



www.csiro.au

Future Grains for Consumer Foods with Extra Health Benefits

Food Futures National Research Flagship

David Topping

National Research
FLAGSHIPS



The Aim

- **The production of new, cereal-based foods with substantiated health benefits to lower the risk and improve the management of diet-related conditions at the population level.**

The Means

**Through the application of advanced technologies,
the generation of fibre-enriched cereals:**

- **New high amylose cereal cultivars**
 - **BARLEYmax™ - high non-starch polysaccharides (NSP), high resistant starch (RS), low glycaemic response (GR) (first products launched) joint venture with ACVL.**
 - **High amylose wheat (animal studies progressing), joint venture with GRDC and Groupe Limagrain.**
 - **Low GI rice**
- **High fibre grains**
 - **Barley and wheat with improved NSP (with Universities of Adelaide, Melbourne and Queensland)**
- **Fructo-oligosaccharides (FOS)**
 - **New cereal sources**

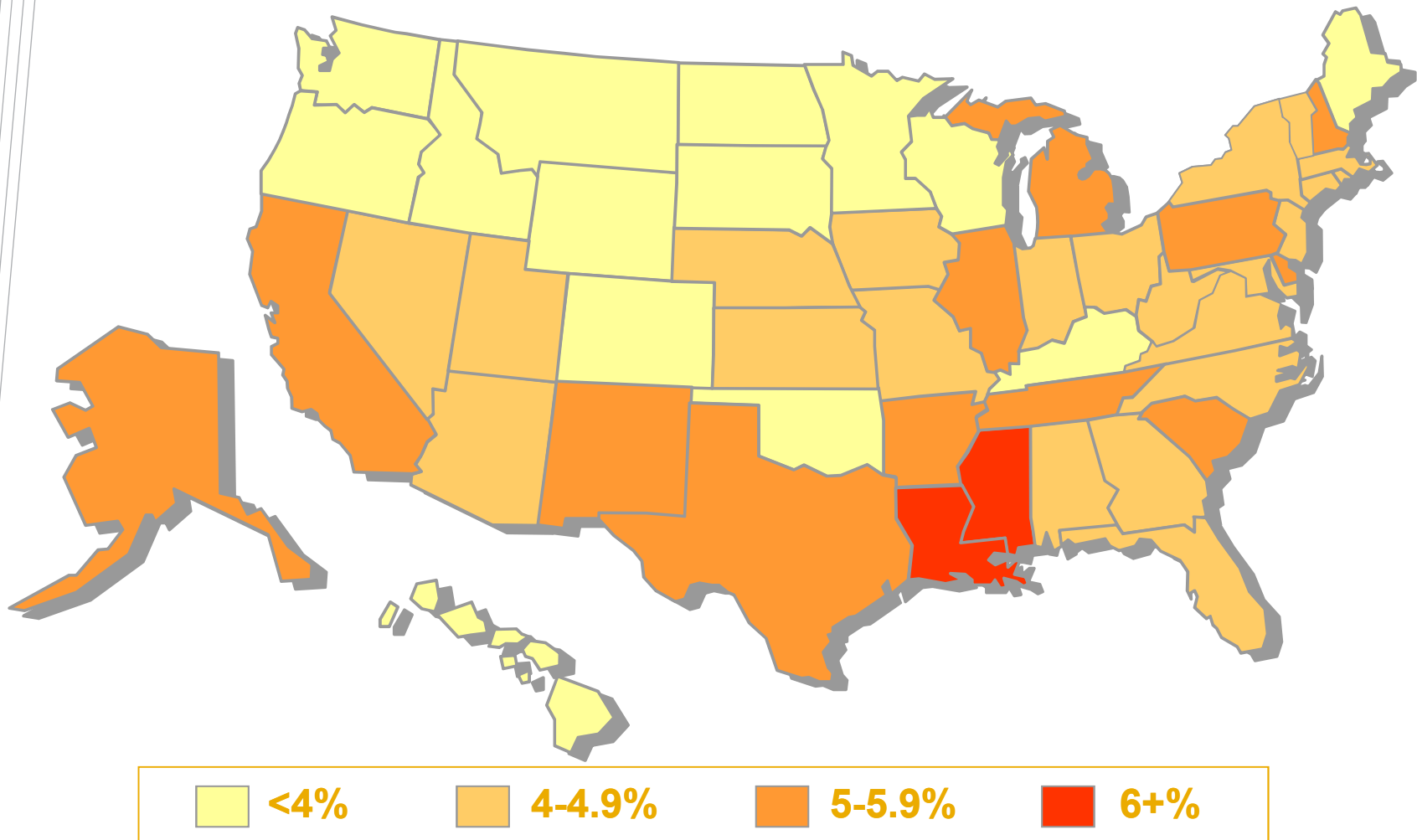
The Basis for Approach

1. **Valid estimates of the (high) costs of preventable diet-related diseases**
2. **Large population studies showing differences in disease rates relating to diet/lifestyle and the appearance of these problems in developing countries in real time.**
3. **A scientific rationale for the actions of dietary fibre, especially for regularity (and for increasing consumption).**
4. **Clear demonstration of the persistently high colo-rectal cancer rates in Australia despite greater population-wide fibre intake.**
4. **The realisation that intakes of a newly-recognised form of fibre (resistant starch, RS) intakes are high in low risk populations.**
5. **Application of new CSIRO measurement technology showing that RS levels in Australian consumer foods are low – suggesting causation and the potential for population-wide prevention.**
6. **The strengths of CSIRO Human Nutrition and Plant Industry and external linkages through the High Fibre Grains Cluster.**

