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.

BIANCA BENASSI
B Med Pharm Biotech (honours)

A thesis submitted to the University of Adelaide for the degree of Doctor of Philosophy

University of Adelaide, School of Molecular and Biomedical Sciences, Discipline of Physiology
AND
CSIRO Human Nutrition, Adelaide

March, 2008
1. INTRODUCTION

1.1 HIGH PROTEIN DIETS 1
1.2 COLORECTAL CANCER 3
1.3 COLORECTAL CANCER AND THE INFLUENCE OF DIET 4
  1.3.1 FIBRE 5
  1.3.2 FAT 6
  1.3.3 RED MEAT 6
  Heterocyclic amines 7
  Polycyclic aromatic hydrocarbons 7
  N-nitroso compounds 8
  Haeme iron 8
1.3.4 MICRONUTRIENTS 8
1.4 COLORECTAL CANCER RISK FACTORS AND THE INFLUENCE OF HIGH PROTEIN DIETS 9
  1.4.1 TOTAL CALORIES 9
  1.4.2 PHYSICAL INACTIVITY AND OBESITY 10
  1.4.3 INSULIN RESISTANCE 10
1.5 TOTAL DIETARY PATTERNS AND COLORECTAL CANCER RISK 11

2. AIMS AND HYPOTHESES 13

AIMS 13
HYPOTHESES 14
3. GENERAL METHOD: THE CYTOKINESIS BLOCK MICRONUCLEUS CYTOME ASSAY

3.1 INTRODUCTION 15
3.2 THE DISCOVERY OF MICRONUCLEI 15
3.3 THE EVOLUTION OF THE CBMN ASSAY INTO A ‘CYTOME’ ASSAY 17
3.4 APPLICATIONS OF THE CBMN CYTOME ASSAY 19
  3.4.1 THE CBMN CYTOME ASSAY AS A BIOMARKER OF CANCER RISK 19
  3.4.2 THE CBMN CYTOME ASSAY AS A BIOMARKER OF OPTIMAL NUTRITIONAL STATUS 20
  3.4.3 THE CBMN CYTOME ASSAY AS A BIOMARKER OF EXPOSURE TO GENOTOXIC AGENTS 21
  3.4.4 THE GENOME HEALTH CLINIC CONCEPT 22
3.5 THE CBMN CYTOME ASSAY PROTOCOL AND DETAILED SCORING CRITERIA 23
  3.5.1 DATA OBTAINED FOR EACH SLIDE 23
  3.5.2 CRITERIA FOR SELECTING BINUCLEATED CELLS WHICH CAN BE SCORED FOR THE FREQUENCY OF MICRONUCLEI, NUCLEOPLASMIC BRIDGES AND NUCLEAR BUDDING 24
  3.5.3 CRITERIA FOR SCORING MICRONUCLEI 24
  3.5.4 CRITERIA FOR SCORING NUCLEOPLASMIC BRIDGES 25
  3.5.5 CRITERIA FOR SCORING NUCLEAR BUDS 25
  3.5.6 CRITERIA FOR SCORING APOPTOTIC CELLS 26
  3.5.7 CRITERIA FOR SCORING NECROTIC CELLS 26
  3.5.8 CALCULATING NUCLEAR DIVISION CYTOTOXICITY INDEX 27

4. STUDY OVERVIEW 29

4.1 SUBJECTS 29
4.2 DIETARY PROTOCOL AND INTERVENTION 30
4.3 CONSORT STATEMENT 32
4.4 WEIGHT LOSS 33
4.5 METHODS FOR SAMPLE COLLECTION AND STORAGE 35
  4.5.1 BLOOD COLLECTION 35
  Isolation and storage of lymphocytes 35
  4.5.2 FAECAL COLLECTION AND STORAGE 36
  Isolation and storage of faecal water 36

5. DNA DAMAGE POTENTIAL OF HUMAN FAECAL WATER MEASURED USING THE CYTOKINESIS-BLOCK MICRONUCLEUS CYTOME ASSAY AND THE WIL2-NS CELL LINE 38

