

## **Short and long read mRNA sequencing and proteomics data of blood cells exposed to different immune stimuli**

### **General principles**

In the context of the [Human Functional Genomics Project / 500FG study](#), researchers from Radboud university medical center's Departments of Internal Medicine, Human Genetics and the Center for Molecular and Biomolecular Informatics have generated short-read and long-read (PacBio) RNA sequencing data and proteomics data from cultured peripheral blood mononuclear cells from anonymized healthy donors exposed to different immune stimuli: lipopolysaccharide (LPS), polyI-polyC, *S. aureus* and *C. albicans* (and RPMI medium as control). The primary objective of this proteogenomics project was to characterize transcript and protein isoforms that are expressed only under certain immune-stimulated conditions. The Project is coordinated by Alexander Hoischen and Peter-Bram 't Hoen.

Access to Project Data will be granted to qualified researchers for approved use and will be governed by the provisions laid out in the associated informed consent of individual data subjects for each cohort and/or of the associated ethics committee approval of the associated cohort, the Data Access Procedure set forth below and the terms of the Data Access Agreement attached hereto. A qualified researcher refers to a senior investigator who is employed or legitimately affiliated with an academic, non-profit or government institution and who has a track record in the field.

Access to Project Data is available by application to the Data Access Committee. Researchers granted access to Project Data must acknowledge the Human Functional Genomics Project and cite the following paper(s):

Access is conditional upon availability of data and on signed agreement by the researcher(s) and the responsible employing institution to abide by the policies and conditions related to publication, data ownership, data return, intellectual property rights, data disposal, ethical approval, confidentiality and commercialization referred herein.

### **Data Available**

The following Project Data are available:

PacBio long-read RNA sequencing data from PBMCs of 1 anonymized healthy individual, stimulated with lipopolysaccharide (LPS), polyI-polyC, *S. aureus* and *C. albicans* (and RPMI medium as control).

Illumina short-read RNA sequencing data (3'cunting) from PBMCs of 5 anonymized healthy individuals, stimulated with lipopolysaccharide (LPS), polyI-polyC, *S. aureus* and *C. albicans* (and RPMI medium as control).

Proteomics profiles from the secretome of PBMCs of 5 anonymized healthy individuals, stimulated with lipopolysaccharide (LPS), polyI-polyC, *S. aureus* and *C. albicans* (and RPMI medium as control).

### **Data Access Committee**

Applications for access to Project Data must be made to the Proteogenomics Data Access Committee (DAC). The Proteogenomics DAC consists of Alexander Hoischen, Peter-Bram 't Hoen and Mihai Netea.

## Data Access Procedure

### *1. Application for Access*

The handling of applications, the issue of Project Data and any associated operations, administration and audits will be performed by the Radboudumc. Applications for Access to Project Data must be submitted using the online EGA data request procedure and using the form in Appendix 1. The information disclosed in the application will be treated as confidential and will only be disclosed to the persons evaluating the application. All incoming applications will be documented, including any conjunct agreements with the applicants. Unless explicitly consented for by the applicant, this information will not be used for purposes other than evaluation of the application. The research topic of the applications which have been granted will be published on the website of the Project. Applications which have not been granted will not be published. In cases where an application contains classified plans, know-how or trade secrets, the applicant may request the conclusion of a separate confidentiality agreement.

### *2. Multiple applications*

Applicants agree to use the Project Data for the approved purpose and project described in the application; use of the data for a new purpose or project will require a new application and approval. The Proteogenomics Data Access Committee (DAC) will consider applications that include named collaborators, but each Institution must sign a separate Data Access Agreement. In the event an applicant wishes to share the data with additional collaborators not previously approved, these additional collaborators must make a separate application for access to the Project Data. In the event two or more applications overlap, the DAC may propose the respective applicants to align their applications.

