Canterbury Medical Research Foundation

Final report for Grant in Aid GIA2020-1

Grant recipient

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Grant details

GRANT TYPE	Grant in Aid	FUNDING ROUND	2020 Grant In Aid
GRANT REFERENCE	GIA2020-1	GRANT AMOUNT	$4,864

Final report

1. Scientific Assessing Committee report

Our previous research found that long term carriage of toxin-producing strains of the gut bacterium *Bacteroides fragilis* is associated with increased risk of colon cancer in our community. Our research proposal detailed a pilot study involving two cohorts, each with two objectives, to enable us to better understand if young children and/or lambs are susceptible to colonisation with these bacteria and, if so, do they become chronically colonised.

We proposed to establish a cohort of 100 children aged between 1 month and 5 year presenting with acute diarrhoeal illness in the Paediatric department of Christchurch Hospital. Our first objective was to determine the incidence of enterotoxigenic *Bacteroides fragilis* (ETBF) carriage in these children, while the second objective was to ascertain whether these bacteria remain as part of the normal bowel flora at 12 months later.

Recruiting a cohort of paediatric patients through the CDHB proved to be more difficult than anticipated so we took a different approach. We contacted a pre-school in Darfield and, with help from parents (who all provided written consent), we obtained 27 stool samples from children living in a rural environment. Our next objective is to recruit a similar number of age-matched children from a Christchurch day-care centre. We will then determine whether carriage of ETBF is similar (or not) across the rural versus the urban cohort. We also intend to ask parents of children who test positive for a second stool sample to determine if these bacteria are still present 12 months later.

Our second objective was to determine carriage rates of ETBF in Coopworth and Romney study flocks maintained by Lincoln University. In 2019 we collected stool samples from 67 Coopworth ewes and their lambs (n=81). Nine months later we collected a second stool sample from the remaining lambs (n=52). We also collected stool samples from Romney ewes and lambs (n=142). These two flocks are kept in adjacent paddocks on the farm.

To date DNA from has been extracted from Coopworth sheep samples and analysed for molecular evidence of ETBF. We find that 43 of the 67 ewes (64%) and 55 of the 81 lambs (68%) are colonised with these bacteria. Moreover, 31 of the 51 lambs (61%) sampled nine months later also show evidence of colonisation. Analysis of the 2019 Romney samples is underway and, to date, findings are similar to those found in the Coopworth sheep.

We subsequently sampled the Coopworth ewes and their lambs in 2020 and will collect follow up samples on these lambs this month. We also propose to repeat this process again this year (2021-2022). Collectively, we anticipate the data we gather from analyses of these samples will give us a better understanding of whether transmission is maternal or environmental. To investigate this further we process to isolate strains of these bacteria from a number of ewes and their lambs with the aim of determining how closely the bacterial isolates are related at a genetic level.

A PhD student (Scott Loeffler) started work on this project in July 2020. Scott has a background in epidemiology and his thesis is centred on the hypothesis that our studies in sheep may provide increased understanding of within- and between-species transmission of a bacterium that we find

associated with increased risk of colorectal cancer.

The Grant In Aid from the CMRF was used for the purchase of commercial kits for the extraction of DNA from these 400 samples.

4. Feedback

5. Media and public statement

Our previous research found that long term carriage of toxin-producing strains of the gut bacterium *Bacteroides fragilis* is associated with increased risk of colon cancer in our community. This finding raises two important questions. Are infected individuals colonised at an early age? If so, this would increase the potential of these toxin-producing bacteria to “drive” pre-cancerous changes over time. Secondly, where do these bacteria come from?

A Grant In Aid from the Canterbury Medical Research Foundation is enabling us to begin addressing these questions. In the first instance we are collecting stool samples from young children to look for molecular evidence of these bacteria. We are also collecting samples from ewes and their lambs. Our finding of toxin-producing strains of *B. fragilis* in these animals highlights the potential of sheep as a model to better understand how these bacteria are transmitted, and whether early life colonisation becomes persistent. Going forward we will also explore the idea that colonised farm animals might be a potential source of infection for humans.

Publication

Date

28/07/2021