AIM 38
HYPOTHESES 38
5.1 INTRODUCTION 39
5.2 METHODS 42
  5.2.1 SUBJECTS AND FAECAL COLLECTIONS 42
  5.2.2 ISOLATION OF FAECAL WATER 42
  5.2.3 CELL CULTURE AND CYTOKINESIS-BLOCK MICRONUCLEUS CYTOME ASSAY 42
  5.2.4 STATISTICAL ANALYSIS 44
5.3 RESULTS 45
5.4 DISCUSSION 50
6. THE EFFECT OF HIGH PROTEIN-HIGH RED MEAT VS HIGH CARBOHYDRATE WEIGHT LOSS DIETS ON BIOMARKERS OF BOWEL HEALTH 54

AIM 54
HYPOTHESES 54
6.1 INTRODUCTION 55
6.2 METHODS 59
6.2.1 CYTOKINESIS BLOCK MICRONUCLEUS CYTOME ASSAY PROTOCOL FOR FAECAL WATER GENOTOXICITY AND CYTOTOXICITY TESTING IN THE WIL2-NS CELL LINE 59
6.2.2 DETERMINATION OF FAECAL MOISTURE 60
6.2.3 SHORT CHAIN FATTY ACIDS AND FAECAL PH 60
6.2.4 PHENOL AND P-CRESOL MEASUREMENT 60
6.2.5 MICRONUCLEUS ASSAY IN PIG AND HUMAN COLORECTAL BIOPSY TISSUE 61
Collection and storage of pig colonic cell biopsy tissue 61
Collection and storage of human mid-rectal cell biopsy tissue 61
Isolation and slide preparation of biopsy tissue 62
6.2.6 STATISTICAL ANALYSIS 63
6.3 RESULTS 64
6.3.1 SHORT TERM INTENSIVE WEIGHT LOSS PHASE 64
Faecal water genotoxicity and cytotoxicity 64
Conventional bowel health biomarkers 64
6.3.2 LONG TERM WEIGHT MAINTENANCE PHASE 69
Faecal water genotoxicity and cytotoxicity 69
Conventional bowel health biomarkers 70
6.3.3 CORRELATIONS 75
Week 0 75
Week 12 75
Week 52 76
6.3.4 MICRONUCLEUS ASSAY IN PIG AND HUMAN COLORECTAL BIOPSY TISSUE 77
Criteria for selecting colonocyte cells which can be scored for the frequency of micronuclei 77
Criteria for scoring micronuclei in colonocytes 77
6.4 DISCUSSION 79

7. THE EFFECT OF HIGH PROTEIN-HIGH RED MEAT VS HIGH CARBOHYDRATE WEIGHT LOSS DIETS ON GENOME STABILITY IN LYMPHOCYTES 84

AIM 84
HYPOTHESES 84
7.1 INTRODUCTION 85
7.2 METHODS 88
7.2.1 CYTOKINESIS BLOCK MICRONUCLEUS CYTOME ASSAY 72 HOUR PROTOCOL FOR ISOLATED LYMPHOCYTES STORED IN LIQUID NITROGEN 88
7.2.2 QUANTIFICATION OF FOLATE IN PLASMA 90
7.2.3 QUANTIFICATION OF VITAMIN B12 IN PLASMA 91
7.2.4 QUANTIFICATION OF TOTAL L-HOMOCYSTEINE IN PLASMA 91
7.2.5 STATISTICAL ANALYSIS 92
7.3 RESULTS 93
7.3.1 SHORT TERM INTENSIVE WEIGHT LOSS PHASE 93
Genome damage biomarkers 93
Cytotoxicity biomarkers 93
Plasma folate, vitamin B12 and homocysteine 93
7.3.2 LONG TERM WEIGHT MAINTENANCE PHASE 97
Genome damage biomarkers 97
Cytotoxicity biomarkers 97
# LIST OF FIGURES

FIGURE 1.1 PREVALENCE OF OVERWEIGHT AND OBESITY BY BMI IN AUSTRALIAN MEN AND WOMEN AGED 25-64 YEARS FROM 1980 TO 1999/2000  
FIGURE 1.2 MOST FREQUENTLY OCCURRING CANCERS IN BOTH MEN AND WOMEN IN AUSTRALIA IN 2000  
FIGURE 1.3 AGE-SPECIFIC INCIDENCE AND MORTALITY RATE OF COLORECTAL CANCER IN MEN AND WOMEN IN AUSTRALIA IN 2000  

