



THE IMPACT OF HIGH PROTEIN-HIGH RED MEAT VS HIGH CARBOHYDRATE WEIGHT LOSS DIETS ON GENOME STABILITY AND BIOMARKERS OF COLORECTAL CANCER RISK IN OVERWEIGHT MEN.

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ABSTRACT

It has been suggested that high protein diets are associated with an increased risk of colorectal cancer due to the higher content of red meat. However, the study of the overall dietary and lifestyle pattern may prove more important than any individual component when assessing colorectal cancer risk. From this, it is proposed that a dietary pattern used for weight loss that is higher in protein but remains low in fat and high in foods rich in fibre and micronutrients that are required for genome stability may not increase the risk of colorectal cancer, thus providing a safe and effective dietary method of weight loss in overweight subjects.

This thesis describes the development of a novel *in vitro* faecal water genotoxicity test using the cytokinesis-block micronucleus (CBMN) cytome assay in the WIL2-NS cell line. This thesis then investigates faecal water genotoxicity and peripheral blood lymphocyte genome stability in overweight men following a weight loss dietary pattern either high in protein, specifically red meat, or high in carbohydrate.

Results from this thesis indicate that the genotoxic potential of faecal water can be successfully assessed *in vitro* using the CBMN cytome assay. A high protein-high red meat weight loss diet did not increase faecal water genotoxicity or peripheral blood lymphocyte DNA damage, measured with the CBMN cytome assay, differently to a high carbohydrate weight loss diet. Faecal water genotoxicity data suggests weight loss and/or caloric restriction following either a high protein or high carbohydrate diet may beneficially modify the carcinogenic load of the colon in the short term, however this needs to be validated in a study that includes a non-weight loss control group. A lack of relationship was seen between faecal water genotoxicity and genome damage in lymphocytes which may suggest that the assessment of both the genome damage potential of the bowel contents and the assessment of the genome stability profile of peripheral blood lymphocytes may be important in comprehensively assessing the impact on genome damage by different dietary patterns.

ABBREVIATIONS

BN	binucleate
CBMN	cytokinesis-block micronucleus
Cyto B	cytochalasin B
DMSO	dimethyl sulphoxide
FBS	foetal bovine serum
HBSS	hanks balanced salt solution
HC	high carbohydrate
HP	high protein
MN	micronucleus
MNi	micronuclei
NDI	nuclear division index
NDCI	nuclear division cytotoxicity index
NPB	nucleoplasmic bridge
NBud	nuclear bud
PHA	phytohaemagglutinin
RDA	recommended dietary intake
SCFA	short chain fatty acid

DECLARATION

This thesis contains no material which has been accepted for the award of any other degree or diploma in any University or other tertiary institution, and to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

I give consent to this copy of my thesis, when deposited in the University library, being available for loan and photocopying.

.....

Bianca J Benassi

.....

Date

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PRESENTATIONS

2007: European Nutrition Conference

Poster presentation: High protein-high red meat and high carbohydrate weight loss diets do not differ in their effect on faecal water genotoxicity.

Poster presentation: High protein-high red meat and high carbohydrate weight loss diets do not differ in their effect on lymphocyte DNA damage using the cytokinesis-block micronucleus cytome assay.

Australian Society for Medical Research SA Scientific Meeting

Ross Wishart Memorial Session, Oral Presentation: Impact of a high protein-high red meat vs high carbohydrate diet on biomarkers of colorectal cancer risk

2006: International Congress on Obesity

Poster presentation: Short term effect of a high protein-high red meat diet vs. a high carbohydrate diet on biomarkers of colorectal cancer risk

International conference on Nutrigenomics and Gut Health

Oral presentation: Inter- and intra-individual variation in DNA damage potential of faecal water assessed in the WIL2-NS cell line

2005: Nutrition Society of Australia national conference

Poster presentation: Benassi B, Clifton P, Fenech M (2005) Inter- and intra-individual variation in DNA damage potential of faecal water assessed in the WIL2-NS cell line, Asia Pac J Clin Nutr, 14 (suppl):S95