Informed Consent Form

Title: Genomics and Epigenomics of the Elderly Response to Pneumococcal Vaccines

NCT number: NCT03104075

Document Date: June 18, 2018

Informed Consent Form

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Title of Research Study: **Genomics and Epigenomics of the Elderly Response to Pneumococcal Vaccines**

Expected Duration of Subject's Participation: 6 visits over a 67-day (about 2 month) period with an optional 7th visit for a second vaccination 1 to 2 years later.

Sponsor: The Jackson Laboratory
Funding Agency: National Institute on Aging (NIA)/National Institutes of Health (NIH)

IRB Number: **16-071J-1**

Name of Research Participant: _____

What Is The Purpose Of This Research Study?

The purpose of this research study is to gain a better understanding of how the immune system responds to two different pneumococcal (pneumonia) vaccines that work in different ways. The two vaccines that are used in this study are recommended and routinely given to healthy older adults 65 and older, and children and adults between the ages 2-64 with certain health conditions. In this study, blood samples will be collected before and after one of the two vaccines is given to you. This is to learn more about how the immune cells in the blood change following vaccination. Scientists will use genomic testing of the immune cells in the blood in this research. This means that they will be looking at which genes are turned on and which are turned off in immune cells before and after the vaccine is given. They will also look at how the numbers of different types of immune cells change after vaccination. Since the elderly are at a higher risk of getting pneumonia and of developing complications from the illness than are younger adults, this research may contribute to the development of new or modified vaccines that may work better in older adults than vaccines that are currently available.

This study will increase our understanding of the impact of aging upon genetic makeup of cells (how our cells are functioning and the codes in the cells that are telling them what to do) and how this relates to the function of the immune system in healthy adults ages 60 and older. The major purpose of collecting this information and DNA and/or RNA from you is to discover and/or study genes that may relate to a stronger or weaker response to one of two pneumococcal vaccines that work in different ways in the immune system.

Why Am I Invited To Participate?
You are invited to take part in this study because you are a healthy adult 60 years of age or older and have never received pneumococcal vaccination. Pneumococcal vaccine is recommended for healthy individuals, ages 65 or older, as part of routine preventive medical care. Pneumococcal vaccine is routinely given to younger people with various chronic diseases. If you elect to participate in this study and you are ages 60-64, you will receive pneumococcal vaccination as a healthy adult, at an earlier age than routine preventive medical care.

How Many Other People Do You Think Will Participate?
We estimate that 40 people will enroll in this study, all at UConn Health.

Is Participation Voluntary?
Participation in this study is voluntary. Before making a decision about whether to participate in this research study with a genetic component, please read this consent form carefully and discuss any questions you have with the researcher. You may also want to talk with family members, your primary care physician or a friend before making a decision.

You can choose not to participate. If you choose to participate in the study, you can change your mind later and stop participating. If you decide not to participate or you withdraw from the study after starting participation, your decision will not affect your present or future medical care you receive at UConn Health. There will be no penalty or loss of benefits to which you are otherwise entitled.

How Long Will My Participation In This Study Last?
As part of this study, you will come to the UConn Center on Aging at UConn Health for a total of 6 study visits over a little more than a two-month period (67 days). There is a 7th visit to get the other vaccine if you choose to receive it. This visit will happen 1 to 2 years later. These visits must occur on specific days around the vaccination given to you in this study as shown in this table:

Visit Number	Time Required	When it will be scheduled
Visit 1	1 hour	7 days before vaccination is given
Visit 2	15-30 minutes	Day of Vaccination
Visit 3	15-30 minutes	1 day after vaccination
Visit 4	15-30 minutes	10 days (± 1 day) after vaccination
Visit 5	15-30 minutes	28 days (± 3 days) after vaccination
Visit 6	15-30 minutes	60 days (± 5 days) after vaccination
Visit 7 (OPTIONAL)	30 minutes	1 to 2 years after Visit 2.

Visits 4-7 will be scheduled on the day indicated, but if this day falls on a weekend or if a health or weather issue arises, they may be scheduled within the number of days in the table above.

What Are the Costs To Me For Participating In This Study?
You may have to take time away from work to come to the appointments. There is no cost to you for the vaccine that you will receive or for laboratory tests that will be conducted as part of this study.