Preventable Socio-economic Impacts

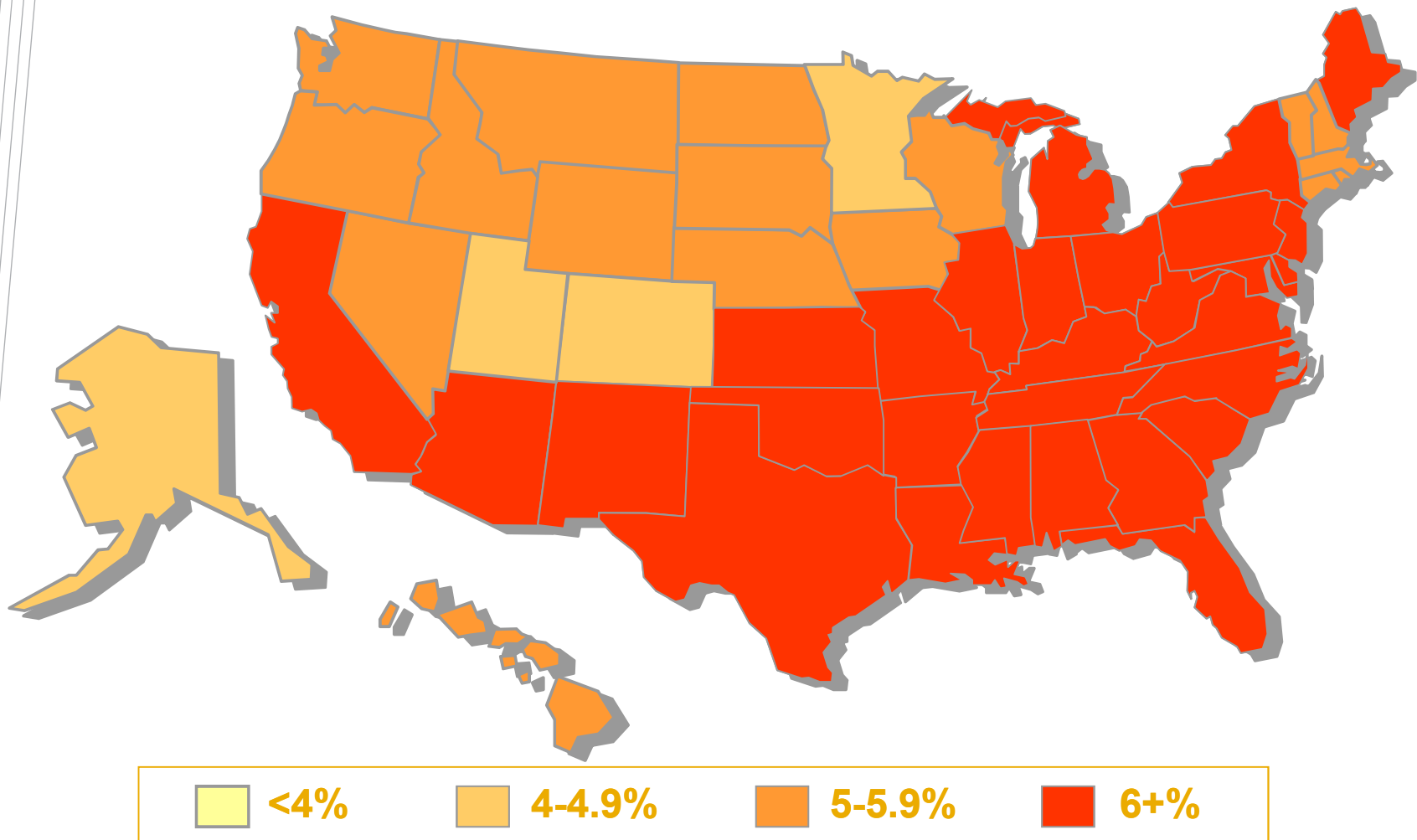
- **Colo-rectal cancer is a major cause of death and disability (4400 deaths, >12,000 new cases annually)**
- **Irritable bowel syndrome (IBS) (Non-fatal but >20% of adult population affected, costs >\$200,000,000 pa)**
- **Inflammatory bowel diseases (high prevalence, risk factor for colo-rectal cancer)**
- **Infectious diarrhoea - remains prevalent (5,000,000 cases annually in Australia, >3,000,000 infant deaths per annum, world-wide)**
- **Diabetes - Affects >8% of Australians and is increasing rapidly in Westernised and emerging countries (especially in South Asia)**

Diabetes by State: United States 1994



Centers for Disease Control and Prevention 2004

Diabetes by State: United States 2004



Centers for Disease Control and Prevention 2004

So - Why Fibre?

- **Based largely on observations (not dietary records), Dennis Burkitt and colleagues noted the very low risk of diet-related diseases for African natives consuming unrefined diets.**
- **These native populations ate diets high in unrefined grains which were thought to be high in fibre.**
- **Stool bulking was high and constipation was so very rare in these groups as to cause comment, consistent with high dietary fibre intakes.**
- **“Fibre” became identified as the protective factor.**
- **Fibre has proved to be very effective for regularity**

Human Small Intestinal Carbohydrate Digestion

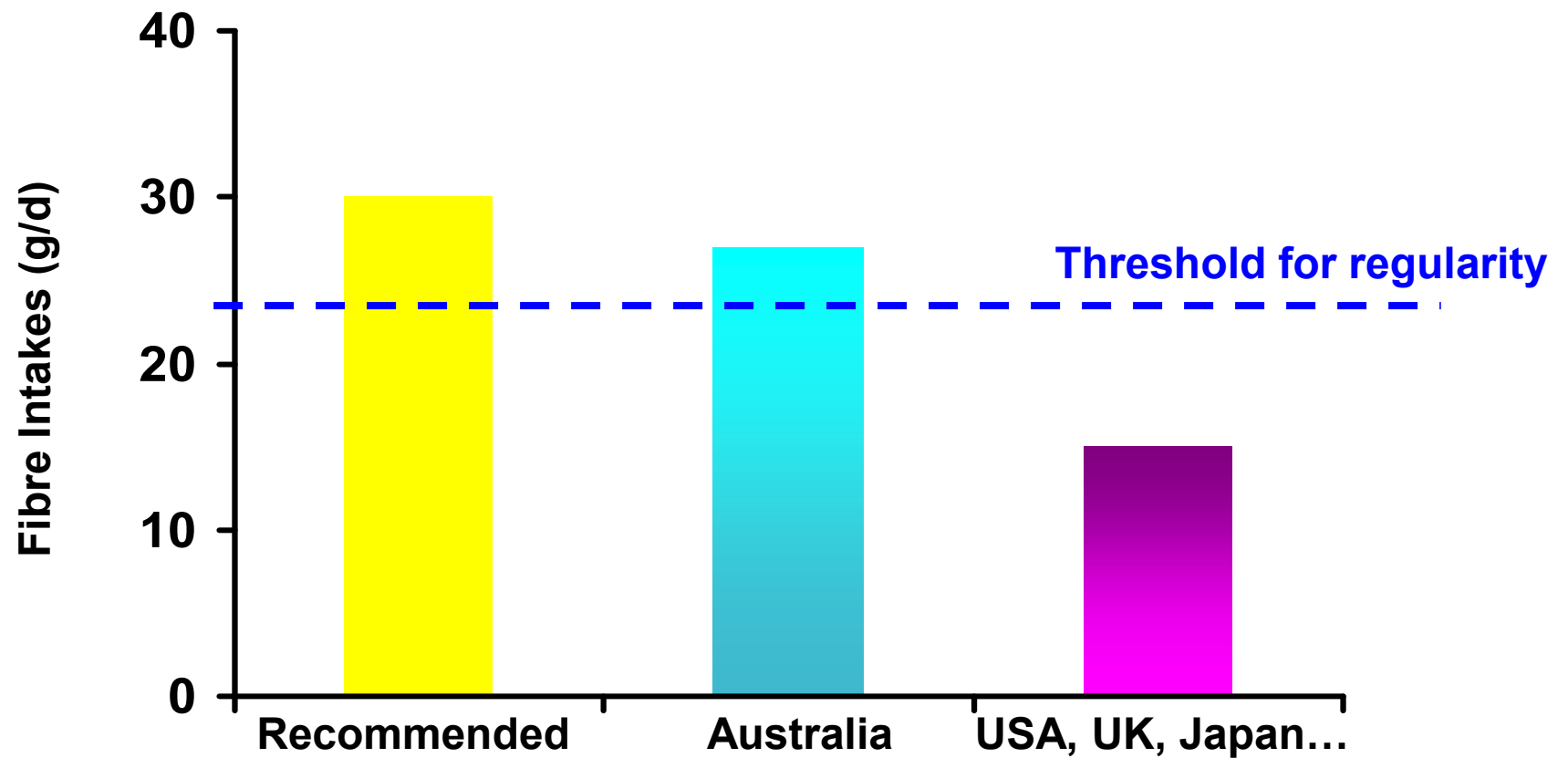
- **Only one human enzyme (α -amylase) can digest polysaccharides and it works on only one carbohydrate – starch.**
- **All other (non-starch) polysaccharides (NSP) are indigestible in the small intestine.**
- **NSP are the main components of dietary fibre – that is why fibre promotes regularity.**
- **Some oligosaccharides (eg fructo-oligosaccharides, FOS) are also indigestible.**

