DGIM Project Summary

(1 page preferred, 2 pages maximum)

Name of Project: Pilot Whole Genome Sequencing and Return of results at UCSF

Investigator(s). (Include phone numbers and email address, indicate PI and primary contact) Aleksander Rajkovic, MD, PhD (aleks.rajkovic@ucsf.edu) – the PI, Sawona Biswas, MS, CGC (Sawona.biswas@ucsf.edu)

Research question(s): In this study, we propose to enroll 1000 adults (aged 18 or above, not suspected to have a genetic condition) recruited at UCSF medical clinics and/or through myChart for clinical whole genome sequencing (WGS). The pilot will investigate best practices for consenting, recruiting, and delivering results along with its role in predictive care. The study in the pilot phase will include about 1000 adults and can be increased to 10,000 individuals in subsequent years. Our immediate aims will compare recruitment success via myChart as opposed to direct recruitment in medical clinics, the demographics of individuals who choose to participate, expectations and perceptions of results to return to participants, concerns about privacy and data sharing. Additionally, the de-identified information in the joint genetic and health information database will be made available for other research projects at UCSF (with IRB and appropriate regulatory oversight).

The primary objective of this study will be to:

1. Develop electronic modalities for patient recruitment (website, MyChart, brochures and questionnaires)
2. Engage different stakeholders across UCSF to develop best recruiting operating procedures within primary care and other clinics. Specifically assess engagement of frontline physicians in managing outcomes of genetic results.
3. Investigate best practices for consenting, recruiting, and delivering results along with its role in predictive care.
4. To establish a common repository of genomic, clinical and social data at UCSF for future research use.

Brief Background/Significance:

As the cost of sequencing continues to drop and the ability of next generation sequencing increases, tests like whole exome and whole genome sequencing will be utilized more abundantly. WGS will revolutionize how we approach genetic diagnostics and risk management. However, little is known about the utility of WGS in healthy populations, the prospective penetrance of disease variants, clinical utility of such test, and whether such data improves long term health outcomes. Primary healthcare physicians will be at the forefront of this change and we want to understand the barriers and best practices for general practitioners in managing genomic results.

Inclusion/exclusion criteria (list)

Inclusion criteria:

- Any adult individual seen at UCSF or any affiliated institution (ages 18-65+) without diminished capacity to consent.
- Adult not suspected to have a genetic syndrome, like 22q11.2 deletion

syndrome, Down syndrome, Turner syndrome, etc. They should be primarily in general good health. Having common multifactorial conditions like diabetes, obesity, hypertension, etc. will not exclude them.
- Adults consulted at the UCSF primary care and dental clinics will be the initial focus for this pilot study.

Exclusion criteria:
- Subjects who are unable to provide a DNA source or medical health record
- The PI decides that the study is not in the best interest of the participant (non-complaint, too stressful, etc.)
- Children/Minors
- Subjects unable to consent for themselves
- Subjects unable to consent for themselves in an emergency setting
- Subjects with diminished capacity to consent
- Fetuses
- Neonates
- Prisoners

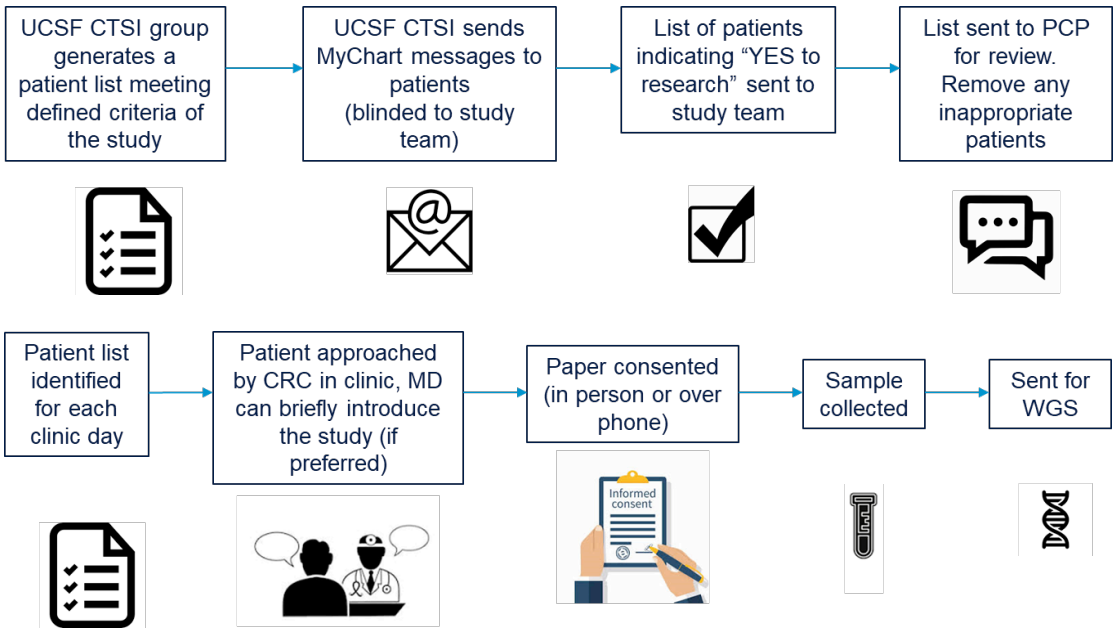
Method of contact/recruitment (be specific)

