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RACP Foundation Research Awards

PROGRESS REPORT

Project / Program Title		The role of chemokine signalling in maintenance of the latent HIV resevoir
Name		Dr Matthew Corder Pitman
Award Received		2016 RACP NHMRC CRB Blackburn Scholarship
Report Date		19 December 2016
Chief Investigator / Supervisor		Prof Sharon Lewin
Administering Institution		The University of Melbourne
Funding Period	Start Date:	1 January 2016
	Finish Date:	15 March 2018

PROJECT SUMMARY

Despite the great successes of antiretroviral therapy (ART) for people living with HIV, treatment is lifelong and there is no cure. In individuals on treatment, HIV can hide in multiple places including in a subset of immune cells called Th 17 cells that are found frequently in the gastrointestinal tract. HIV infected individuals on antiretroviral therapy have ongoing inflammation in the gut which is thought to be a consequence of a leaky gut wall. This inflammation impairs the immune response and may potentially allow for HIV to persist at this site.

Vitamin D inhibits Th17 cell formation, strengthens the integrity of the gut wall and reduces inflammation in individuals without HIV infection. Vitamin D may also activate virus production in infected cells which may allow the immune system to recognise and kill these cells. It may thus allow the body to get rid of the hiding virus and contribute to an HIV cure.

We aim to assess the effect of high dose vitamin D on Th17 cells, integrity of the gut wall, diversity of gut bacteria, inflammation and the amount of virus that persists in HIV infected participants on ART. We plan to randomise 30 participants to either high dose vitamin D or placebo for 24 weeks. We will collect blood, urine and rectal swabs at 0, 12, 24 and 36 weeks and analyse each of these effects in the lab. We will also measure calcium levels at each time point to ensure the treatment is safe. Participants and researchers will not know which treatment participants are being administered until after all results have been analysed. If calcium levels in blood or urine are high, the vitamin D or placebo dose will be reduced to every second day.

PROJECT AIMS / OBJECTIVES

Determine the effect of high dose vitamin 0 3 supplementation in HIV infected participants on suppressive antiretroviral therapy on:

- Immune cell frequency, function and activation (including T cell subsets, monocytes, dendritic cells and natural killer cells) using flow cytometry
- Gut barrier integrity and gut microbiome using ELISA and 16S rRNA sequencing respectively
- HIV persistence using PCR and RT-PCR
- Safety using serum and urinary calcium measurements and adverse event reporting

SIGNIFICANCE AND OUTCOMES

Treatment for HIV is lifelong and there is no cure. HI V-infected individuals on ART have an increased risk of complications of chronic inflammation such as malignancy, ischaemic heart disease and nephropathy. As a cheap, safe, widely available and easily administered drug, vitamin D would serve as an optimal adjunct to antiretroviral therapy in an HIV cure regimen if proven efficacious.

If this pilot study shows a trend toward reduction in HIV persistence, I would like to coordinate a larger study powered to determine whether high dose vitamin D3 has efficacy as part of an HIV cure regimen. I am also interested in assisting in the coordination of other translational HIV cure research.

PUBLICATIONS / PRESENTATIONS

I am currently working on a review paper discussing the role of chemokines, Th17 cells and the gut in HIV persistence.