Dietary Fibre and Improved Regularity in Older People

	Fibre	Aperients	Bowel Actions	Average time to stop aperient use
	(g/d)	(no/d)	(no/d)	(wk)
Baseline	13.9	1.3	0.9	
End	25.4	0	1.4	5.4

Source: Baghurst et al (1984)

Population Fibre Intakes



The Size of the Challenge -Fibre

The recommended intake of dietary fibre is 30g/person/day.
US - average ~15g/person/day (typical of a wide number of countries).

If all at-risk US consumers reached the target overnight, consumption would rise to

$250,000,000 \times 15 \times 365 = 1.37$ million tonnes of fibre per year

or

10.3 billion 400 g packets of wheat bran breakfast cereal.

This is a global issue and clearly modifying the entire food supply quickly is impossible – hence selective cereal breeding and altered processing (ie the Universities/CSIRO *High Fibre Grains Cluster*).

Dietary Fibre and NSP in Transgenic Barley

Line	Treatment	TDF	NNSP		
			Soluble	Insoluble	Total
GP	Pearled	13.3	4.5	4.3	8.8
GP	Dehulled	13.5	5.7	3.1	8.8
1	Dehulled	20.4	8.4	4.6	13.0
4	Dehulled	21.1	8.3	4.3	12.6
4	Dehulled	19.0	7.5	6.7	14.2
5	Dehulled	16.7	6.4	2.6	9.0



Tony Bird

The Dietary Fibre Paradox

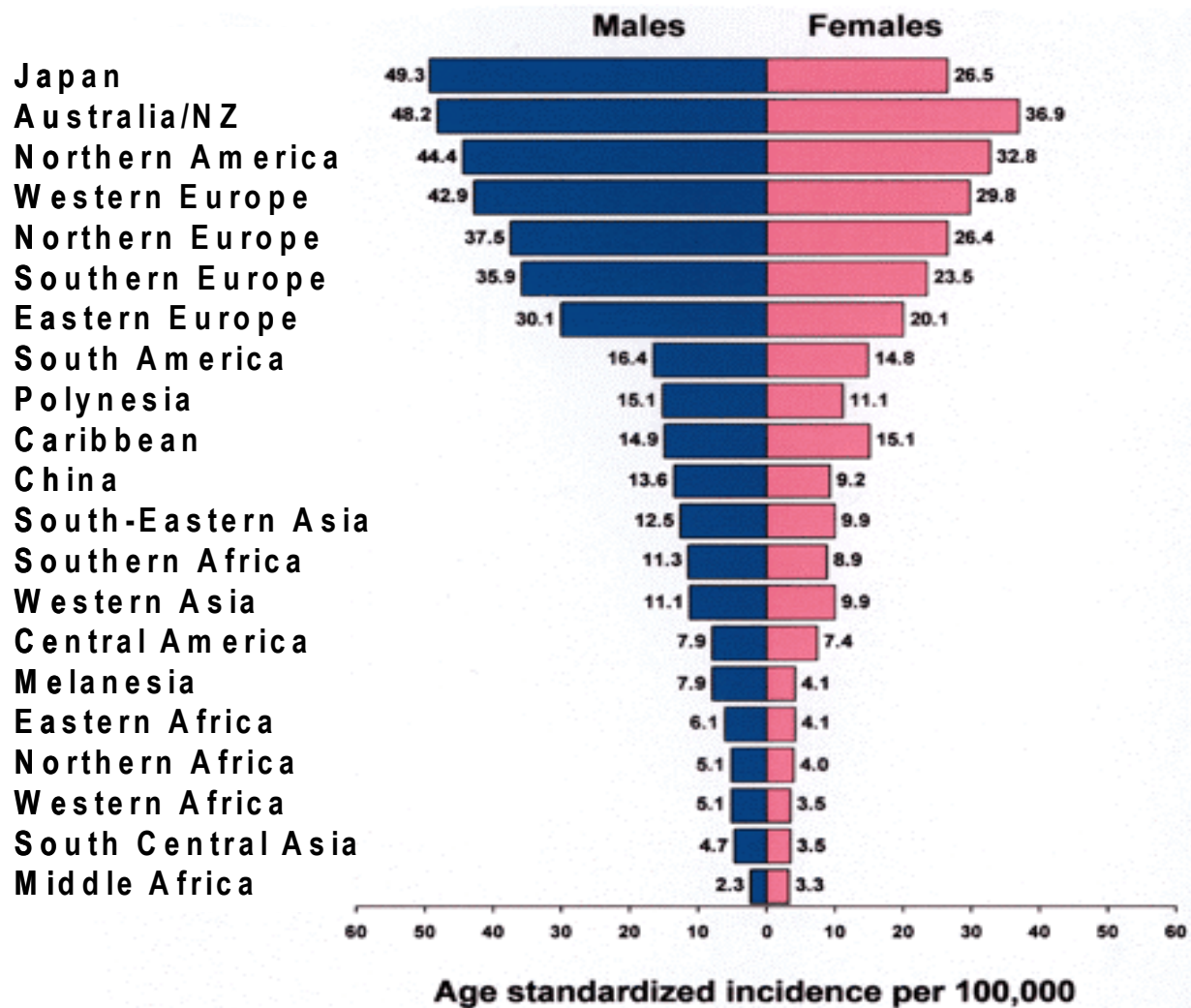
- **Australia – High (largely cereal) fibre intakes (~27 g/person/d), high colo-rectal cancer rates**
- **South African blacks – Low (largely cereal) fibre intakes (~15g/person/d), low colo-rectal cancer rates**
- **The explanation - the African natives' cooking practices for their staple – whole grain maize flour.**
- **It is eaten cold after cooking – this retrogrades the starch ie RS (starch escaping small intestinal digestion).**
- **RS works largely through fermentation by the large bowel microflora, NSP (traditional “fibre”) largely though bulking.**

This is not new....