| FIGURE 3.1. DETECTION OF CHROMOSOME DAMAGE USING THE MICRONUCLEUS ASSAY. | 16 |
| FIGURE 3.2. THE POSSIBLE FATES OF CYTOKINESIS-BLOCKED CELLS FOLLOWING EXPOSURE TO A CYTOTOXIC/GENOTOXIC AGENT | 18 |
| FIGURE 3.3 COMPARISON OF THE DOSE-RESPONSE EFFECT OF ACUTE X-RAY EXPOSURE AND FOLIC ACID DEFICIENCY ON MN INDUCTION IN CBMN CYTOME ASSAY CULTURED LYMPHOCYTES | 21 |
| FIGURE 3.4. DIAGRAMMATIC EXAMPLES OF THE VARIOUS TYPES OF CELLS FOUND IN THE CBMN CYTOME ASSAY | 24 |
| FIGURE 3.5. DIAGRAMMATIC EXAMPLES OF GENOME DAMAGE EVENTS SCORED IN BINUCLEATE CELLS | 26 |
| FIGURE 3.6. PHOTOGRAPH EXAMPLES OF THE VARIOUS CELLS FOUND IN THE CBMN CYTOME ASSAY | 27 |
| FIGURE 3.7. PHOTOGRAPH EXAMPLES OF GENOME DAMAGE EVENTS SCORED IN THE CBMN CYTOME ASSAY | 28 |

| FIGURE 4.1. CONSORT DATA | 32 |
| FIGURE 4.2 EFFECT OF 12 WEEKS FOLLOWING A HIGH PROTEIN-HIGH RED MEAT OR A HIGH CARBOHYDRATE DIETARY PATTERN ON BODY WEIGHT | 33 |
| FIGURE 4.3 EFFECT OF 12 AND 52 WEEKS FOLLOWING A HIGH PROTEIN-HIGH RED MEAT OR A HIGH CARBOHYDRATE DIETARY PATTERN ON BODY WEIGHT | 34 |

| FIGURE 5.1. SCHEMATIC PROTOCOL OF FAECAL WATER CBMN CYTOME ASSAY EXPERIMENT | 44 |
| FIGURE 5.2. DOSE RESPONSE EFFECT OF FAECAL WATER CONCENTRATION ON NDCI AND NECROSIS ASSESSED IN THE WIL2-NS CELL LINE | 45 |
| FIGURE 5.3. DOSE RESPONSE OF FAECAL WATER ON CBMN CYTOME ASSAY GENOME DAMAGE BIOMARKERS (MN, NPB, NBUDS) ASSESSED IN THE WIL2-NS CELL LINE | 46 |