What Will I Be Asked to Do?

Participation in this study will involve the following procedures:

***Blood Draw*:** Blood will be drawn from a vein in your arm by a needle stick. The amount of blood drawn at each visit will be about 10 teaspoons (50 mL) at Visits 1, 3, 4, 5 & 6 (see table above for timing of visits), and 2 teaspoons (10 mL) at Visit 2. If you choose to attend optional Visit 7 for a second vaccination, 10 teaspoons of blood will be drawn at that visit.

Risks Associated with a Blood Draw: There may be a minor amount of discomfort due to the phlebotomy (needle stick and blood draw). There is a minor risk of bruising (< 1%), infection at the phlebotomy site (< 1%) or dizziness following the blood draw (<1%).

Safeguards Taken: Blood will be drawn by experienced, trained research staff in a clinic setting on a hospital campus. The area where the needle is to be inserted will be wiped with a disinfectant before and after the needle is inserted. Only sterile needles will be used. The puncture site will be covered with a bandage.

Vaccination with one of two randomly assigned FDA- approved pneumococcal vaccines: One of two FDA- approved pneumococcal vaccines, Prevnar-13 (Pfizer) or Pneumovax-23 (Merck), will be randomly assigned to you (by chance assignment, similar to flipping a coin) for administration in this study. You have an equal chance of being assigned Prevnar 13 or Pneumovax 23. Each vaccine is administered the same way by a shot in the muscle of your upper arm. Once your vaccine assignment has been determined by the study nurse, you will be vaccinated with the assigned vaccine then informed of which vaccine you received. You will be given information sheets about the vaccine that you received and a form that documents the date, the vaccine that you were given and the lot number of the vaccine given to share with your doctor.

Risk from Vaccination with ***Prevnar-13***
In adults aged 50 years and older, the commonly reported side effects to the Prevnar-13 vaccine were pain at the injection site (this happened in more than 50% of people that got the vaccine), tiredness (around 30%), headache or muscle pain (around 20%), joint pain, decreased appetite, redness at the site if the injection, limitation to arm movement (around 10%), and around 5% of people experienced chills or rash.

In adults, immune responses to Prevnar 13 (the number of antibodies in the blood available to respond to pneumonia germs) were lower when given on the same day as one type of flu vaccine. Prevnar-13 does not protect against getting pneumonia that is caused by types of pneumonia germs that are not included in the vaccine. Vaccines against 13 types of pneumonia germs are included in Prevnar-13.

Safeguards taken for Vaccination with ***Prevnar-13****:* The vaccine will be given by a Registered Nurse at one time, by a shot given in the muscle of the upper arm. You will be required to remain on site for 30 minutes after vaccine administration so that you can be monitored for adverse events.

Risk from Vaccination with ***Pneumovax-23***
The most common side effects to vaccination with Pneumovax-23 are: pain, soreness or tenderness where the shot was given (this occurred in around 60% of people that got this vaccine), swelling

or firmness where the shot was given (around 20%), headache (18%), redness where the shot was given (16%), weakness and tiredness (13%), and muscle soreness (12%).

Pneumovax 23 will not prevent disease caused by types of pneumonia germs other than those included in the vaccine. There are vaccines against 23 types of pneumonia germs included in Pneumovax 23.

People that were vaccinated with Pneumovax 23 and the shingles vaccine (Zostavax®) on the same day did not get as much protection from shingles from the vaccine as people who got the vaccines 4 weeks apart.

*Safeguards taken for Vaccination with **Pneumovax 23***:
In addition to safeguards listed under vaccination with Prevnar 13, you will be asked about recent or planned shingles vaccination within 28 days (4 weeks) from date of planned vaccination for this study. To help you to get the best response to all vaccines that you receive, we may wait to give you the pneumonia vaccine until 28 days have passed between getting the shingles vaccine and pneumonia vaccine shots.