The higher defecation frequency and the much shorter transit time in black children are not explicable in terms of the levels of fibre intake.

Walker ARP, Walker BF Arch Dis Child (1985) Bowel behaviour in young black and white children. 60: 967-970.

Incidence of colorectal cancer globally



Source: Global cancer statistics 2002

Prevalence of colon cancer in Australia

- Colorectal cancer is the leading cause of cancer deaths and disability
- Large health care cost (>\$2 billion pa, 80% treatment)
- Incidence increasing, death rate steady

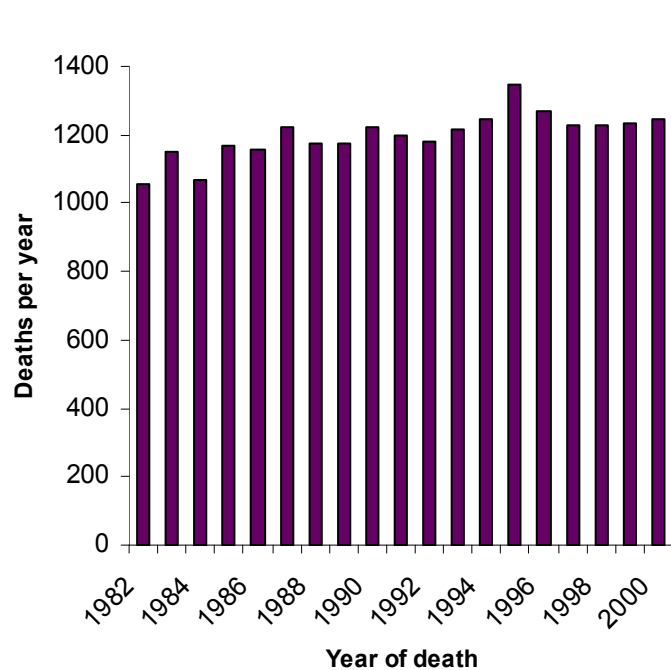


Figure 1(a). Age adjusted colon cancer deaths per year in Victoria.

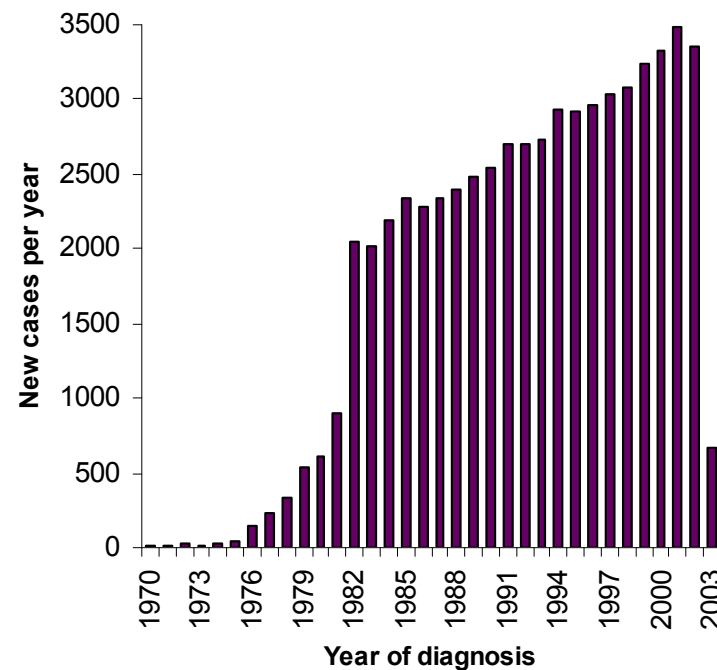
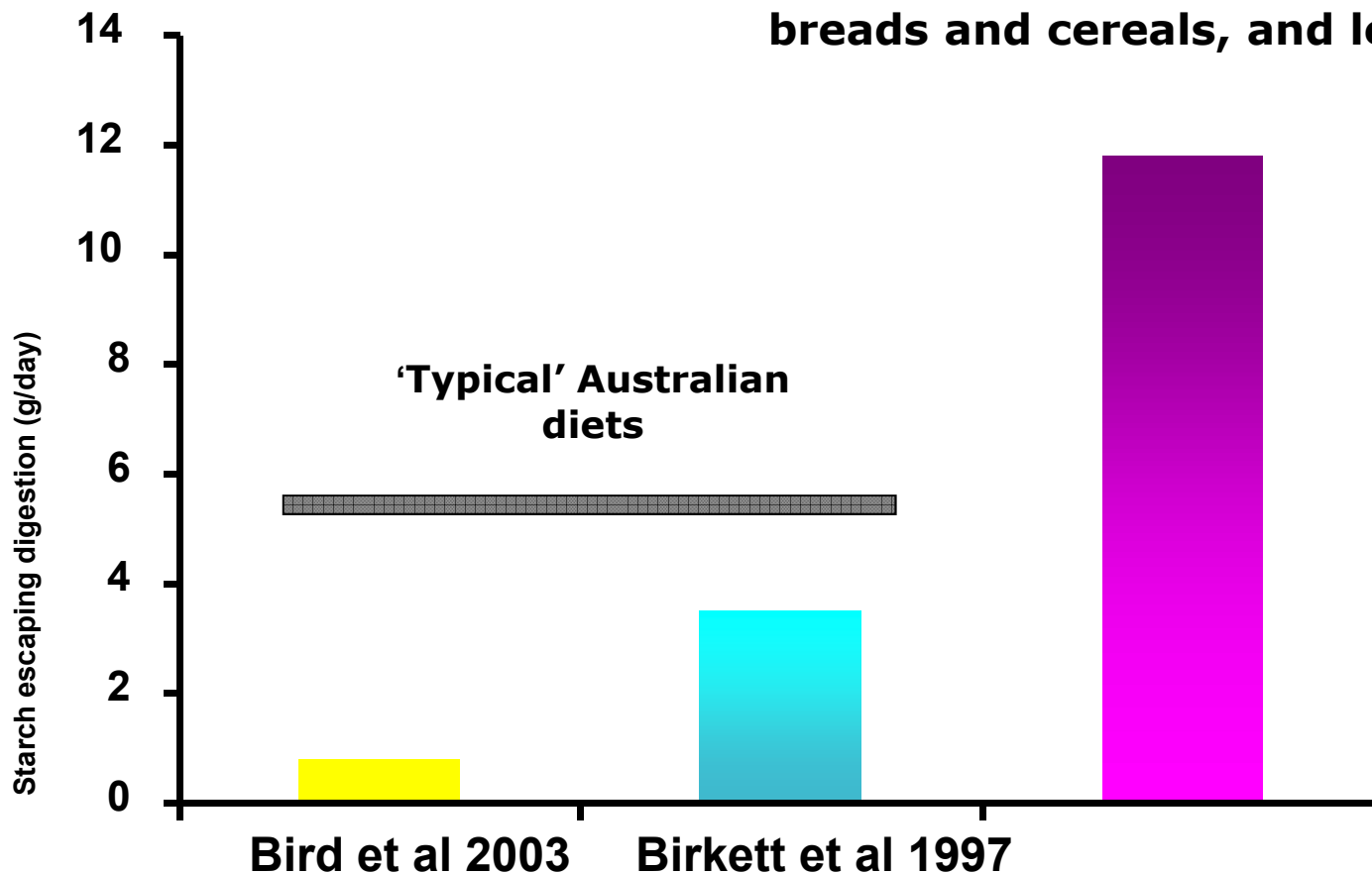


