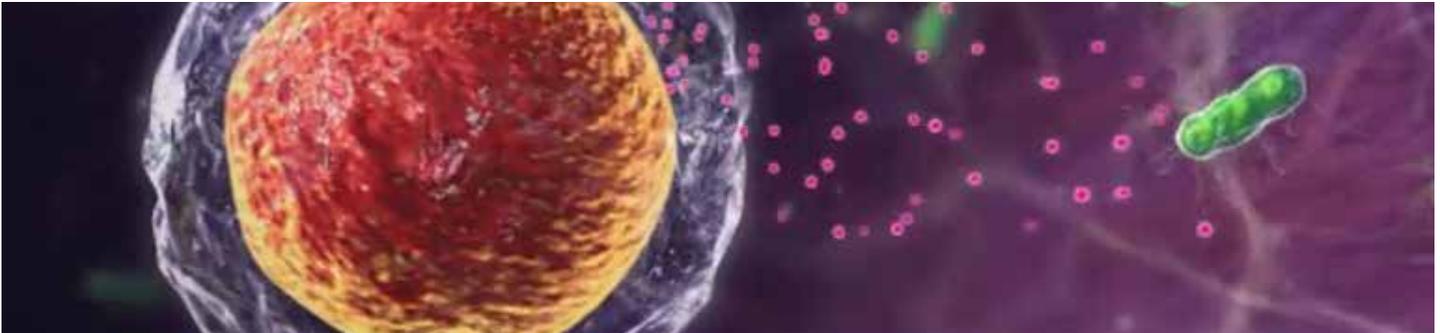


# The Pitt Men's Study



## Wonder Genes?

Diana Campbell and Giovanna Rappocciolo, PhD

There exists a small proportion of HIV-infected individuals who are able to control the progression of the disease for a long time without antiretroviral therapies, individuals collectively referred to as non-progressors (NP). Studying

their responses to the infection can reveal important clues about the development of better therapies or even an effective vaccine.

In our laboratory, we have studied a very specific mechanism by which HIV infects target cells, the CD4 T cells. HIV can infect CD4 T cells directly, as free virus, or alternatively by “*trans* infection”.

To *trans* infect, HIV exploits the ability of some immune cells that capture virus, and then deliver it to the target CD4 T cell. This is made possible by the fact that these specialized immune cells, called antigen presenting cell (APC), are already programmed to interact with the CD4 T cells to fulfill their role

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## Inside the Issue

- **Cover** New research indicates that the cholesterol makeup of certain cells may hinder the spread of HIV in the body; Pitt PhD candidate Diana Campbell and her faculty mentor Dr. Giovanna Rappocciolo reveal what this might mean for future treatment.
- **Page 2** Got a friend in need? Pitt researcher Dr. Mack Friedman conveys the important effect that social support has on lowering your viral load.
- **Page 3** Red, green, blue, green, red...join the conversation about what to do as volunteers get older and show age-related changes to their thinking.
- **Page 3** While the summer is coming to a close, PMS medical director Dr. Ken Ho discusses episodic PrEP and the ways that HIV-negative men might prepare for beach trips in the future.
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# Social Support Linked to Lower Viral Loads

New research indicates that forming close relationships can help HIV+ men to lower their viral loads. In a study published in *AIDS Care*, Dr. Mack Friedman found that HIV+ gay and bisexual men with greater levels of social support exhibited greater viral load suppression and lower average viral loads.

Dr. Friedman—a faculty member of the Pitt Graduate School of Public Health, and former Pitt Men's Study employee—piggy-backed off of a wealth of evidence showing that social support confers health benefits. Other studies have found that social support leads to medication

adherence and HIV viral load suppression among the general HIV population. Before Dr. Friedman's paper, no one had examined the effects of social support among HIV+ gay and bisexual men: the population which accounted for over 60% of new HIV diagnoses throughout the US.

Dr. Friedman used data collected by the MACS, focusing in particular on the question, "is there someone you can talk to about things that are important to you—someone you can count on for understanding or support?" Of the 712 participants whose data the study examined, 63% said they had three or less of these

understanding confidants. Research from this paper and others demonstrates that gay and bisexual men often have lower levels of social support social support, which may affect their ability to fully suppress their viral loads. Lower levels of social support are especially prevalent among those of low income, those who identify as African American and/or Hispanic/Latino, and those age 40 or less. In a time when social isolation in America is increasing, Dr. Friedman concludes his paper by arguing for more concentrated efforts to increase social support in the HIV+ community.