### *3. Assessment criteria*

Applications which seek to reserve Project Data for unspecified research goals will not be taken into consideration. Applications for access to Project Data must be Specific, Measurable, Attainable, Resourced and Timely (SMART). Specifically, the DAC will assess each application to determine whether:

- i. it has been submitted by a qualified researcher or researchers, who is employed by or legitimately affiliated with a recognised research institution that can provide institutional responsibility for appropriate research governance;
- ii. its proposed use of the Project Data is in accordance with and meets the objectives of the Human Functional Genomics Project and the objectives of the associated cohorts and collections;
- iii. its proposed use of the Project Data constitutes research in the context of the individual sample donor consent process, and is likely to be understood as such by the individual sample donors;
- iv. it would breach any of the ethical permissions or restrictions in the consent forms for any component cohort;
- v. all required ethico-legal approvals, restrictions and commitments for the proposed use of the Project Data have been obtained and adhered to;
- vi. the proposed research has any adverse potential impact, specifically whether the proposed research could affect minorities;
- vii. the nature of the funding of the application and the applicant;
- viii. the research proposal has been peer-reviewed, and, if not, whether the proposal satisfies applicable scientific standards;
- ix. the requested data are, quantitatively and qualitatively, suitable and not excessive for the applicant's proposed research;

- x. there are any similar applications pending or granted;
- xi. the proposed use of the Project Data has the potential to produce information that will enable identification of the individual sample donors.
- xii. In the event the applicant(s)' proposed use of Project Data involves use of his/their own data the applicant has warranted that he has obtained all required ethico-legal approvals, restrictions and commitments, without limitation his data subject consent and approval of his pertinent medical ethical review board, for his proposed use of his data in combination with the Project Data, as appropriate.

#### 4. Access decision

The DAC will decide on an application within a reasonable period of time after it has received all pertinent information. If the DAC grants an application, additional agreements may be made regarding authorships along the lines set forth in the Publication Policy attached to the Data Access Agreement. Rejections of applications will be motivated.

#### Mode of Access to Data; restrictions and authentication

The DAC will make the pseudonymised Project Data available through the European Genome Phenome Archive (EGA), hosted at the European Bioinformatics Institute. Issue of Project Data may be subject to restrictions pursuant to data subject's or ethics committee's consent. The issue of Project Data and the Data Access Agreement will be administered by Radboudumc.

#### Data Access Conditions

Access to Project Data is conditional on prior receipt by the DAC of the Data Access Agreement attached as *Appendix 2* hereto, signed and dated by the applicant(s) and the responsible employing Institution(s).

Authors who use Project Data must:

1. Acknowledge the Human Functional Genomics Project using the following wording:

*"The authors acknowledge all efforts from the researchers involved in setting up the 500FG cohort within the Human Functional Genomics Project (reference 1 below). The authors thank all volunteers from the 500FG cohort of the Human Functional Genomics Project for their participation."*

2. Cite in the reference list the papers describing the generation of the data:
  1. Understanding human immune function using the resources from the Human Functional Genomics Project. *Nat Med* **22**: 831–833 (2016)
  2. Functional Genomics Approach to Understand Variation in Cytokine Production in Humans. *Cell* **167**(4): 1099-1110 (2016)

## **Application Form for Access to Human Functional Genomics Project Proteogenomics Data**

**PLEASE SUBMIT COMPLETED, SIGNED AND DATED FORM BY EMAIL TO: [peterbram.thoen@radboudumc.nl](mailto:peterbram.thoen@radboudumc.nl)**

### **Application Form for Access to HFGP Data**

**1. Name and position of the Applicant, including employment or affiliation with any organization**

Please ensure that a full postal and email address is included for each applicant.

**2. Title of the study**

In less than 30 words.

**3. Research Question**

Please describe the study in no more than 750 words. Include:

- a. outline of the study design;
- b. an indication of the methodologies to be used;
- c. proposed use of the Project Data;
- d. preceding peer-reviews of the study (if any present);
- e. specific details of what you plan to do with the Project Data;
- f. timeline;
- g. key references.

**4. Consent and Approvals**

If your proposed use of Project Data involves use of your own data, please confirm that you have obtained all approvals required by the rules and regulations of your jurisdiction, including your institution's institutional rules, and the consent of your data subjects, for your use of your own data in the study, by ticking the following box: Yes, we have ☐.

**5. The nature and amount of Project Data applied for**

Please specify the data you request access to (cohort & type).

