INVESTIGATION OF MILK PROTEIN BIOACTIVITY

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INTRODUCTION

- Program for genomic and proteomic approach to milk bioactives
- Evaluation of milk-derived proteins in tissue specific experimental models – regeneration and repair
OBJECTIVES

- To establish a quantitative cellular bioassay for “wound” repair

- To compare and establish mouse models for analysis of milk protein/peptide bioactive effects on gastrointestinal tract (GIT) growth and repair

Human umbilical vein endothelial cell (HUVEC)
In vitro Tissue Remodeling

- Milk proteins screened for bioactivity using HUVEC cultures

- Effect on cell survival (Apoptosis Protection Index)

- Cell migration – “wound” repair
BSA abundant whey protein = good model bioactive
BSA protects endothelial cells

- BSA effect ≥ to HSA
Restriction of molecular movement ablates BSA activity
In *vitro* wound repair

- Developed modified cell based repair assay

  - flat metallic wire = uniform & clear edges
  - Simulated wound for different time points (BCS, Media alone, BSA, HSA)
  - Measured by image analysis
- Albumin marked effect on cell migration and wound repair
- BSA equivalent to HSA
Compared GIT development in 4 mouse strains - QSi5, FVB, C57 and CBA

- Used weaned C57 mice
- 4 groups x 9-weeks:
  - no-treatment, AA, BSA, WP; n=8
- Measured:
  - Body weight
  - GIT length
  - Morphometric analysis of GIT
Increased body weight gain in WP and BSA treated mice
Increased GIT length in BSA and WP treated group
Increased villi length and crypt depth in BSA and WP treated groups
Induced colitis

Model for inflammatory disease of human gastrointestinal tract (IBD)

- C57 mice
- Induction with 5% dextran sodium sulfate (DSS) for 5 days
- 5 groups: (Normal, No treatment-control, Antibiotic treatment-control, BSA, WP); n=10 + 10 days treatment
  - Measured: body weight, intestinal length
  - Analysed colon histology
  - Disease activity index (DAI)
Improved recovery with BSA > WP treated mice
Recovery of colon length BSA > WP treated mice
Disease activity index (DAI) (body weight; hemoccult; stool consistency; inflammation)

BSA and WP reduced DAI = sig therapeutic effect ≤ to Abs
Developed *in vitro* and *in vivo* systems to assess protein bioactivity

Demonstrated that BSA has a positive effect on tissue repair similar or greater than whey protein effect

Potential adjunct treatment in IBD

**Future direction**

- GIT gene expression analysis in progress
- Broaden application to milk bioactive peptides
• Peter Williamson- Supervisor
• Rosanne Taylor
• Hans Zoellner-Oral Pathology

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