inconsistency shall be resolved by giving precedence in the following order:

A. Research Agreement;
B. Appendix A-Statement of Work;

17. COUNTERPARTS. This Agreement may be executed in duplicate counterparts, which taken together shall constitute one single representation between the Parties.

ATTESTED

Dr.Gangadhara Somayaji K.S.
Registrar
Yenepoya(Deemed to be University)
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The Parties have caused this Agreement to be executed by their authorized representative.

Yenepoya (Deemed to be University)	University of Siena
By:	By:
Name: Dr. Gangadhara Somayaji	Name: Prof. Gianni Pozzi
Title: Registrar of Yenepoya (Deemed to be University)	Title: Head of Department of Medical Biotechnologies
Date: 07.10.2021	Date:
By:	By:
Name: Dr. Ranajit Das	Name: Prof. Alessandra Renieri
Title: RECIPIENT Research PI	Title: SENDER Research PI
Date: 07.10.2021	Date: 11/10/2021

Registrar
Yenepoya (Deemed to be University)
University Road, Deralakatte
Mangalore 575 018

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APPENDIX A
STATEMENT OF WORK

Title: Impact of Host Genome on COVID-19 clinical variability
Short title: GEN-COVID

SENDER PI: Prof. Alessandra Renieri, Department of Medical Biotechnologies

(short name of Research Institute or SME) **PI**: Dr.__Ranajit Das, Yenepoya Research Centre, Yenepoya (Deemed to be University), India_____, *(name of Research Institute or SME)*

The Scope of Work:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia has spread rapidly across the world and a major outbreak is currently ongoing in the northern regions of Italy. While the majority of individuals presents mild symptoms, a subgroup of critically ill patients is admitted to intensive care units and requires mechanical ventilation. The proportion of critically ill patients varies across countries and depends on the specific type of screening strategy enforced in the population. Patients admitted to intensive care units tend to be older and being diagnosed with previous comorbid conditions.

Nonetheless these factors do not completely explain differences in disease severity between individuals. We hypothesize that genetic susceptibility can play a role in explaining differences in individual disease susceptibility, severity and prognosis. Exploring genetic determinants of viral infection and outcome is important for several reasons. First, it might permit the identification of high and low risk individuals to improve clinical management of patients. Second, it might point out targets for existing drugs which can be repurposed to treat COVID-19 patients (for example, an observation such as CCR5-del32 and protection from HIV could, if it implicates an already targeted gene, lead rapidly to promising trials).

The primary aim of this project is to compare the genetic profile of laboratory-confirmed COVID-19 patients with mild *vs* severe symptoms. In secondary analysis we will compare all infected patients with a population control sample, incorporate immunoglobulin G response in the phenotype definition, and evaluate how the genetic profile is associated with patient outcomes.

The collector the University of Siena (Sender) will extract DNA on samples from COVID-19 patients collected across Italy.

The use of the derived data is regulated under the EU GDPR 2016/679 and legal provisions by the Italian national authority. Limits for the use of biosamples and data is also related to the terms of the informed consent obtained and the relative ethical approval (Prot n. 16929 of 16 March 2020). Informed consent constituted the legal basis for the collection and sharing of the data.

Clinical information will be collected during the patient visit together with blood drawn. A minimal set of clinical information will be directly reported in a study specific form which can be filled online or emailed to the coordinating center Additional clinical information will be extracted by accessing the electronic clinical records of the patient. This information will be obtained following informed consent limits.

Sender will produce using either in house resources or external resources genetic data (GWAS; WES; WGS)

This study aims to identify rapidly novel genetic variants associated with disease severity and progression to inform patient management and to provide novel insights for therapeutic development or repurposing.

DESCRIBE HERE THE SPECIFIC PART OF THE PROJECT

The objectives of the study are:

• Identify novel genetic variants that show significant variation between COVID-19 patients who are asymptomatic or show mild to moderate symptoms, versus those who show severe manifestations, employing a case-control based approach.
• Evaluate the likely association between hosts' genomic ancestry and the severity of COVID-19 manifestation, combining the COVID-19 patient data (common variants) with ancient and modern-day human genome data.

DELIVERABLE:

1. Part of data generated by Sender will be transferred to Recipient for data analysis

2. Results of statistical analysis of the data will be immediately transferred to Sender (within 2 weeks from the date of the data transfer)

3. The Recipient will provide the Sender with a first report within 30 days from the date of the data transfer and a report reflecting the complete data analysis within 60 days

4. Any relevant scientific results could be also released by Recipient to the scientific community under the approval of Sender

5. Any release to scientific community will be made by Recipient as aggregate data only under the approval of Sender. Individual level data cannot be released or published by Recipient

6. Any transfer from Recipient to third parties of data sent by Sender is forbidden

7. Any transfer from Recipient to third parties of results generated by Recipient on data sent by Sender is forbidden

8. Any transfer of results generated by Recipient through the creation of databases is forbidden

9. It is forbidden to profile individuals and to re-identify it unless Sender allows it for clinical reasons.

This agreement is valid for three years, can be renewed if both parties agree and after this period individual level data must be cancelled.