*Risks from **OPTIONAL second vaccination** one year after initial vaccine (Visit 7):*

*Risk to participants randomized to **Prevnar 13** in this study who opt to receive **Pneumovax 23** one to two years after initial vaccination.*
At one year between vaccinations, this sequence (Prevnar then Pneumovax) is consistent with routine care recommendations; therefore risk is consistent with that of standard medical care. Information about immune response to the two vaccines given in this order is available only for antibody response to the 12 varieties of pneumonia that the two vaccines have in common, and for these, vaccination with Pneumovax one year later results in similar lab test levels as the first Prevnar 13 vaccination.

Safeguards taken for this sequence of vaccines: Prior to administration of Pneumovax (your 2nd vaccine since you received Prevnar first), your medical and medication history will be reviewed by a qualified member of the study team to confirm that you are eligible to receive vaccination with Pneumovax. The vaccine will be administered by a Registered Nurse as a single dose, by a shot given in the muscle of the upper arm. You will be required to remain on site for 30 minutes after vaccine administration so that you can be monitored for adverse events.

*Risk to participants randomized to **Pneumovax 23** in this study who opt to receive **Prevnar 13** one year after initial vaccination.*
In patients 60-64 years old, antibody response to the 13 types of pneumonia in Prevnar 13 was found to be slightly lower when given a year after Pneumovax 23 than when Prevnar is given as the first vaccination. There is no available information about immune response to all 23 types of pneumonia in Pneumovax 23 when followed by Prevnar 13.

Safeguards taken for this sequence of vaccines: Prior to administration of Prevnar one to two years after the Pneumovax vaccination, your medical and medication history will be reviewed by a qualified member of the study team to confirm that you are eligible to receive vaccination with

Prevnar. The effectiveness of these vaccines will depend on your body's immune response to each vaccine and on the germ community that you are exposed to during everyday life. Both Pneumovax and Prevnar vaccines are recommended, one dose each, for all adults ages 65 and older and anyone 2 through 64 years of age with certain chronic health conditions. The current CDC recommendations for patients who were previously vaccinated with Pneumovax before age 65, are for vaccination with Prevnar, too, with the vaccines given at least one year apart.

Survey Administration: You will be asked about your health habits and medical history.

Risks Associated with Survey Administration: You may feel uncomfortable answering some of the questions. There are no physical risks associated with the survey.

Safeguards Taken: You may always choose not to answer a question that makes you feel uncomfortable.

Risk to Confidentiality: There is a potential risk to confidentiality due to collection of protected health information at research visits and storage of this information in the research record.

Safeguards taken: All study visits will occur in a private room at the UConn Center for Aging at UConn Health in Farmington, CT. Research records will be accessible only to approved study personnel directly involved in conduct of this study.

Research records will be labeled with a participant ID number (PID), an assigned unique identifier that is not derived from your personal identifiers (name, birthday, social security number, etc.).

Any study documents (Informed Consent Form, HIPAA Authorization, Visit 7 Opt-in form, etc) that contain your name or signature will be kept in a separate file apart from the research record and will be stored in a secure location accessible only to authorized members of the study team. A master key that links your name and other identifiers and the PID will be maintained in a separate and secure location by the study staff at the UConn Center on Aging. This key will not be provided to Dr. Banchereau or to other researchers at the Jackson Laboratory at any time. As a study co-investigator, Dr. Banchereau may attend meetings with the study team at which identifiable information is present. He will not record this information.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by NIH National Institute of Allergy and Infectious Diseases (NIAID) which is funding this project. You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of information about elder, spousal abuse, reportable communicable diseases. The investigators on this study will report this information to State officials if it becomes known to them. The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

Risk to Privacy from sharing of recoded samples or genomic data

To promote faster discovery of new or more effective ways to prevent, diagnose or treat disease, scientists share health and genomic (about genes how they work) information (data) in online scientific databases and share samples for use in other studies. Data and samples from this study are coded before they are provided to the Jackson Laboratory for processing and genomic analysis. This means that all information that could identify you has been removed from the sample and the information provided with the samples. Genomic data, although coded, could potentially be used to identify you although this is considered to be unlikely at this time.

Safeguard taken: You will be given the option to agree or not agree to sharing of your recoded (given new code other than your research code) samples for use in other studies. You will be asked whether you agree to sharing of recoded data in a public and/or a controlled access database at the end of the study. Your responses will be included in the study database (whether you agree/do not agree to sharing) so that your wishes may be respected, although your identity will not be included in the data.