Our study has relatively broad criteria for patient recruitment and a general practice setting. We will initially focus on the three clinics whose medical directors: Mitchell Feldman, Susan Smith, Micheal Reddy have agreed to participate.

In-clinic recruitment:
Flyers at the clinic will notify patients of the study. The flyers will be posted on the bulletin boards, patient waiting areas, registration desks, bathrooms, hallways, and other patient accessible locations within the clinic space. A recruiter, who will rotate between clinics, will have a booth advertising the study. The booths will be placed at convenient locations within the primary care clinics in cooperation with the staff.

MyChart:
Patients will also be approached through pan-MyChart messages with minimal study information to seek interested participants. Patients from these clinics to participate, as well as physician referral. MyChart messaging and infrastructure will be maintained by the UCSF CTSI group. A list of patients interested in the study will be shared by the CTSI group with the study team, who will review it will the primary care clinician, to omit any patients, who are not appropriate for the study. After confirmation from the physician, the patient will be approached for the study by the coordinator from the study team.

BIOS study participants:
Additionally, participants enrolled in the BIOS study (17-22669) study who opted for participating in future genomic studies at UCSF. We will therefore recruit patients within those clinics/mediums as part of this pilot. Since all patients within these clinics are adults, they are eligible for the study, except individuals meeting the exclusion criteria.



Benefits/burden for participants (clearly identify potential for harm):

Benefits of the study: All patients will get WGS and results back. Each participant will get ancestry and ACMG 59 gene findings back. The physical risks from blood drawing or obtaining saliva are very small. There is usually a short-lived pain with a needle stick for a blood draw and there may be bruises at the place of the needle stick. There is also a very small chance of infection, excess bleeding or fainting (feeling lightheaded) from blood drawing. The risk involved will not be any different from that experienced during any clinical blood test. The amount of blood taken will not be enough to cause anemia. Saliva sample collection and buccal swab collection are non-invasive and don't pose any significant risks. Emotional and psychological risks are also possible. Some people are concerned that research about genetic causes of illness may give information that is not only about themselves, but also about their relatives and other groups of people who are like them. We will not provide information about the health of participants to other family members or other people, apart from the participant providing the signed consent. Issues of adoption and paternity (biological fatherhood) may be discovered from this study. We will not discuss such information with study subjects unless it has direct medical implications for them or their families, which is unlikely.

Any benefits or burden to DGIM practitioners?

Benefits include:

- Increase awareness and education among general practitioners on Genetics
- Inform the larger community on how to educate general practitioners and manage patients with genetic test results from whole genome sequencing
- Participate in the care of patients with centralized genomic and phenotypic information
- Participate in other UCSF grants or research projects facilitated by this project

Burden:

- Identifying candidates to recruit for this project will include the DGIM physicians to aid in vetting the patients and interacting with the study team

members.

- We expect only 3-5 % of cases or 30-50 individuals out of the 1000 to have a finding in the ACMG gene list. All those cases will be managed by Genetics for result disclosure and follow up determination. But the DGIM physician might get involved in the care as he/she will be the primary contact for the patient.

Timeline for recruitment (projected start and stop dates)

March 2020 – July 2021

Funding source

UCSF strategic Funds (School of Medicine)

Potential for DGIM collaborators? (We encourage DGIM resident and fellow involvement in particular)

Currently we have interacted with Elad Ziv, MD and Mitchel Fieldman

Do you agree to notify us when recruitment is completed? Yes

Date form completed: 02/04/2020

Link to learn more about ACMG 59:

https://www.ncbi.nlm.nih.gov/clinvar/docs/acmg/

Overall Study Design: