PEG Study Onboard Training

Scarlett Yu

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7/9/2024

Training Overview

1. CITI Training and Data Security Agreement
2. General Office Background
3. Data Entry Training

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CITI Training & Data Security Agreement

CITI Training

- UCLA - HIPPA
- Group 1: Human Subjects Research

Data Security Agreement

- Confidential Data User Agreement & Office Security Agreement

Requirement

- Read and sign the data + office security agreement
- Complete the CITI training and HIPAA training
- Email the three documents above to Yufan Gong (ivangong@ucla.edu).

Sample Certificates/Agreement

CITI PROGRAM

Completion Date 27-Oct-2021
Expiration Date N/A
Record ID 45821365

This is to certify that:

Yue Yu

Has completed the following CITI Program course:

Not valid for renewal of certification through CME.

UCLA HIPAA
(Curriculum Group)
UCLA HIPAA
(Course Learner Group)
1 - Stage 1
(Stage)

Under requirements set by:

University of California, Los Angeles (UCLA)

CITI
Collaborative Institutional Training Initiative

Verify at www.citiprogram.org/verify/?w0d3e6ee8-bc52-4fe3-8880-4a21ae3ca731-45821365

UCLA - HIPPA

CITI PROGRAM

Completion Date 27-Oct-2021
Expiration Date 26-Oct-2024
Record ID 45820759

This is to certify that:

Yue Yu

Has completed the following CITI Program course:

Not valid for renewal of certification through CME.

Human Research
(Curriculum Group)
Group 1: Human Subjects Research
(Course Learner Group)
1 - Basic Course
(Stage)

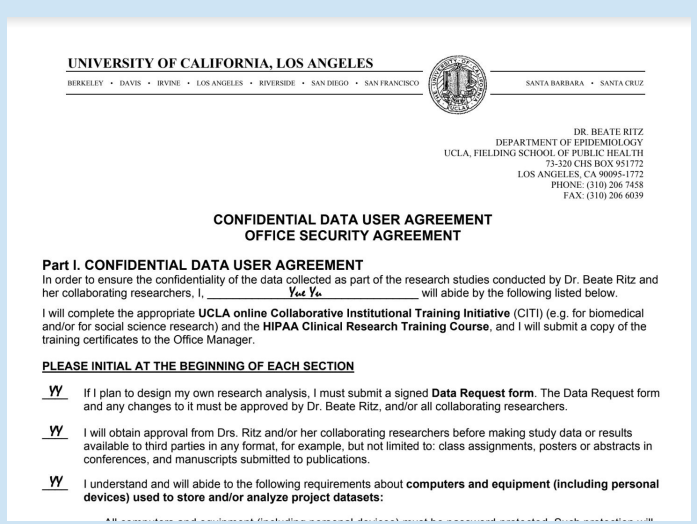
Under requirements set by:

University of California, Los Angeles (UCLA)

CITI
Collaborative Institutional Training Initiative

Verify at www.citiprogram.org/verify/?w85c376c2-3f6d-4299-9d77-3b57021d3085-45820759

Group 1: Human Subjects Research



UNIVERSITY OF CALIFORNIA, LOS ANGELES

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DR. BEATE RITZ
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FAX: (310) 206 6039

CONFIDENTIAL DATA USER AGREEMENT
OFFICE SECURITY AGREEMENT

Part I. CONFIDENTIAL DATA USER AGREEMENT
In order to ensure the confidentiality of the data collected as part of the research studies conducted by Dr. Beate Ritz and her collaborating researchers, I, Yue Yu will abide by the following listed below.

I will complete the appropriate **UCLA online Collaborative Institutional Training Initiative** (CITI) (e.g. for biomedical and/or for social science research) and the **HIPAA Clinical Research Training Course**, and I will submit a copy of the training certificates to the Office Manager.

PLEASE INITIAL AT THE BEGINNING OF EACH SECTION

YY If I plan to design my own research analysis, I must submit a signed **Data Request form**. The Data Request form and any changes to it must be approved by Dr. Beate Ritz, and/or all collaborating researchers.

YY I will obtain approval from Drs. Ritz and/or her collaborating researchers before making study data or results available to third parties in any format, for example, but not limited to: class assignments, posters or abstracts in conferences, and manuscripts submitted to publications.

