

PROTOCOL TITLE:Development of a research infrastructure for understanding and addressing multiple myeloma disparities

**Development of a Research Infrastructure for Understanding and Addressing
Multiple Myeloma Disparities**

**[NCT Not Yet Assigned]
December 2, 2019**

1) Protocol Title

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Protocol Version Date: 12/02/2019

2) Objectives

- To develop sample selection, study materials, and protocols to recruit and survey ethnic/racial minority patients with multiple myeloma.
- To evaluate the feasibility of using cancer registry data to identify and recruit a cohort of ethnic/racial minority patients diagnosed with multiple myeloma in California.
- To evaluate the feasibility of surveying ethnic/racial minority patients with multiple myeloma to ascertain etiological and survival-related factors.
- To better understand multiple myeloma etiology, survival, and to develop race-appropriate multiple myeloma models

3) Background

Multiple myeloma (MM) is a malignancy of the plasma cells that accounts for nearly 13,000 deaths in the U.S. each year, representing 2.1% of all cancer deaths and 20% of all hematological malignancy deaths. Despite recent advances in treatment, such as the availability of immunomodulators and proteasome inhibitors, only about half of MM patients survive at least five years after diagnosis. MM is also associated with important disparities, with African Americans (AA) having 2- to 3-fold higher incidence and mortality rates than non-Hispanic Whites. The reasons for this disparity are unclear and indicate an important unmet need that should be addressed through AA-specific studies.

To better understand MM etiology, survival, and to develop race-appropriate MM models, the Precision MEDicine, EqUity and Disparities Research in MultipLe MyeLoma (MEDULLA) Consortium was established. MEDULLA is based out of the five University of California (UC) Comprehensive Cancer Centers (Davis, Los Angeles, San Francisco, San Diego and San Francisco) and includes experts in cancer outcomes, disparities, and genetic etiological research. The long-term goal of MEDULLA is to identify and address the causes of MM disparities.

The objectives of the proposed study are to develop and evaluate protocols for ethnic/racial minority-specific research using cancer registry data. In conjunction with the Cancer Registry of Greater California (CRGC), we have developed procedures to identify, recruit, and survey ethnic/racial minority patients with MM. To pilot the study, we aim initially to test the feasibility of this protocol by contacting 400 eligible patients (100 AAs, 100 Latinos, 100 Asian American/Native Hawaiian/Pacific Islander-AANHPI and 100 non-Hispanic Whites as a comparison group) to conduct a pilot survey through which we will ascertain etiological and survival-related factors for MM. Ultimately, we hope the findings from this pilot

PROTOCOL TITLE:Development of a research infrastructure for understanding and addressing multiple myeloma disparities

will yield insight into the best practices for recruiting minorities with MM and serve as the basis for larger population-based studies of MM etiology and survival.

4) Inclusion and Exclusion Criteria

Eligible patients will include AAs, Latinos and AANHPIs who were diagnosed with a first primary, pathologically confirmed MM within the previous five years and who were at least 21 years of age at the time of diagnosis. We will also include, as a comparison group, non-Hispanic White patients. Patients must have been diagnosed in one of the 48 counties of California. Patients must be alive at the time of study and able to provide informed consent. We will not include those who are unable to consent, pregnant women, or prisoners.

Initially, we will randomly select 100 eligible patients from each race/ethnicity mentioned above to participate in the pilot study. Once the pilot is completed, we will aim to contact all eligible patients reported to the CRGC until 2024.

5) Study Timelines

This study will take place over five years (Dec. 2019 through Nov. 2024), and all analysis will be completed by the end of the study.

Each participant will only be involved in the study for the time it takes to complete the survey and provide a biospecimen sample.

6) Study Endpoints

The study endpoint is the analysis of the information collected through the survey due to the funder by Nov. 2024.

7) Procedures Involved

This pilot study is being funded by the National Cancer Institute as an administrative supplement to the UC Davis Cancer Center Support Grant. Drs. Luis Carvajal-Carmona and Rosemary Cress will co-lead this project. Dr. Carvajal-Carmona is the lead of the MEDULLA Consortium. He is the Associate Director for Basic Science and the co-leader of the Population Sciences and Health Disparities Program at the UC Davis Comprehensive Cancer Center. Dr. Cress is an Adjunct Professor in the Department of Public Health Sciences at UC Davis as well as a Research Program Director with CRGC at the Public Health Institute (PHI). The CRGC is a grantee of the California Department of Public Health (CDPH) to collect cancer data for residents in its catchment area and is part of the California Cancer Registry. Dr. Cress will oversee all work by CRGC staff.

Drs. Carvajal-Carmona and Cress have coordinated with MEDULLA investigators and CRGC research staff to develop a questionnaire for racial/ethnic minorities with MM. The survey (draft attached) focuses on demographics, risk factors, cancer

PROTOCOL TITLE:Development of a research infrastructure for understanding and addressing multiple myeloma disparities

treatment, quality of life, and social determinants of health. All survey items are adapted from previously tested and validated surveys. The survey is expected to take approximately 30-45 minutes to complete. Final materials will be submitted to IRB before human subject contact is initiated.