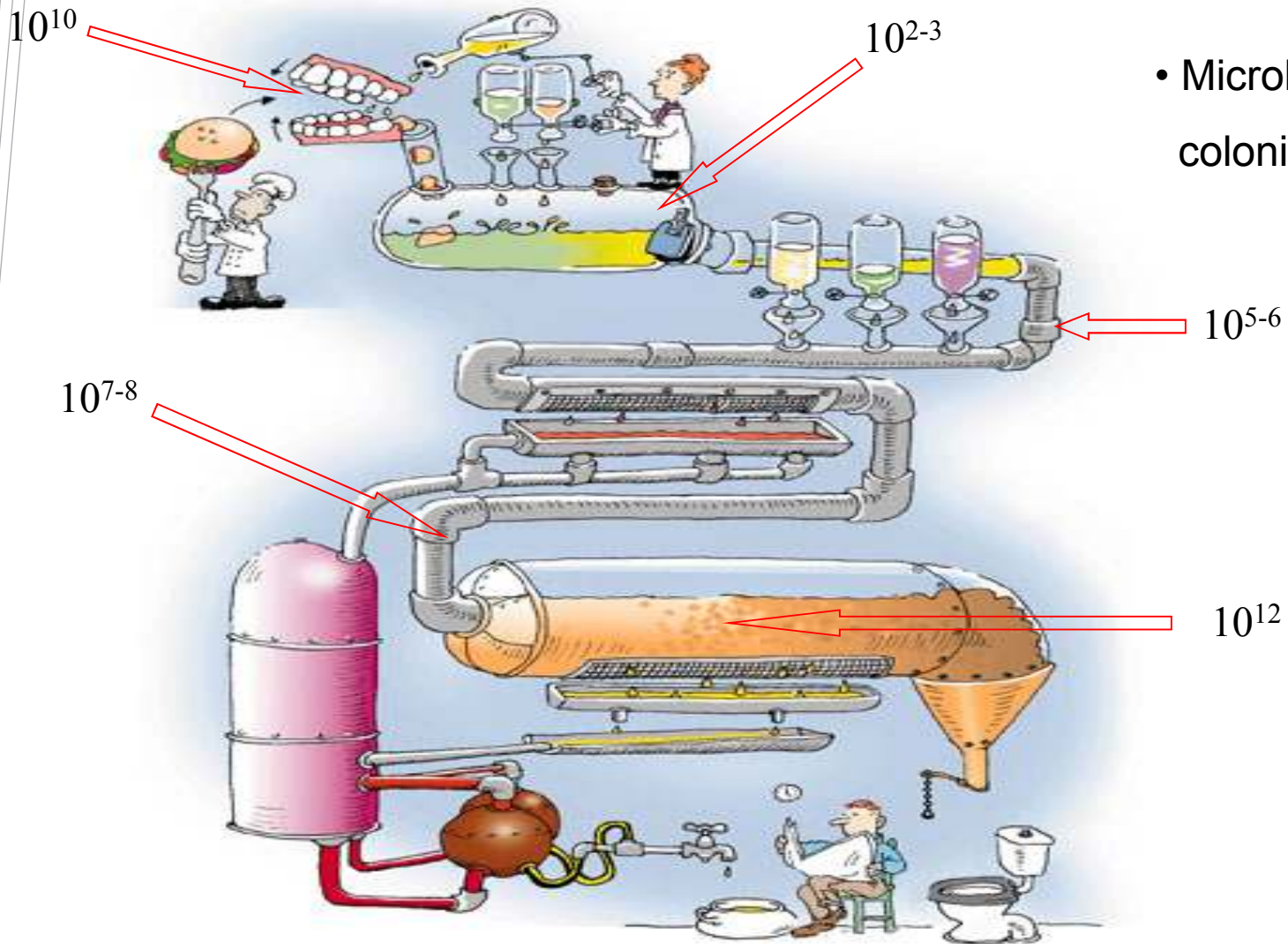
Figure 1(b). Number of Colon cancer cases in Victoria is increasing (2003 figures to April).

Modern Diets are low in RS

Modified diet – Resistant starch increased by including wholegrain breads and cereals, and legumes