Please tick the boxes below, if you request any or all of the following associated phenotype data:

Age (within certain bins): ☐;                      Sex:    ☐;

**6. Resources, Feasibility & Expertise**

Please confirm that you have secured funding for your proposed use of the Project Data and that you will carry out your research within a reasonable period of time after the granting of this application: by ticking the following box: Yes, we will ☐.

Please describe your experience and expertise, and that of your collaborators, and how this will be applied to the proposed study (in 250 words).

Please provide a list of recent publications (max. 10).

## 7. Access Conditions

Please declare that you have read and agree to abide by the terms and conditions outlined in the HFGP Data Access Agreement and the Publication Policy attached hereto as Appendix 1, by ticking the following box:  
Yes, we will ☐.

Signed by:

.....

Name of Applicant:

Affiliation of Applicant with Institution:

.....

Place:.....

Date:.....

.....

Legal representative of Applicant's Institution:

Name of Applicant's Institution:

.....

Place:.....

Date:.....

Stamp or Seal of Applicant's Institution:

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## **Appendix 2**

### **Data Access Agreement**

This agreement governs the terms on which access will be granted to the Project Data generated by the Human Functional Genomics Project. In signing this agreement, you are agreeing to be bound by the terms and conditions of access set out in this agreement. For the sake of clarity, the terms of access set out in this agreement apply both to the User and the User's Institution (as defined below). User Institution and User are referred to within the agreement as "You" and "Your" and shall be construed accordingly.

#### **Definitions:**

"Project" refers to the proteogenomics project executed within Radboudumc

"Project Data" refers to the RNAseq and proteomics data generated by the Project.

"Data Subject" refers to the person whose sample has been used to generate Project Data.

"User" refers to a researcher who has successfully applied for access to Project Data.

"Publications" refers to, without limitation, articles published in print journals, electronic journals, reviews, books, posters and other written and verbal presentations of research.

"User Institution" refers to the organization with which the User is employed, affiliated or enrolled.

#### **Terms and Conditions:**

In signing this Agreement:

1. You agree to use Project Data only for the advancement of scientific and medical research.
2. You agree not to use, and not to allow use of, Project Data or any part thereof for the creation of products or services for sale or for any commercial purpose, whether sale by You or by third parties.
3. You acknowledge that the Project Data You receive is pseudonymised and that the Data Access Committee (DAC) will under no circumstances provide You with any means to identify any Data Subject. You agree not to use Project Data to identify or contact individual Data Subjects. You agree to preserve, at all times, the confidentiality of information and Project Data. In particular, You undertake not to use, or attempt to use Project Data to compromise or otherwise infringe the confidentiality of information on Data Subjects and their right to privacy.
4. You agree to disclose Project Data only to those of Your employees who strictly need access to it for the purpose of your approved study (Authorized Recipients), and who are bound by a duty of confidentiality which is at least as strict as provided for in this agreement.
5. You agree to ensure that any Authorized Recipient who has access to Project Data is advised of the confidentiality of Project Data. Upon request by the DAC, you agree to furnish the DAC the names of all Authorized Recipients who have gained access to Project Data. You agree that You are responsible for all breaches of confidentiality and of the terms of this agreement by your Authorized Recipients.