CRGC staff, under Dr. Cress supervision, will identify eligible participants using the criteria described above based on diagnostic information in the CRGC database. We will be following CCR policies and procedures for release of data. CRGC staff will extract patients contact information from the registry and will provide this information to research staff at UC Davis, who will work under Dr. Carvajal-Carmona's supervision.

The UC Davis Research team will initially mail each eligible participants a postcard and a survey study packet that will include: 1) Simple instruction sheet 2) An introductory letter that details the study 3) Information sheet that details on informed consent 4) Survey instruction sheet 5) A paper copy of the survey 5) Incentive selection sheet and option to continue to the second part of study 6) Brochures about the cancer registry and the UC Davis Comprehensive Cancer Center, and return pre-paid envelope. The following steps will be taken to follow up on the study packet mailing:

- 1) If no response is received within two weeks of the mailing, research staff will follow up with non-respondent participants by telephone.
 - a. If participant has received the post card and study packet, the research team will answer any additional questions they may have and ask to see if they will be participating in survey or remove them from the participant list.
 - b. If participants has not received postcard and wishes to continue with the research study, a new study packet will be mailed. Correct Address will be confirmed.
 - c. If participant is wanting to opt out, ask to see if they have received the packet, ask to see if they would like to take the survey over the phone. If not we will then remove them from the participant list.
 - i. The study team will conduct the survey via telephone interview using the phone survey request script. In order to conduct survey over the phone, the research team will need to verify identity of participants and acquire their verbal consent before they can ask survey questions over the phone. Research team will also need to contact participant if their survey has been sent back incomplete.

Once the first study packet is returned and completed, and the participant selected to continue participating in the second part of the study, a second study packet for biospecimen collection will be sent. The bio-specimen study packet will include 1) informed consent sheet 2) simple instruction sheet 3) saliva kit 4) incentive selection sheet and return pre-paid envelope. If the survey packet was returned and the

PROTOCOL TITLE:Development of a research infrastructure for understanding and addressing multiple myeloma disparities

participant selected the opt out option for the bio-specimen study packet, the research team will do a final contact phone call to confirm their selection and answer any additional questions they may have. If they still wish to opt out, we will then remove them from the participant list for the bio-specimen collection.

Justification for Patient Contact: We plan to call patients two times if they fail to respond to the initial mailing. Additional mailings and phone calls are justified to explain the benefits of the study and enhance participation rates. We will also do a check for survey completeness, and will follow up with patient if survey is not fully completed.

For patients who consent to participate in the survey and bio-specimen study, will be asked to consent. On the survey consent, the participant will be explained either verbally over the phone or in a letter attached to the survey that by completing this survey they are consenting to participate. For the saliva sample, a participant will have to sign a consent form that is included for the donation of 2ml of saliva, if the saliva is mailed back without the consent form, we will contact participant to send us back the form, once consent and saliva is received together, then we will use the saliva for the study. The saliva sample, will be used for genetic studies. Saliva samples will be used to isolate genomic DNA and carry out genotyping and sequencing.

A waiver of HIPAA authorization is not required as the data or specimens will be de-identified and are obtained under the statutory authority of the CCR to disseminate data for research purposes, and the distribution occurs in the context of a state-mandated disease registry's operations. The CCR is not a covered entity nor a business associate to any of the facilities and physician offices that report cases of cancer under the state mandate. The terms and conditions of data access and release are established by CDPH.

We will request the IRB permission to provide participants with incentives for survey completion (\$20) and saliva sample donation (\$30).

8) Data and/or Specimen Management and Confidentiality

All data will be collected and maintained within the firewalls of UC Davis. All personnel are trained on maintaining confidentiality of patient data through physical and electronic processes. All research staff who will be working on the project have current Human Subjects training certificates and have signed confidentiality agreements. All CCR policies and procedures for release of data will be followed promptly.

The data will not be released outside the UC Davis firewall. All data will be password protected and stored on a controlled access computer. Only research staff

PROTOCOL TITLE:Development of a research infrastructure for understanding and addressing multiple myeloma disparities

associated with the study will have access to the data. All research records will be password protected and stored on controlled access computers. Any paper copies will be in locked cabinets in locked rooms that are only accessible by study staff. No paper will be left unattended. All study materials will not leave our secure building and will never be left unattended in unsecured locations.

No personal identifiers will be included in the analytic files. After all surveys are completed, data will be electronically stored on a secure computer server. Paper copies will be shredded. No identifying information will be kept on the paper surveys prior to them being destroyed. Unique study ID numbers will be assigned, and the key will be password protected on a secure computer server.

No identifying information will be published. The only identifying information that will be used is the participant's name, address, and phone number to mail the study packet and conduct follow-up phone calls, if necessary. Contact information will be destroyed after research collection is completed and unique study ID numbers have been assigned to all material we will mail to participants to ensure confidentiality.

Once everything is de-identified, we may share data or genetic information with dbGaP, a database of genotypes and phenotypes through the NIH for additional research. Protocols for additional research will be submitted to IRB for approval before use of this data or genetic information.