**REPRIEVE**  
Randomized Trial to Prevent Vascular Events in HIV

**Join our Clinical Research Study about heart disease prevention in people with HIV.**

Pitavastatin is a statin that, along with diet, has been approved by the FDA for the treatment of high cholesterol. It also lowers triglyceride levels in the blood. The main purpose of this clinical trial is to see if pitavastatin can prevent heart disease and heart disease related deaths in people with HIV infection who are taking HIV medications.

This study lasts about 6 years (21 visits) and you may be eligible if:

- You have HIV and are between the ages of 40 and 75.
- You have been on antiretroviral therapy (ART) for at least 6 months.
- You have a CD4+ cell count > 100.
- You have no history of cardiovascular disease (history of heart attack or stroke, etc.).
- You are not currently using a statin drug.

*For more information and to see if you may qualify for this exciting study, please contact:*

**Renee Weinman, Recruitment Coordinator**

**412-383-1748**

[weinmandr@upmc.edu](mailto:weinmandr@upmc.edu)



## Age of Cohort Increases Cause for Concern

Whether or not the MACS participants like to admit it, they are getting older. As of the most recent MACS meeting, the median age of active participants was just shy of 57 years old. Thanks to effective antiretroviral therapy, HIV and AIDS-related dementia is mostly a problem of the past. However, now that HIV+ people are living longer, they are sometimes subject to the same cognitive declines other people experience as they age. In relation to all of this, MACS researchers in Chicago have asked whether or not to accept informed consent forms from study participants who show evidence of cognitive decline. Furthermore, MACS researchers are looking for more ways to detect cognitive decline in participants.

Dr. Jim Becker, the principal investigator of the neuropsychological component of the Pitt Men's Study, presented some possible options to the study's community advisory board. Dr. Becker addressed the possibility of adding new questions to interviews, or administering a short new survey to participants. The survey, though, is intended to be taken by an "informant," who knows the participant well and sees them often. Dr. Becker also discussed the possibility of asking all of the men in the study over 70 if there is someone who knows them well and sees them often, and then asking questions to these people that might help to detect cognitive impairments as they arise. Unfortunately, the study by Dr. Mack Friedman summarized on page 2 of this newsletter indicates that many of the men in the MACS might not have someone who knows them well and sees them often.

Fortunately, only 13 men in the entire MACS study have been diagnosed with dementia, 6 of whom are members of the Pitt Men's Study. As always, more information about changes to the study will be available to participants as actions become more concrete. Finally, it is thanks to the continued dedication of the study members that allows for better care of PMS members and their peers as they age.

## Study Finds Vacation Prep Potentially Effective

Dr. Ken Ho, PMS Medical Director

PrEP is a method of HIV prevention that involves the use of antiviral medication by people who are HIV negative and who are at significant risk for getting HIV. Designed to be taken once a day, Truvada is a combination of two HIV medications that was approved by the Food and Drug Administration for use as PrEP. Clinical trials have demonstrated that PrEP is highly effective at protecting HIV but only when the medication is taken consistently. These studies have also established that Truvada is safe when monitored appropriately.

There has been interest in whether PrEP can be used intermittently around high risk periods or "seasons of risk". Advantages of intermittent or episodic PrEP include reduced cost, fewer side effects, and the potential for improved adherence. Almost all of clinical trials of PrEP have studied daily dosing of PrEP but one study, called IPERGAY, did show 86% reduction in HIV infection in gay men who took Truvada versus a sugar pill when given around the time of sex. It is important to emphasize that episodic PrEP is not currently recommended by the Centers for Disease Control. More research is needed before episodic PrEP can be considered a standard of care.

The University of Pittsburgh is currently conducting a study of "vacation PrEP" which will look at the feasibility and acceptability of using PrEP around a period of high risk, such as a vacation. If you are interested in learning more about this study or other HIV prevention studies at the University of Pittsburgh, please call Sherri Karas at (412) 383-1313.