| FIGURE 6.1 SCHEMATIC PROTOCOL OF FAECAL WATER CBMN CYTOME ASSAY | 59 |
| FIGURE 6.2 INDUCED DNA DAMAGE BY FAECAL WATER ASSESSED USING THE CBMN CYTOME ASSAY WITH 12 WEEKS INTENSIVE WEIGHT LOSS ON A HIGH PROTEIN-HIGH RED MEAT OR HIGH CARBOHYDRATE DIET | 65 |
| FIGURE 6.3 INDUCED CYTOTOXICITY BY FAECAL WATER ASSESSED USING THE CBMN CYTOME ASSAY WITH 12 WEEKS INTENSIVE WEIGHT LOSS ON A HIGH PROTEIN-HIGH RED MEAT OR HIGH CARBOHYDRATE DIET | 66 |
| FIGURE 6.4 FAECAL PH, WEIGHT AND MOISTURE WITH 12 WEEKS INTENSIVE WEIGHT LOSS ON A HIGH PROTEIN-HIGH RED MEAT OR HIGH CARBOHYDRATE DIET | 67 |
| FIGURE 6.5 FAECAL SCFA, PHENOL AND P-CRESOL WITH 12 WEEKS INTENSIVE WEIGHT LOSS ON A HIGH PROTEIN-HIGH RED MEAT OR HIGH CARBOHYDRATE DIET | 68 |
| FIGURE 6.6 INDUCED DNA DAMAGE BY FAECAL WATER USING THE CBMN CYTOME ASSAY WITH 12 WEEKS INTENSIVE WEIGHT LOSS AND 9 MONTHS WEIGHT MAINTENANCE ON A HIGH PROTEIN-HIGH RED MEAT OR HIGH CARBOHYDRATE DIET | 71 |
| FIGURE 6.7 INDUCED CYTOTOXICITY BY FAECAL WATER USING THE CBMN CYTOME ASSAY WITH 12 WEEKS INTENSIVE WEIGHT LOSS AND 9 MONTHS WEIGHT MAINTENANCE ON A HIGH PROTEIN-HIGH RED MEAT OR HIGH CARBOHYDRATE DIET | 72 |
| FIGURE 6.8 FAECAL PH, WEIGHT AND MOISTURE WITH 12 WEEKS INTENSIVE WEIGHT LOSS AND 9 MONTHS WEIGHT MAINTENANCE ON A HIGH PROTEIN-HIGH RED MEAT OR HIGH CARBOHYDRATE DIET | 73 |
| TABLE 3.1 | PROTOCOLS USED FOR CBMN CYTOME ASSAY IN PERIPHERAL BLOOD LYMPHOCYTES AND PRIMARY CELL CULTURES | 23 |
| TABLE 4.1 | SUBJECT CHARACTERISTICS AT BASELINE | 29 |
| TABLE 4.2 | COMPOSITION OF STUDY DIETS | 30 |
| TABLE 4.3 | WEIGHT LOSS AFTER 12 WEEKS FOLLOWING A HIGH PROTEIN-HIGH RED MEAT OR A HIGH CARBOHYDRATE DIETARY PATTERN | 33 |
| TABLE 4.4 | WEIGHT LOSS AFTER 12 AND 52 WEEKS FOLLOWING A HIGH PROTEIN-HIGH RED MEAT OR A HIGH CARBOHYDRATE DIETARY PATTERN | 34 |
| TABLE 5.1 | CBMN CYTOME ASSAY DNA DAMAGE AND CYTOTOXICITY MARKERS FOR 1% FAECAL WATER IN THE WIL2-NS CELL LINE FOR SIX DIFFERENT INDIVIDUALS. | 47 |
| TABLE 5.2 | CBMN CYTOME ASSAY DNA DAMAGE AND CYTOTOXICITY MARKERS FOR 1% FAECAL WATER IN THE WIL2-NS CELL LINE FOR ONE INDIVIDUAL (SIX TIMES). | 48 |
| TABLE 5.3 | INTER- AND INTRA-INDIVIDUAL COEFFICIENT OF VARIATION (CV) OF CBMN CYTOME ASSAY DNA DAMAGE AND CYTOTOXICITY MARKERS FOR 1% FAECAL WATER IN THE WIL2-NS CELL LINE. | 49 |
| TABLE 5.4 | INTER- AND INTRA-INDIVIDUAL ‘FOLD INCREASE TO CV RATIO’ FOR CBMN CYTOME ASSAY DNA DAMAGE AND CYTOTOXICITY MARKERS FOR 1% FAECAL WATER IN THE WIL2-NS CELL LINE. | 49 |
| TABLE 6.1 | CBMN CYTOME DNA DAMAGE BIOMARKERS INDUCED* BY FAECAL WATER WITH 12 WEEKS INTENSIVE WEIGHT LOSS ON A HIGH PROTEIN-HIGH RED MEAT OR HIGH CARBOHYDRATE DIET. | 65 |
| TABLE 6.2 | CBMN CYTOME CYTOTOXICITY BIOMARKERS INDUCED* BY FAECAL WATER WITH 12 WEEKS INTENSIVE WEIGHT LOSS ON A HIGH PROTEIN-HIGH RED MEAT OR HIGH CARBOHYDRATE DIET. | 66 |
| TABLE 6.3 | CHANGE IN FAECAL PH, WEIGHT AND MOISTURE WITH 12 WEEKS INTENSIVE WEIGHT LOSS ON A HIGH PROTEIN-HIGH RED MEAT OR HIGH CARBOHYDRATE DIET. | 67 |
| TABLE 6.4 | EXCRETION RATE OF FAECAL SCFA, PHENOL AND P-CRESOL WITH 12 WEEKS INTENSIVE WEIGHT LOSS ON A HIGH PROTEIN-HIGH RED MEAT OR HIGH CARBOHYDRATE DIET. | 68 |
| TABLE 6.5 | CBMN CYTOME DNA DAMAGE BIOMARKERS INDUCED* BY FAECAL WATER USING THE CBMN CYTOME ASSAY WITH 12 WEEKS INTENSIVE WEIGHT LOSS AND 9 MONTHS WEIGHT MAINTENANCE ON A HIGH PROTEIN-HIGH RED MEAT OR HIGH CARBOHYDRATE DIET. | 71 |