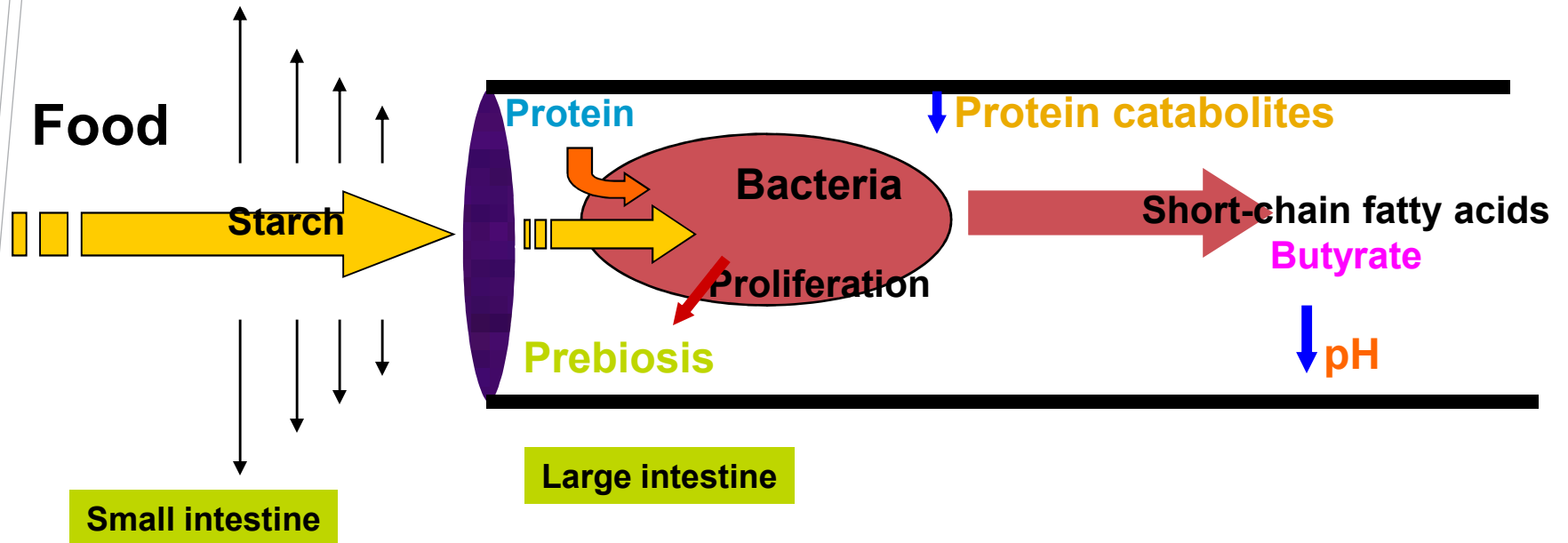


Gastrointestinal Tract Microbiology



- Microbial colonisation

RS – Metabolic Mechanisms



Major Products

In adults

- **SCFA – mostly acetate, propionate, butyrate**
- **More bacteria**
- **Gases**

In breast-fed babies

- **SCFA – principally acetate**
- **Other carboxylic acids – lactate, formate**
- **Ethanol**
- **More bacteria**
- **Gases**

Specific Effects of Butyrate

- **Inhibition of growth of a range of tumour cell lines and promotion of differentiation in vitro.**
- **Promotion of repair of damaged DNA in cells in vitro.**
- **Induction of apoptosis in cancer cell lines and rats with experimentally induced cancer**
- **Major metabolic fuel for isolated colonocytes.**
- **Stimulation of colonic electrolyte transport.**

RS fermentation favours butyrate production (NSP and OS fermentation do not).

Faecal SCFA (including butyrate) are high in black Africans relative to whites.

Faecal SCFA in Africans and Whites

SCFA (mmol/kg)	Africans	Whites	P value
Total	142	69	< 0.001
Butyrate	18	12	< 0.01

Source: Segal et al (1995)

High RS Cereals for Public Health

- **Good evidence for a positive role for RS in human health**
- **RS is a recognised fibre component**
- **Technology is available to manipulate starch composition to raise RS in staple consumer foods.**
- **BARLEYmax™ is the first grain.**

What is BARLEYmax™ ?

BARLEYmax™ is a hull-less barley variety with a single base-pair change in a gene coding for Starch Synthase IIa giving an altered composition with favourable nutritional and sensory properties™

BARLEYmax™ is designed to be the main component of foods to supply RS (and fibre).

The benefits of BARLEYmax™ are supported by an extensive research programme.

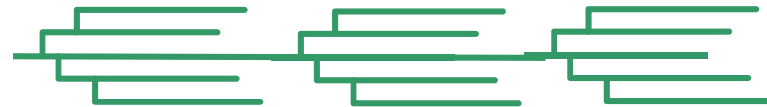
Amylose, RS and BARLEYmax™

Starch is a major component of cereal grains (65-70%). It is composed of glucose with either a 1,4 (linear) or a-1,6 (branched) linkages

Amylose
(~25%)

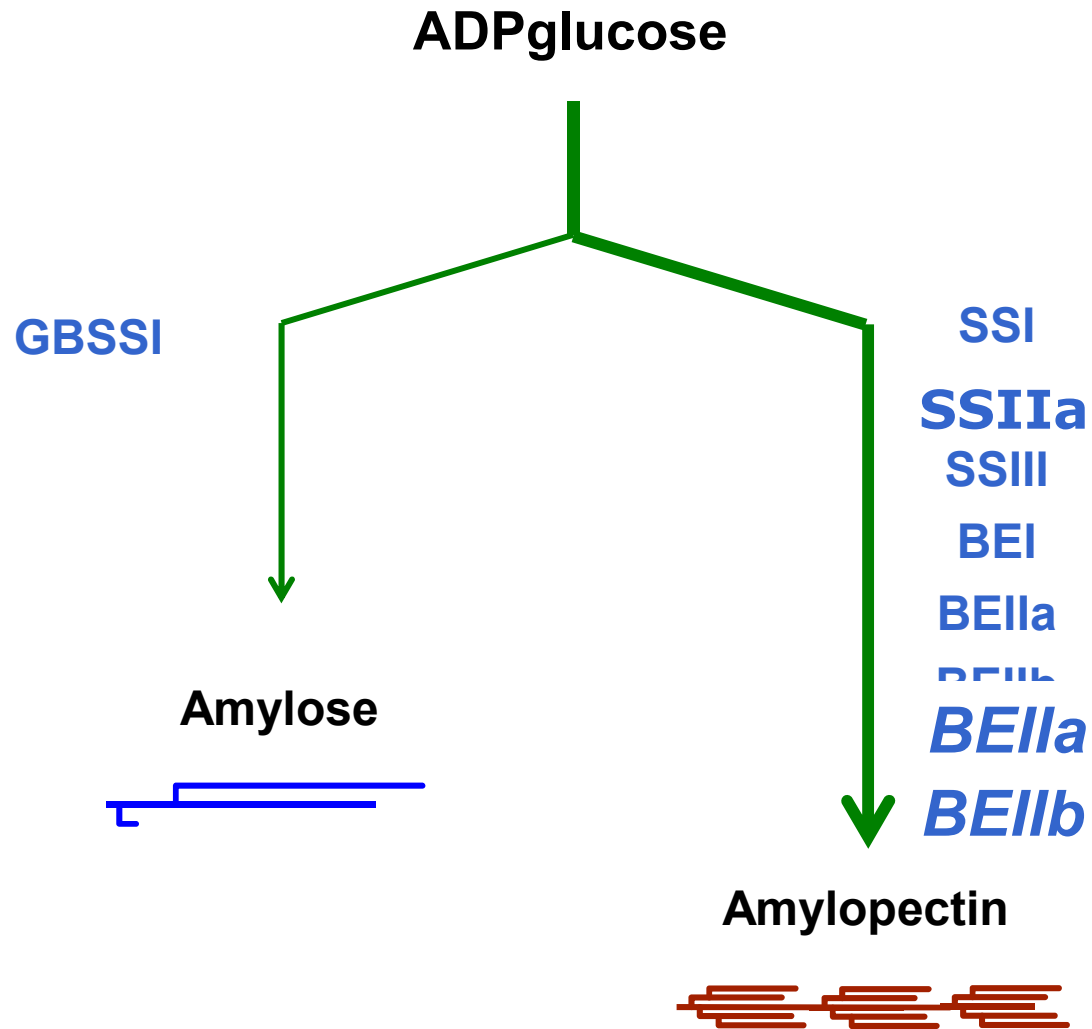


Amylopectin
(~75%)