# PMS Welcomes New Employees

Bill Buchanan, PMS Clinic Coordinator

Those of you who know me know that change and I are not on the best of terms. But I'm getting more comfortable with it after the addition of two new clinicians to our staff: Lisa Graham, PA-C, and Daniel Rzewnicki.



Our new Physician Assistant, Lisa Graham, is from Kentucky. This is particularly apparent around the time of the Derby. If you're in clinic that day, you will be treated to big hats and perhaps some scrumptious bourbon balls (which we only indulge in after clinic, I promise – hic!).

Lisa earned her Bachelor of Science in Biology at Kentucky Wesleyan College before attending the University of Kentucky to become a Physician Assistant. She worked at Bluegrass Care Clinic, an HIV clinic at the University of Kentucky, before moving to San Antonio, Texas to work at FFACTS (Family Focused AIDS Clinical Treatment Services). In 2015 she moved to Pittsburgh to be closer to family and worked at UPMC Montefiore Hospital and the Allegheny County Health Department before joining the PMS staff in February.

Being at PMS is a natural fit for Lisa. "Because of my interest in the history of HIV/AIDS I enjoy being part of a study that has contributed so much to the field. I also like being involved in HIV from the research perspective after several years delivering care."

When she's not doing physical exams, drawing blood, sending result letters, and reviewing medical records, Lisa enjoys tending her vegetable and herb garden which ties naturally to other pastimes – cooking healthy foods and grilling. She also loves spending time spoiling her dogs and teaching her husband new tricks.

Dan Rzewnicki, our new med tech, was so excited to work at the Pitt Men's Study that he graduated

from college on Saturday and started work on Monday. "I knew I wanted to work at Pitt more than anywhere else. I love the city. It's close to my hometown, and it's a hub of important research. And this job fits so many of my interests that I didn't want to let such a good opportunity slip away."

A native of Leechburg, PA, he served as editor-in-chief of his school newspaper, the Trottyveck, for which he wrote a blog entitled "What Grinds My Gears." He also played on the varsity football team and served as team captain. (Never mind that the Blue Devils won only four games in as many years.)

Dan did his undergraduate work at Grove City College from which he graduated *cum laude* with a major in English and minors in biology and psychology. He was founder and president of the Grove City chapter of *To Write Love on Her Arms*, "a non-profit movement dedicated to presenting hope and finding help for people struggling with depression, addiction, self-injury, and suicide" ([www.twloha.com](http://www.twloha.com)). He also found time to work as an EMT and at the Grove City Outlet's Brooks Brothers store (so he's a sporty dresser as you'll see at your next appointment).



An avid reader, Dan counts Marilyn Robinson's *Gilead*, John Steinbeck's *East of Eden*, and Walker Percy's *The Last Gentleman* among his favorites, and he spends a lot of time riding his bicycle around his new home town of Pittsburgh, PA.

Dan plans to apply to the Master's Program at Pitt's Graduate School of Public Health with an eye on adolescent and young adult mental health. "I think that there are more and better ways that we can educate young

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# Steroids for T Cells?

Paolo Piazza, PhD

**H**IV is one devious virus. It mutates its antigenic makeup every time the patient's immune system tries to shut it down for good so that new HIV variants can emerge that will eventually escape immune surveillance.

Evading the immune system is not the only outcome of these changes in antigenic makeup: the HIV specific killer T cells (which is what we'll call the immune system from now on, for clarity) become spent and incapable of changing rapidly enough to fight the changing virus. One way to get around this problem is to teach these "old" cells (also called memory T cells) new tricks and make them good killers again; however this approach is proving difficult due to their exhaustion after years of HIV infection.

Another approach, which is being tried here at the University of Pittsburgh in my laboratory led by Dr Charles Rinaldo, requires recruiting a type of killer T cells that have never seen HIV before (we call them "naïve", and yes, they do exist even in people infected with HIV for many years!). In a scientific article that we recently published (\*) we use dendritic cells obtained from the same blood to trigger these HIV-naïve killer T cells into becoming effective soldiers. Under these conditions, the naïve T cells work much better than the old, ineffective killer T cells (the "memory" type) which have been around since the subject was infected but have failed to control HIV. Unfortunately, the naïve killer T cells are rare (literally a few per million) and therefore we need a great many cells to be able to perform these studies (at least one

unit of blood). We think that these in vitro experiments are an important, first step because they show how we can 1) isolate and activate these naïve killer T cells and 2) these naïve killer T cells are much better than their "older" cousins in eliminating HIV.