| TABLE 6.6 | CBMN CYTOME CYTOTOXICITY BIOMARKERS INDUCED* BY OF FAECAL WATER USING THE CBMN CYTOME ASSAY WITH 12 WEEKS INTENSIVE WEIGHT LOSS AND 9 MONTHS WEIGHT MAINTENANCE ON A HIGH PROTEIN-HIGH RED MEAT OR HIGH CARBOHYDRATE DIET. | 72 |
| TABLE 6.7 | CHANGE IN FAECAL PH, WEIGHT AND MOISTURE WITH 12 WEEKS INTENSIVE WEIGHT LOSS AND 9 MONTHS WEIGHT MAINTENANCE ON A HIGH PROTEIN-HIGH RED MEAT OR HIGH CARBOHYDRATE DIET. | 73 |
| TABLE 7.1 | FREQUENCY OF CBMN CYTOME ASSAY GENOME DAMAGE BIOMARKERS IN PERIPHERAL BLOOD LYMPHOCYTES WITH 12 WEEKS INTENSIVE WEIGHT LOSS ON A HIGH PROTEIN-HIGH RED MEAT OR HIGH CARBOHYDRATE DIET. | 94 |
| TABLE 7.2 | FREQUENCY OF CBMN CYTOME ASSAY CYTOTOXICITY BIOMARKERS IN PERIPHERAL BLOOD LYMPHOCYTES WITH 12 WEEKS INTENSIVE WEIGHT LOSS ON A HIGH PROTEIN-HIGH RED MEAT OR HIGH CARBOHYDRATE DIET. | 95 |
| TABLE 7.3 | MEAN PLASMA MICRONUTRIENTS AND HOMOCYSTEINE AFTER 12 WEEKS INTENSIVE WEIGHT LOSS ON A HIGH PROTEIN-HIGH RED MEAT OR HIGH CARBOHYDRATE DIET. | 96 |
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.
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<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>BN</td>
<td>binucleate</td>
</tr>
<tr>
<td>CBMN</td>
<td>cytokinesis-block micronucleus</td>
</tr>
<tr>
<td>Cyto B</td>
<td>cytochalasin B</td>
</tr>
<tr>
<td>DMSO</td>
<td>dimethyl sulphoxide</td>
</tr>
<tr>
<td>FBS</td>
<td>foetal bovine serum</td>
</tr>
<tr>
<td>HBSS</td>
<td>hanks balanced salt solution</td>
</tr>
<tr>
<td>HC</td>
<td>high carbohydrate</td>
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<tr>
<td>HP</td>
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<td>MN</td>
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<tr>
<td>MNi</td>
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<td>NDI</td>
<td>nuclear division index</td>
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<td>nucleoplasmic bridge</td>
</tr>
<tr>
<td>NBud</td>
<td>nuclear bud</td>
</tr>
<tr>
<td>PHA</td>
<td>phytohaemagglutinin</td>
</tr>
<tr>
<td>RDA</td>
<td>recommended dietary intake</td>
</tr>
<tr>
<td>SCFA</td>
<td>short chain fatty acid</td>
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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
First and foremost I would like to thank Dr Michael Fenech for the opportunity to complete my PhD with his laboratory and for being such a fantastic supervisor, I am truly grateful for all your support, encouragement and advice. I would also like to thank my co-supervisors Prof Peter Clifton and A/Prof Pat Buckley for their support.

Thank you to all the members of the Genome Health and Nutrigenomics laboratory staff, especially Carolyn Salisbury for answering my endless number of questions!

Thank you also to my family and friends for all your support and love. A big thank you also to the ‘work girls’, Sasja Beetstra, Denise Furness, Jane Bowen and Maryam Hor for your support, discussions, laughter and of course, fabulous morning tea sessions!

A special thank you to Matthew Evans, (I'm sure the last few years were just a tough on you!), thank you for you support, patience, encouragement and love.

I am very grateful to the University of Adelaide and CSIRO Human Nutrition for their monetary support for my studies and travel to the 2007 European Nutrition Conference in Paris and the Nutrigenomics and Gut Health Conference in New Zealand.
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