6. You agree to store Project Data on a computer with adequate security controls that prevent unauthorized access to or loss of Project Data and to maintain appropriate control over the Project Data. You represent and warrant that You have in place, and You agree that You will keep having in place, state of the art technical and organizational security measures preventing unauthorized access and loss of Project Data or other forms of unlawful processing of Project Data, including without limitation, physical security measures, access controls, security and privacy technologies, security checks in relation to personnel, security incident response management and audit arrangements. You agree to notify forthwith the administrator of the Project, Radboudumc, of any violations of the foregoing.
7. You represent and warrant that you have obtained and adhered to all required ethico-legal approvals, restrictions and commitments, without limitation data subject consent and approval of the pertinent medical ethical review board, for Your proposed use of Your data in combination with the Project Data.
8. In the event the Project Data is issued to You subject to any Data Subject's restrictions, you hereby assume the obligation to abide by these restrictions as Your own obligation towards the Data Subject. You agree that Data Subjects can enforce such restrictions as well as any pertinent provisions of this agreement as third-party beneficiaries and, in the event they choose to do so, that You will not object to Data Subjects being represented by an association or other bodies if they so wish. You agree that a Data Subject who has suffered damage(s) as a result of any violation by You of pertinent provisions in this Agreement or of applicable legislation, is entitled to receive compensation from You for the damage(s) suffered. You agree that, in the event of such a violation, the Data Subject may bring an action before a court within the Data Subject's jurisdiction against You.
9. You agree not to attempt to link Project Data to other information or archive data available for the data sets provided to You under this agreement, even if access to that data has been formally granted to you, or it is freely available without restriction, without the required consents and approvals. You agree to retain control over Project Data, and NOT TO DISTRIBUTE (individual-level or aggregated) Project Data provided under this agreement, in any form, to any entity or individual.
10. You agree not to transfer, share or disclose Project Data, in whole or in part, to or with anybody else, whether or not he or she is affiliated with Your institution, unless he or she is a named and approved collaborator under the Proteogenomics Data Access Procedure.
11. You agree to use Project Data for the purpose and project described in your application, as approved by the Proteogenomics Data Access Committee; use of the data for a new purpose or project or by another researcher will require a new application and approval. Substantive modification of the original application requires submission of an amendment to the original application.
13. You accept that Project Data will be reissued from time to time, with suitable versioning. If the reissue is at the request of sample donors and/or subject to other ethical scrutiny, you will destroy earlier versions of the Project Data.
14. You agree to destroy the Project Data after the resulting paper has been published. To meet journals' requirements for availability of Project Data for reviewers to see and readers to use, you agree to refer to the availability of the Project Data as deposited with EGA, under the terms hereof. You agree that the availability of the data resulting from your study of the Project Data for reviewers to see and readers to use is subject to this Access Policy, Procedure and this Data Access Agreement.



15. You agree to acknowledge in any work based in whole or in part on Project Data, the published paper from which the Project Data derives, the version of the data, and the Human Functional Genomics Project, as per the wording provided in the paragraph “Data Access Conditions”.
16. You accept that the DAC and the original Project Data generators:
  - a) bear no legal responsibility whatsoever for the accuracy, completeness or comprehensiveness of the Project Data; and
  - b) accept no liability for direct, indirect, consequential or incidental, damages or losses arising from any use of Project Data by anyone, including without limitation any clinical use and any commercial use thereof, or arising from the unavailability of, or break in access to, the Project Data for whatever reason.
17. You understand and acknowledge that Project Data are protected by copyright, database right and other intellectual property and proprietary rights, and that duplication, sale, licensing or any other form of disposing or distribution or making available, of all or part of the Project Data on any media is not permitted.
18. You acknowledge that the Project Data are made available to you under this agreement on the title of unassignable, non exclusive “loan”. You recognise that nothing in this agreement shall operate to transfer to You any rights, including but not limited to intellectual property rights and database rights, in or relating to Project Data.
19. You accept that this agreement will terminate immediately upon any breach of this agreement by You and You will be required to destroy any Project Data held.
20. You accept that it may be necessary for the Data Access Committee or its appointed agent to alter the terms of this agreement from time to time in order to address new concerns. In this event, the Data Access Committee or its appointed agent will contact You to inform You of any changes and You agree that Your continued use of Project Data shall be dependent on the parties entering into a new version of the agreement.
21. You agree that You will submit a report to the Proteogenomics Data Access Committee, if requested, on completion of your study of the Project Data. Such report will include the data resulting from your study of the Project Data. The Proteogenomics Data Access Committee agrees to treat the report and all information, data, results, and conclusions contained within such report as confidential information.
22. You accept that Project Data may be protected by and subject to national and international laws and that You are responsible for ensuring compliance with any such applicable law. The Proteogenomics Data Access Committee reserves the right to request and inspect Your data security and management documentation to ensure the adequacy of data protection measures in countries that have no national laws comparable to that which pertain in the European Economic Area (EEA).
23. This agreement shall be construed, interpreted and governed by the laws of the Netherlands.

Signed by:

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Name of Applicant:

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Legal representative of Applicant’s Institution:

Affiliation of Applicant with Institution:

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Place:.....

Date:.....

Name of Applicant's Institution:

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Place:.....

Date:.....

Stamp or Seal of Applicant's Institution:

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