(\*) Smith, K.N., Mailliard, R.B., **Piazza, P.A.**, Fischer, W., Korber, B.T., Fecsek, R.J., Ratner, D., Gupta, P., Mullins, J.I., Rinaldo, C.R.. Effective Cytotoxic T Lymphocyte Targeting of Persistent HIV-1 during Antiretroviral Therapy Requires Priming of Naïve CD8+ T Cells. 2016. *MBio*, 7(3):473-16, 2016. PMID: 27247230

## HIV Inflammation Linked to CKD

**A** recently published article in *The Journal of Infectious Diseases* indicated that chronic inflammation that is a result of HIV infection may contribute to chronic kidney disease and other conditions. The paper highlighted data from a MACS study that involved 715 men, 188 of whom were from the Pitt Men's Study.

One of the strengths of the study was its direct measurement of glomerular filtration rates (GFR), an assessment of how well the kidneys flush toxins from urine. All of the men in MACS have an estimated GFR calculated from their blood draws at each visit, but this study allowed for a more precise determination of kidney function.

This study compared kidney function and inflammation between HIV+ and HIV- men. While positive and negative men displayed essen-

tially the same median GFR's and serum creatinine levels (a second assessment of kidney function), but more positive men had very low or very high GFR levels. In other words, while the median GFR measurements did not differ between the two groups, kidney function did not necessarily appear to be equal for the two groups. Furthermore, when measuring biomarkers in the blood for inflammation, even HIV+ men with suppressed viral loads had more markers for inflammation than their HIV- counterparts. Finally, the study showed that men with higher inflammatory markers had lower levels of kidney function.

The study starts a very important conversation about future research projects in the HIV field in that it reveals that HIV+ individuals may be troubled by hidden complications. It suggests that the inflammation resulting from HIV infection may cause heretofore unanticipated problems for people as they age. The study also sparks a conversation about the ways that HIV-associated inflammation may affect other chronic conditions such as cardiovascular disease and rheumatoid arthritis. The study confirms the importance of continued research in HIV and in HIV+ individuals as they age. Most importantly, it shows the need to investigate inflammation and other complications that may affect the HIV+ population as they continue to live longer lives.

# Still Relevant After All These Years?

Bill Buchanan, M.M., Clinic Coordinator

From time to time I'm asked if the study is still relevant, does participating in the Pitt Men's Study still matter. The answer is an unqualified, loud, and resounding **YES!**

With your help, the Pitt Men's Study and the entire Multicenter AIDS Cohort Study have made significant, groundbreaking contributions to HIV research. Well over 1,000 scholarly articles, part of the legacy of your participation, are testament to that. As a result our HIV-infected men, in large part, have undetectable viral loads and restored immune systems, and the face of HIV/AIDS has turned from a terminal illness to a chronic but treatable disease.

So haven't we done our job? Isn't the mission fulfilled? The truth is that for every answer research provides a number of new questions arise. Questions like: how does being positive, even if undetectable, affect long term health; what differences might there be in the long term health of HIV+ and HIV- men; how do we keep all of our men as healthy as possible long into their Golden Years? In short, we now need to and are studying aging.

Thirty-two years ago when this study started who would have thought we'd have the luxury of studying aging? Yet here we are, mining our vast repository of samples and data and incorporating it with what we collect and observe in the future in order to answer incredibly important questions about cardiovascular, pulmonary, renal,

and neurological health and more - an increasingly global outlook that still includes, but is not restricted to, HIV. *Your continued participation makes this possible.*

Your continued participation also leads us ever closer to vaccines that could prevent infection, control the virus without taking daily meds, and even cure people of HIV. To do so we use blood and data from *both our positive men AND our negative men* to continue to unlock the secrets of HIV and the immune system. You think we'd have that all figured out by now, but the truth is that our immune system is complex beyond our wildest dreams and HIV is a wily opponent. There are so many things we still need to learn, and those things will lead to progress, not just in HIV, but across a broad spectrum of medical fields.