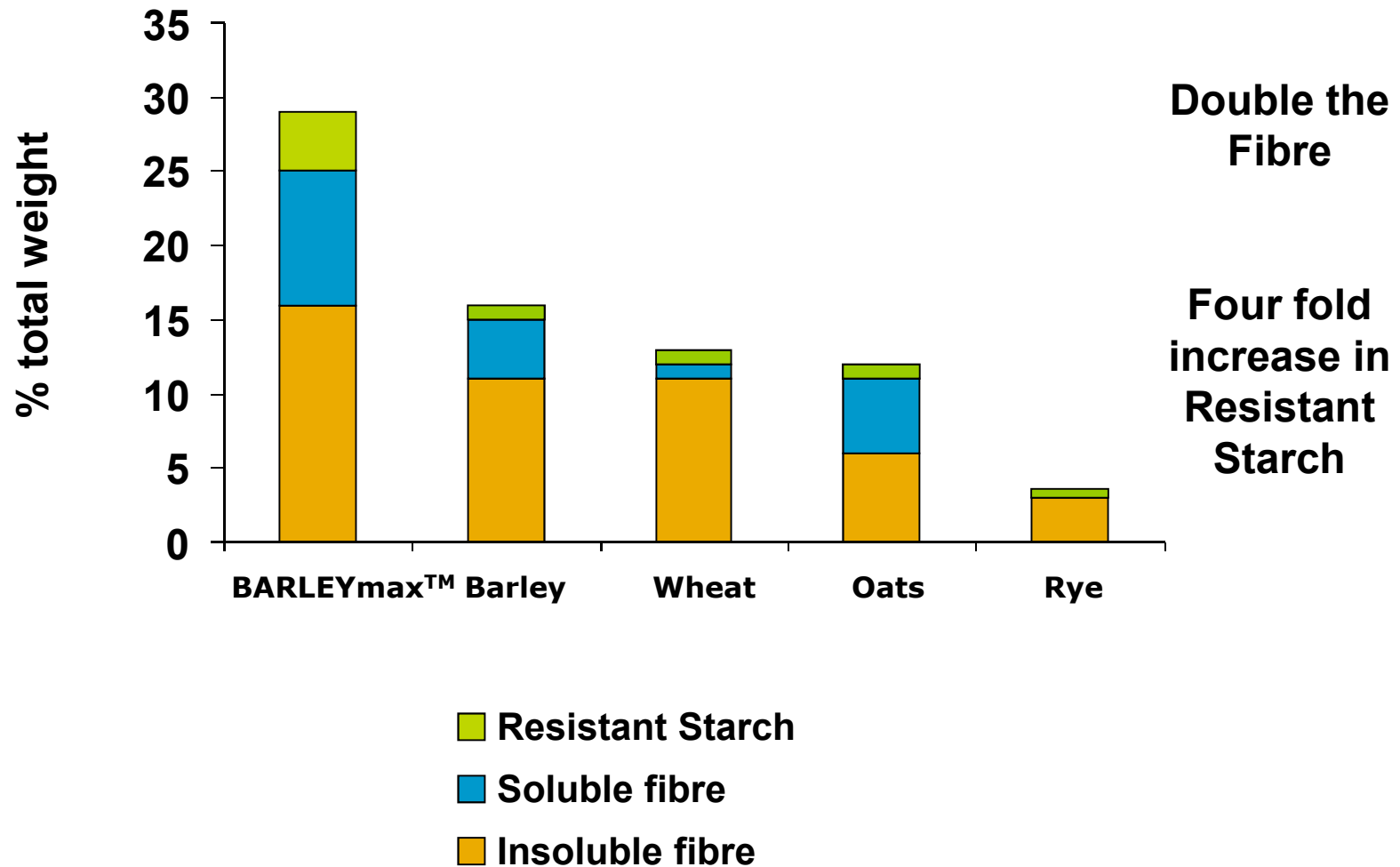


Amylose tends to form enzyme resistant aggregates which are digested more slowly while amylopectin is digested more easily. BARLEYmax™ has a higher amylose content but less total starch (25-30%).

Starch Synthesis Genes



New Grains – BARLEYmax™



The BARLEYmax™ Development Path

Once the grain has been identified, this is the sequence:

- 1. Detailed analysis – for diet or food formulation**
- 2. *In vitro* studies – to establish key features**
- 3. Small animal trials – baseline effectiveness (and disease modelling)**
- 4. Pig trials – to establish human relevance**
- 5. Pilot scale food processing**
- 6. Acute and/or long term human trials**
- 7. IP position and/or publication**
- 8. Licensing (as appropriate)**