YY I understand and will abide to the following requirements about **computers and equipment (including personal devices) used to store and/or analyze project datasets:**

Confidential Data User Agreement & Office Security Agreement

All lab members must complete and submit these three documents before starting to work!

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General Office Background

About PEG Study

Schedules and Personnel

Office Layout

Key Application

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About PEG Study

Duration

- 23-year study (started in 2001)

Focus:

- Links between **P**arkinson's disease, the **E**nvironment, and **G**enes

Collaboration:

- UCLA School of Public Health
- UCLA Movement Disorder Clinic (Neurology Dept.)
- UCLA Human Genetics
- Local healthcare providers in Kern, Fresno, and Tulare counties, CA

Funding:

- National Institute for Environmental Health Sciences (NIEHS)

Significance:

- First federally funded Parkinson's study focusing on rural populations

PEG
Brain & Gut Study

UCLA Fielding School of Public Health

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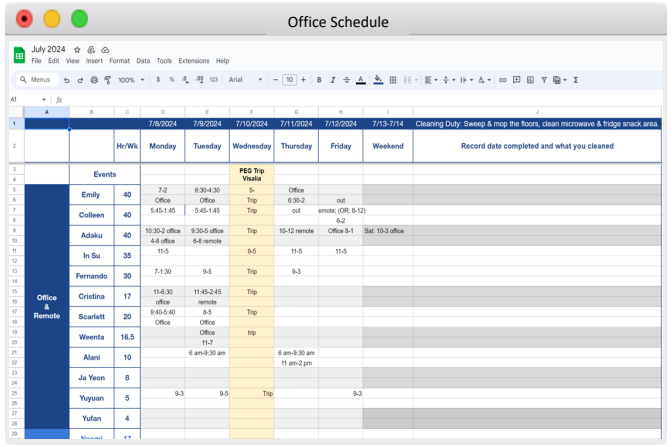
Office Schedule and Personnel

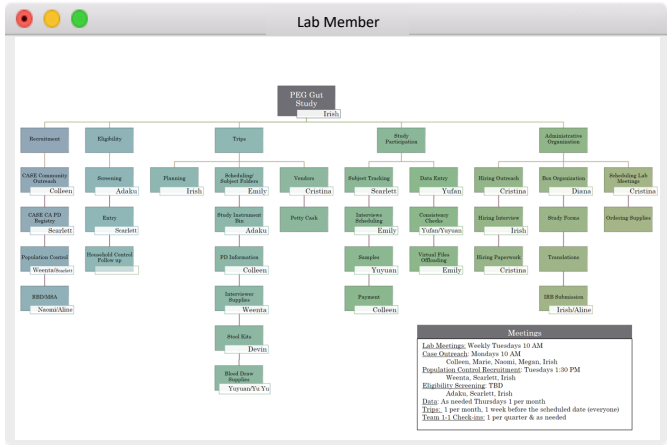
Office schedule

- A Google sheet indicates lab member's working schedule
- Please always keep it updated
- Cristina will send out through email every month

Personnel

- Lab member responsibility flowchart & bios
  - BOX Path: PEG_GUT > PEG Dictionary >
  - BOX Link: https://uclahs.box.com/s/b91os9rzodpb9i7w6s6ckjs37ln4h9cn





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Office Layout

Main PEG office (73-274/73-284)

- Key cabinet: all cabinets need to be locked at the end of the day
- Computers and passwords
- Printers
- Recruitment station, form shelves
- **Main office key application:** Contact Cristina Ruiz (cruiz311@g.ucla.edu)

Supply room (73-254)

- Storage for extra office supplies

Secure room (73-310)

- Good to use as private interviewing space, key logging records required

Copy room (76-087)

- Bulk printing/copying, printing code required – check with lab members for the code

Study Participants

Case – PD patient

- PD patient

Controls – originate

- (ideally randomly sampled) from the same population that gave rise to the cases
- Types
  - HH control
  - Population control

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Study design

Study population (n = 15,792)

- Derived from the Atherosclerosis Risk in Communities (ARIC) study
  - longitudinal cohort study
  - middle-aged individuals, randomly sampled from four US communities
  - measured for multiple risk factor phenotypes related to health and chronic disease

Study sample (n = 1,456)

- 1,456 European-Americans with the metabolomic and whole genome sequence data from the ARIC study.