*Such research benefits both HIV + and HIV- men.* The knowledge that we gain will lead to *longer, healthier lives for all of us, but we need your continued participation to complete this work.*

Some ask, "Why am I so important? One person can't make that much difference, right?" *Well, you are and you do.* Our study is strong because we have a large cohort with a variety of men, not a small, homogeneous sampling. And because each and every one is of us is unique, *who knows who among us may hold a key that unlocks a mystery.*

I get that fatigue, age, illness, distance, traffic and parking in Oakland, and a host of other factors discourage some from participating. If this is you, *call me at 412-624-2008 or 1-800-987-1963. Let's*

*find a way to facilitate your continued or renewed participation.*

Anything worthwhile takes effort, and a boatload of effort has gone into making this study the success that it is, effort on the part of our researchers and staff for sure but more so the effort of *each and every one of you.* We've accomplished great things, but we're not done, not by a long shot.

*Help us continue the hard work that lies ahead. Help us create an even more vast and impactful legacy that will benefit generations to come. I thank each and every one of you for your participation and look forward to working with you 'til we git 'er done.*



## Visit Your Website!

Visit [pittmensstudy.com](http://pittmensstudy.com) to see this newsletter, and others, in the full color version. Also on the website, you will find study news and updates, information for volunteers, study history, and more.

# Funding Continues for MACS MRI Study

Jim Becker, PhD

The Pitt Men's Study received news that National Institutes of Health funding will continue for the MACS-wide MRI study for another five years. This collaborative project among all of the MACS sites is under the leadership of Pitt's Dr. James Becker, who also heads the neuropsychological (NP) component of the PMS. All of the men who are currently participants in the MRI study will be asked to continue their participation for two more MRI scans. We will also enroll

additional men into the study so that across all four of the MACS sites there are a total of 400 men participating. We will enroll men over the age of 50, but are particularly interested in men in their 60s and 70s. Understanding how the conditions associated with aging (such as high blood pressure and diabetes) affect the brain and cognition is important both in men with HIV disease as well as men who are not infected. The research team met in Baltimore in August to finalize the details, and expect to begin contacting participants in September.

## From The Cover

in the activation of the immune system. By using these APC as Trojan horses, HIV has found a way to exploit this interaction to spread with high efficiency. But, as with everything in nature, evolution has its counterpunch. We have discovered that APC from the non-progressors were very inefficient in transmitting HIV as they would normally do. We also discovered that these cells have lower cholesterol levels than expected. But what does cell cholesterol have anything to do with HIV?

Cholesterol is an important part of the cell, particularly the cell membrane. When new HIV particles are assembled inside the cells and are ready to be shipped out to infect other targets, they need to travel through the cell membrane. Cell membrane cholesterol plays a fundamental part in this. Importantly, we used MACS repository blood to find that low APC cholesterol and consequent poor ability to sustain *trans* infection was present in non-progressors *prior* to seroconversion to HIV. These findings strongly suggest that this is an inherited trait, and we are now working to identify which genes may be involved.

This study was possible only because of the availability of frozen specimen that were collected from the PMS volunteers over time. We are also working on understanding the exact mechanisms by which cell cholesterol metabolism is altered in the non-progressor and how this affects the trafficking of HIV in and out of the cell and how cholesterol lowering medication may interfere with the normal ability of APC to transfer virus. We are also studying how the effect of antiretroviral therapies

may be eluded by this cell to cell transmission of HIV. None of these studies will be possible without the help and cooperation of the PMS volunteers and the support of the PMS staff and physicians.

## Contact Us

### The Pitt Men's Study

P.O. Box 7319, Pittsburgh, PA, 15213

(412) 624-2008 (800) 987-1963

<http://pittmensstudy.com/>

Charles R. Rinaldo, PhD  
Principal Investigator

Ken Ho, MD  
Medical Director

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## From Page 4

people about how to care for themselves, mentally and physically. I also think that we continue to give younger and younger people more and more technology, and we haven't fully considered how that might affect their health."

# Stig · ma

A Mark of Disgrace or infamy; a stain or reproach, as on one's reputation



Stigma surrounding HIV affects treatment and prevention of the disease, and erodes the belief that those infected can lead normal lives.

Join the Pitt Men's Study for a commemoration of World AIDS Day, and help provide hope for everyone affected by HIV.

End The Stigma

World AIDS Day 2016

November 30, Heinz Chapel