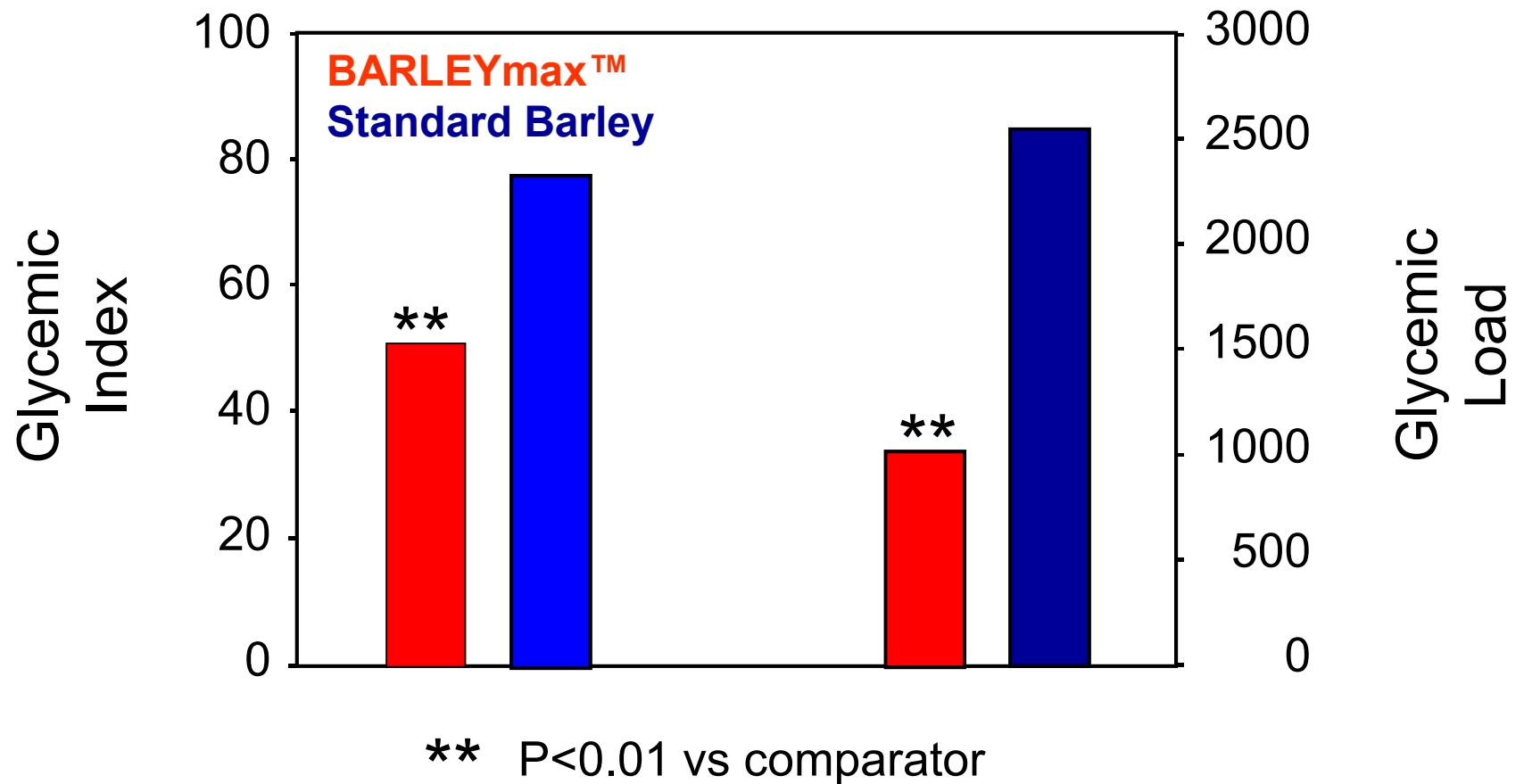
BARLEYmax™ (Himalaya 292) Foods

- **Rolled flakes (100%)**
- **Bread (20%)**
- **Savoury cracker biscuit (37%)**
- **Sweet muffin (21%)**

The volunteers in our trials liked the products – the taste test.



Glycemic Index & Glycemic Load of Barley Breakfast Cereals



BARLEYmax™ and Human Bowel Function

Diet	Faecal weight (g/d)	Faecal moisture (g/100 g)	pH	Defecation frequency (motions/48 h)
Refined wheat	150 ^a	73.8	7.2 ^a	2.0
Wholemeal wheat	187 ^b	76.8	7.2 ^a	2.2
BARLEYmax™	200 ^b	77.3	7.0 ^b	2.1

Human Feeding Study - Faecal SCFA Output

Diet	Faecal SCFA excretion (mmol/d)			
	Acetate	Propionate	Butyrate	Total
Refined wheat	9.2 ^a	1.8 ^a	2.8 ^a	14.4 ^a
Wholemeal wheat	10.7 ^{ab}	2.3 ^{ab}	3.8 ^a	17.3 ^{ab}
BARLEYmax™	13.7^b	2.7^b	5.4^b	22.6^b

BarleyMax™ commercial products



**Popina Food Services, Goodness Superfoods
Released 2009**

RNAi Suppression of BEII genes in Wheat

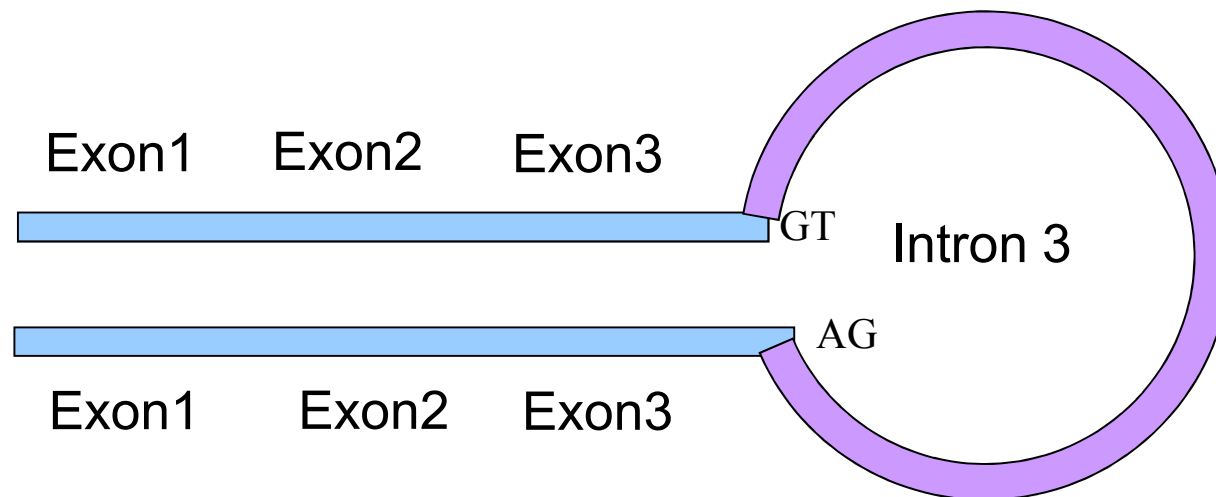
Wheat –

- a global staple
- most wheat consumer foods are low RS
- great potential for high RS functional foods

Using RNAi to decrease amylopectin branching to generate high amylose starches

RNAi Down-Regulation of SBEIIa and SBEIIb

- Targeted use of RNAi technology to down-regulate the BEIIa and BEIIb gene using a “hairpin” construct



- Transformed wheat using SBE IIa and SBE IIb RNAi constructs
- Positive SBE IIa and SBE IIb transformants were identified by both PCR and Southern blot hybridisation

High Amylose Wheat and Caecal Variables in Rats

Diet	pH	Acetate (μmol)	Propionate (μmol)	Butyrate (μmol)	Total (μmol)
Standard Wheat	6.23 (0.05)	44 (4)	14 (2)	31 (6)	88 (10)
High Amylose Wheat	5.90 (0.14)	106 (18)	38 (7)	57 (8)	202 (25)

Standard errors in parentheses

ACKNOWLEDGEMENTS

CPI - Canberra High Fibre Grains Cluster

Matthew Morell
Zhongyi Li
Regina Ahmed
Sadiqur Rahman
Peter Chandler
Steve Jobling

Geoff Fincher (UA)
Rachel Burton (UA)

Tony Bacic (UM)

CFNS Adelaide

Tony Bird
Manny Noakes
Jennifer Keogh
Roger King

Mike Gidley (UQ)
Barbara Willimas (UQ)

Commercial Partners

ACVL Ltd
Austgrains
Popina

Commercialisation

Bruce Lee
Rob Defeyter
Lindsay Adler
Anne Howard
Geoff Ball