What Are the Benefits Of Participating In This Study?

You may benefit from the pneumonia vaccination(s) provided in this study. This research study will take a long time to complete. You will not benefit directly from the information we gather in the study but other people may benefit in the future if this information leads to new or improved vaccines. There is also the possibility that no benefit will come from this study.

Will I Be Compensated For Participating In This Study?

To compensate you for your time, you will receive $50 for each visit attended as a check payable to cash. This check will be issued at Visit 6 for a total of $300. If you choose to attend the optional Visit 7, you will also receive a $50 check payable to cash after this visit. If you withdraw from the study, a check will be issued to you for all visits attended to the date of withdrawal. You must bring identification to pick the check up in person at your study visit or thereafter. If you receive over $600 from participating in research studies over the course of the calendar year that money must be reported to the IRS as income. For checks payable to cash, no replacement checks will

be issued if lost or stolen. You can also choose not to receive any compensation. Please indicate your preferences by initialing below:

Please make the check(s) payable to cash. _____
I prefer not to receive compensation for this study. _____

You will not be charged for the cost of vaccines used in this study.

This research may lead to the development of a commercial product. This product may have economic benefit to UConn Health and/or the Jackson Laboratory for Genomic Medicine (JAX). If such a product is developed, UConn Health and/or JAX do not intend for you to share in the economic benefit.

What Alternative Procedures or Treatments Are Available To Me?

You have the option not to participate in this study. There is no risk to you from choosing not to participate. You may choose to receive pneumonia vaccines through your medical provider as part of your routine medical care. You may choose not to receive pneumonia vaccinations. You may be at greater risk of developing pneumonia infection if you choose this alternative.

How Will My Personal Information Be Protected?

We will protect the confidentiality of your data to the best of our ability, but cannot guarantee 100% protection. The following procedures will be used to protect the confidentiality of your data. Study staff will keep all study records (including any codes to your data) locked in a secure location.

All study information will be placed in separate research record and will not be placed in your medical record. Research records will be labeled with a code and all contents of the research record will be labeled with only that code. A master key that links names and codes will be maintained in a separate and secure location. All electronic files (e.g., database, spreadsheet, etc.) containing identifiable information will be password protected. Any computer hosting such files will also have password protection to prevent access by un-authorized users. Data that will be shared with others will be coded as described above to help protect your identity. Any laptop computers that will be used will be encrypted. Any lab results will be labeled with the PID and will be stored only in your research record.

You should know that the Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health/National Institute on Aging, and UConn Health representatives may inspect records. They may inspect records to ensure that the study is being done correctly.

At the conclusion of this study the researchers intend to publish an article on their findings. Information will be presented in summary format and you will not be identified in any publications or presentations. There still is a slight chance that someone may be able to link the summary information to you because of the unique nature of genetic studies. This may expose you and your family to unwanted publicity. However, we will follow the steps outlined in this form to protect your confidentiality to the best of our ability.

A description of this clinical study will be available on http://www.ClinicalTrials.gov. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

What Will Happen to the Samples and Information I Provide During the Study?

Upon completion of each study visit, the blood sample that you provide will be securely transferred to Jackson Laboratory for processing, storage and analysis. The sample will be labeled with the PID and date, not your name or other direct identifiers. The results of research blood testing will not be provided to you or placed in your medical record. The samples given to Jackson Laboratory will be coded with the PID number, date of collection and the visit number of collection. Genetic information will not be placed in your medical record. The research record will not be available to employers, insurance companies or others that obtain information from your medical record.

Upon completion of the planned study analysis, the sample will be kept in storage until fully utilized. Any remaining sample kept in storage will be given a new unique code (random recode) that will link the recoded study information to the recoded sample. These recoded samples may be shared with other researchers and used in other projects.

Please **initial** your choice below:
I agree to have my recoded samples stored and shared with other researchers and used in other research studies. ____ Yes ____ No

Recoded information (data) that is collected or generated in this study may be shared in online scientific databases by Jackson Laboratory investigators once the study is completed. Recoded genomic data may be shared in public and/or controlled-access scientific databases.