9) Data and/or Specimen Banking

De-identified surveys and genetic data will be stored under firewall in UC Davis Cancer Center and UC Davis Genome center on password protected servers. De-identified biospecimens and DNA samples will be stored in the Carvajal-Carmona laboratory at the genome center. Data, biospecimens and DNA will be stored indefinitely.

10) Provisions to Monitor the Data to Ensure the Safety of Subjects

NA

11) Withdrawal of Subjects

Should subjects withdraw from the original study, we will remove/destroy all data, biospecimens and samples belonging to them.

12) Risks to Subjects

Risk level is minimal. There is no physical or economic risk. The greatest potential risk is loss of confidentiality, but, as described above, this risk will be minimized due to the policies and procedures UC Davis follows to protect the confidentiality of study participants. Other than for recruitment purposes, all data collected will be de-identified.

An additional minimal risk is potential negative emotional responses to questions about cancer and life experiences, but we have designed our survey to be of minimal psychological risk. Participation in this study is voluntary, and subjects

PROTOCOL TITLE:Development of a research infrastructure for understanding and addressing multiple myeloma disparities

may decline to participate or skip any question they do not wish to answer. Participation in the biospecimen collection of saliva is non-invasive safe procedure, which may make the subject uncomfortable for a couple of seconds as saliva from the mouth is collected into a small test tube.

13) Potential Benefits to Subjects

Cancer survivors may be motivated to participate in an effort to understand potential cause(s) of their cancer. Otherwise, there are no direct benefits to participation.

14) Multi-Site Research

NA

15) Community-Based Participatory Research

NA

16) Sharing of Results with Subjects

NA, results will not be shared with subjects.

17) Prior Approvals

The Carvajal-Carmona lab has BUA approval (#R1713) to store and process the type of biospecimens collected for the study, to carry out omics experiments and cell line/tissue culture work. We will also request approval for the California state IRB to obtain patient information from the Cancer Registry. This study will therefore require IRB approvals from UC Davis and from the state.

18) Provisions to Protect the Privacy Interests of Subjects

As described above, all research staff are trained to protect the confidentiality of cancer data.

19) Compensation for Research-Related Injury

NA

20) Economic Burden to Subjects

NA

21) Drugs or Devices

NA

PROTOCOL TITLE:Development of a research infrastructure for understanding and addressing multiple myeloma disparities

22) [ClinicalTrials.gov](https://clinicaltrials.gov) Registration

NA

Section 1: NIH Funded Studies

If yes to BOTH, the study must be registered on Clinicaltrials.gov.

Yes	
<input checked="checked" type="checkbox"/>	This study is funded by the NIH . (If this study is not funded by NIH, go to Section 2.)
<input type="checkbox"/>	One or more human subjects will be prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

Section 2: Studies subject to FDA jurisdiction

If yes to ANY the study must be registered on Clinicaltrials.gov.

Yes	
<input type="checkbox"/>	This is a prospective clinical study of health outcomes in human subjects that compares an intervention with an FDA-regulated device against a control. This is not a small clinical trial to determine the feasibility of a device, or a clinical trial to test prototype devices where the primary outcome measure relates to feasibility and not to health outcomes.
<input type="checkbox"/>	This is a pediatric postmarket surveillance of a device as required under section 522 of the Federal Food, Drug, and Cosmetic Act.
<input type="checkbox"/>	This is a controlled clinical investigation, other than a phase I clinical investigation, of a drug subject to section 505 of the Federal Food, Drug, and Cosmetic Act or to section 351 of the Public Health Service Act.

To view a flowchart describing applicable clinical trials subject to FDA jurisdiction click [here](#).

Section 3: Publishing the results

If yes to BOTH the study must be registered on Clinicaltrials.gov.

Yes	
<input type="checkbox"/>	This study prospectively assigns people or a group of people to an intervention, with or without concurrent comparison or control groups, to study the cause-and-effect relationship between a health-related intervention <i>and</i> a health outcome.
<input type="checkbox"/>	The PI has access to and control over all the data from the clinical trial and has the right to publish the results of the trial and plans to publish the results in a journal that follows the ICMJE recommendations .

This requirement includes studies of behavioral interventions.

Section 4: Registration on Clinicaltrials.gov is not required

Yes	
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PROTOCOL TITLE:Development of a research infrastructure for understanding and addressing multiple myeloma disparities

x	I have read sections 1-3 above and registration on clinicaltrials.gov is not required for this research.
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23) Criteria for 10 Year Approval

NA, this is a five-year study

If yes to all items below this research may qualify for a 10-year approval period.

Yes	
<input type="checkbox"/>	This research involves no more than minimal risk.
<input type="checkbox"/>	This research does not receive any federal or state government funding or funding from a private funder who requires annual review per contract.
<input type="checkbox"/>	This research is not subject to FDA jurisdiction.
<input type="checkbox"/>	This research does not include prisoners as participants.
<input type="checkbox"/>	This research is not subject to SCRO oversight.
<input type="checkbox"/>	This research is not subject to oversight by the Research Advisory Panel of California (RAP of C).
<input type="checkbox"/>	No personnel involved in the design, conduct, or reporting of this research have a new unreported related financial interest (RFI) in this study.