Whole genome sequence data

- contains 12,820,347 rare variants (i.e., minor allele frequency, less than 5%)

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Statistical methods

Slide windows across the genome

- Convex-Concave Rare variant Selection (CCRS)
  - a statistical approach based on penalization methods
  - to address the multitude of analytic challenges

Select the most promising window associated with the metabolites

- ΔAIC and likelihood ratio test

Define model statistical significance

- permutation test

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Results

Table 1. Name and the range of metabolites after log transformation

Name	Average (range)	Name	Average (range)
Octanoylcarnitine	−0.101 (−0.621, 0.542)	*Deoxycarnitine*	−0.066 (−2.074, 1.640)
Decanoylcarnitine	−0.100 (−0.786, 0.657)	*Carnitine*[a]	−0.042 (−2.130, 2.365)
Cis-4-cenoylcarnitine	−0.080 (−1.198, 1.061)	*Glutarate*	−0.130 (−1.136, 1.124)
Laurylcarnitine	−0.076 (−0.820, 0.642)	*Leucine*	−0.092 (−1.133, 0.945)
Glutarylcarnitine	−0.080 (−0.943, 0.786)	*Lysine*	−0.081 (−0.696, 0.489)
Isovalerylcarnitine	−0.129 (−1.388, 1.134)	*N6acetyllysine*	−0.066 (−0.635, 0.620)
Isobutyrylcarnitine	−0.088 (−0.799, 0.748)	*Citrate*	−0.094 (−1.805, 1.676)
Propionylcarnitine	−0.091 (−1.720, 1.243)	*Succinate*	−0.061 (−0.891, 0.935)

[a]Variants that are not transformed.

Table 2. Baseline characteristics of ARIC European-Americans participants and those with metabolomics and genomic data

	ARIC European-Americans	
	Whole dataset	Subset under study
N	11,478	1,456
Age (years)	54 (6)	55 (6)
Male (%)	47.3	45.9
Diabetes (%)	9.1	8.0
Current smoker (%)	24.8	25.8
Hypertension (%)	27.3	31.7
Systolic bp (mmHg)	118.5 (17.0)	119.4 (18.4)
Diastolic bp (mmHg)	71.5 (10.0)	71.7 (10.8)
Glucose (mg/dL)	105.6 (32.1)	105.7 (29.8)
BMI (kg/m^2)	27.0 (4.9)	27.3 (5.0)
HDL (mg/dL)	50.4 (16.8)	50.0 (16.5)
Total cholesterol (mg/dL)	215.0 (40.8)	216.2 (40.3)
Triglycerides (mg/dL)	138.1 (93.0)	144.5 (110.1)
eGFRCKD-EPI ($mL/min/1.73\ m^2$)	0.48 (0.08)	0.47 (0.09)

The numbers in parentheses represent standard deviations.

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Results

Table 3. Summary information for two significant windows influencing two metabolites

	Chr	Location	Physical distance	Genes	*P*-value of LRT	$AIC_i - AIC_{selected}$
Lysine	10	101774069-83714	9,646 bp	*FGF8* *NPM3*	1.752×10^{10}	>4.2
Cis-4- decenoyl-carnitine	14	47401220-11509	10,290 bp	*MDGA2*	4.239×10^{7}	>2.4

Table 4. Summary information of promising variants in two significant windows influencing two metabolites

Chromosome no. position	Associated metabolite	MAC	Estimated effect size	Standard deviation	*P*-value
chr10.101775830	*Lysine*	24	−0.127	0.0434	0.0035
chr10.101776036	*Lysine*	69	−0.090	0.026	0.0005
chr10.101783714	*Lysine*	21	0.172	0.046	0.0002
chr14.47403473	*Cis-4-decenoyl carnitine*	58	0.235	0.053	9.202×10^{6}
chr14.47408133	*Cis-4-decenoyl carnitine*	23	−0.284	0.083	6.547×10^{4}
chr14.47411509	*Cis-4-decenoyl carnitine*	14	−0.433	0.1065	4.729×10^{5}

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Thank you!

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