Please **initial** your choice below:
I agree to have my recoded health information and genomic data shared in public scientific databases for use in future studies.
____Yes ____ No

I agree to have my recoded health information and genomic data shared in controlled-access scientific databases. ____Yes ____ No

If you agreed to sharing of your recoded data or samples above, you can change your mind at any time. Please contact Dr. Kuchel at 860-679-6796 to inform him if you wish to withdraw permission for sharing of samples or data. Dr. Kuchel will inform the Jackson Laboratory investigator of the PID of samples or data to be removed from shared datasets or samples, but will not provide your name. The Jackson Laboratory researcher will locate the recoded data or sample and will remove it from sharing. Any samples or data that were shared before you changed your mind may not be retrievable.

What Happens to the Sample if I Withdraw from the Study?

If you choose to withdraw from the study after your sample(s) has been obtained, we will analyze the collected samples for the study. Data collected before your withdrawal from the study will remain in the research database and will be used in study analyses. If you withdraw, you may change your mind about sharing samples as described in the section above.

Will I Find Out the Results Of This Research Study?

You will not be told any of the results of the research, nor will the results of the study be added to your medical record. Results will not be made available to you because they will not have relevance to your individual medical care.

What If This Research On My Samples Reveals Other Information?

In addition to the research we intend to do, it is possible that unexpected and/or unrelated information will be discovered that is not the focus of this study. This information will not be disclosed to you. However, if the study doctor feels that your blood sample shows abnormalities during research testing, he may contact you and advise you to follow-up with your physician to request standard clinical assessments to evaluate your overall health and detect a wide range of disorders. The study doctor will give you a choice to either have him contact your physician on your behalf or to provide you with information to follow-up on your own with your physician.

What If I Decide To Stop Participating In The Study?

You are free to stop taking part in this study at any time.

If you decide to stop taking part in the study, your relationship with your doctors or UConn Health will not be affected. If you decide to withdraw we ask that you let us know by calling at 860-679-6796 or by sending a written notice to Dr. George Kuchel, UConn Center on Aging, UConn Health, 263 Farmington Ave. Farmington, CT 06030.

Can Someone Else Make Me Stop Participating In This Study?

The researcher may prevent you from continuing in this study. This may happen under any of the following circumstances:

- Failure to follow the instructions of the study staff
- The Principal Investigator decides that continuing your participation could be harmful to you.
- You need treatment not allowed in the study
- The study is cancelled.
- Other administrative reasons.
- Unanticipated circumstances.

Injury from Participation

UConn Health does not provide insurance coverage to compensate for injuries incurred during this research. However, compensation may still be available. A claim may be filed against the State of Connecticut seeking compensation. For a description of this process contact a representative of the UConn Health's Institutional Review Board at 860-679-1019 or 860-679-4851 or 860-679-4849.

UConn Health does not offer free care. However, treatment for a research related injury can be obtained at the UCHC for the usual fee.

What if I Have Questions?

The Principal Investigator is willing to answer any questions you have about the research. You are encouraged to ask questions before deciding whether to take part. You are also encouraged to ask questions during your study participation. If you have questions, complaints or concerns about the research, you should call the Principal Investigator, Dr. Kuchel, at 860-679-6796.

If you have questions about your rights as a research subject you may contact a coordinator at the Institution Review Board at 860-679-1019, 860-679-4851, or 860-679-4849.

You may also call a coordinator at the Institutional Review Board if you want to talk to someone who is not a member of the research team in order to pass along any suggestions, complaints, concerns or compliments about your involvement in the research, or to ask general questions or obtain information about participation in clinical research studies.

Please do not call the IRB number for medical related issues or to schedule or cancel an appointment.

Consent To Participation:

By signing this form you acknowledge that you have read, or have had read to you, this informed consent document, have talked with research personnel about this study, have been given the opportunity to ask questions and have them satisfactorily answered, and voluntarily consent to participate in this project as described in this form.

By signing this form the individual obtaining consent is confirming that the above information has been explained to the subject and that a copy of this document, signed and dated by both the person giving consent and the person obtaining consent, along with a copy of the Research Participant Feedback Form, will be provided to the participant.

Role	Printed Name	Signature	Date
Subject			
Person obtaining consent			