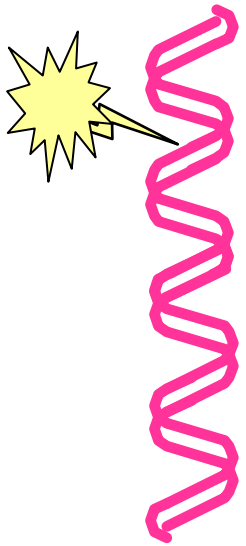
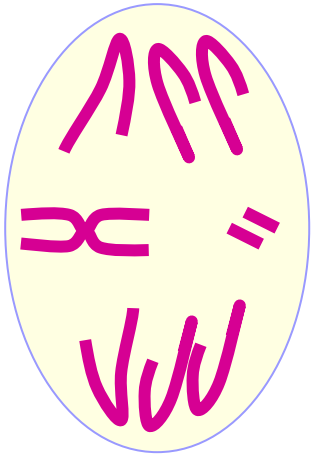
Opportunities for Dietary Control of Health and Disease Prevention

Dr Michael Fenech

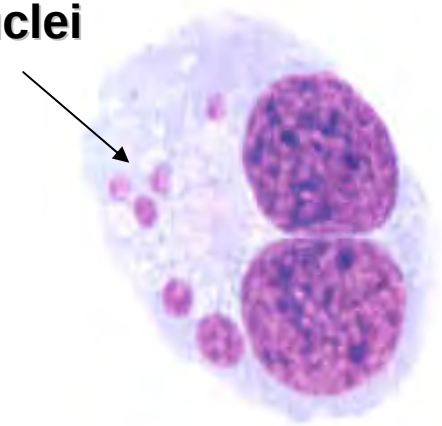
Theme Leader: Nutrigenomics and Genome Health

Genome damage





Micronuclei



CYTOKINESIS-BLOCK MICRONUCLEUS (CBMN) ASSAY

- Oxidative stress
- Nutrient deficiency
- Excess calories

→

- Strand breaks in DNA
- Chromosome malsegregation
- DNA hypomethylation
- Telomere shortening

→

Human cells with damaged & unstable genomes

Genome damage increases with age

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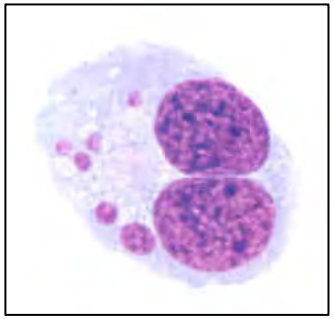

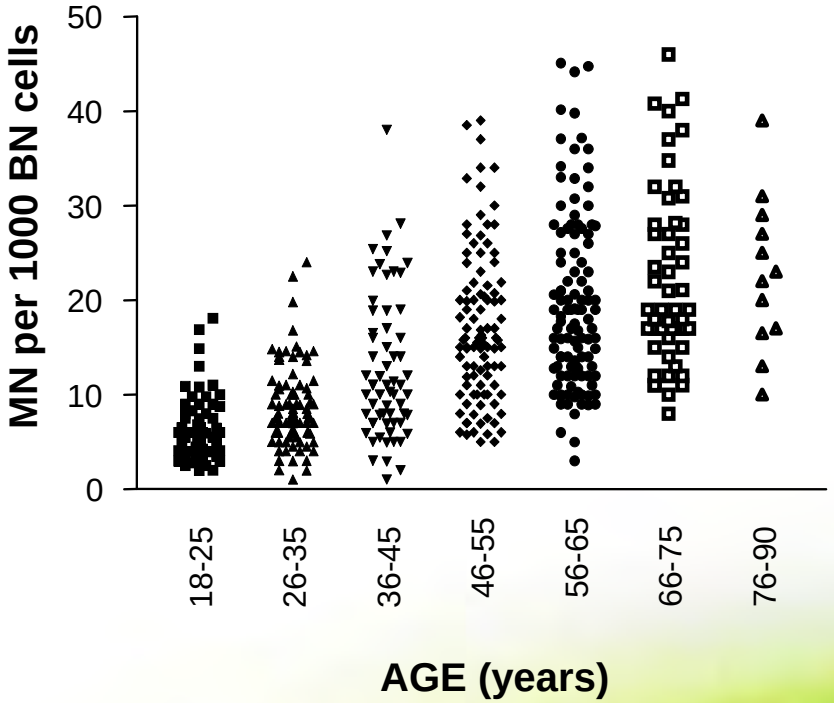

Fenech et al. 2000

Risk of cancer increases with higher DNA damage (MN frequency)

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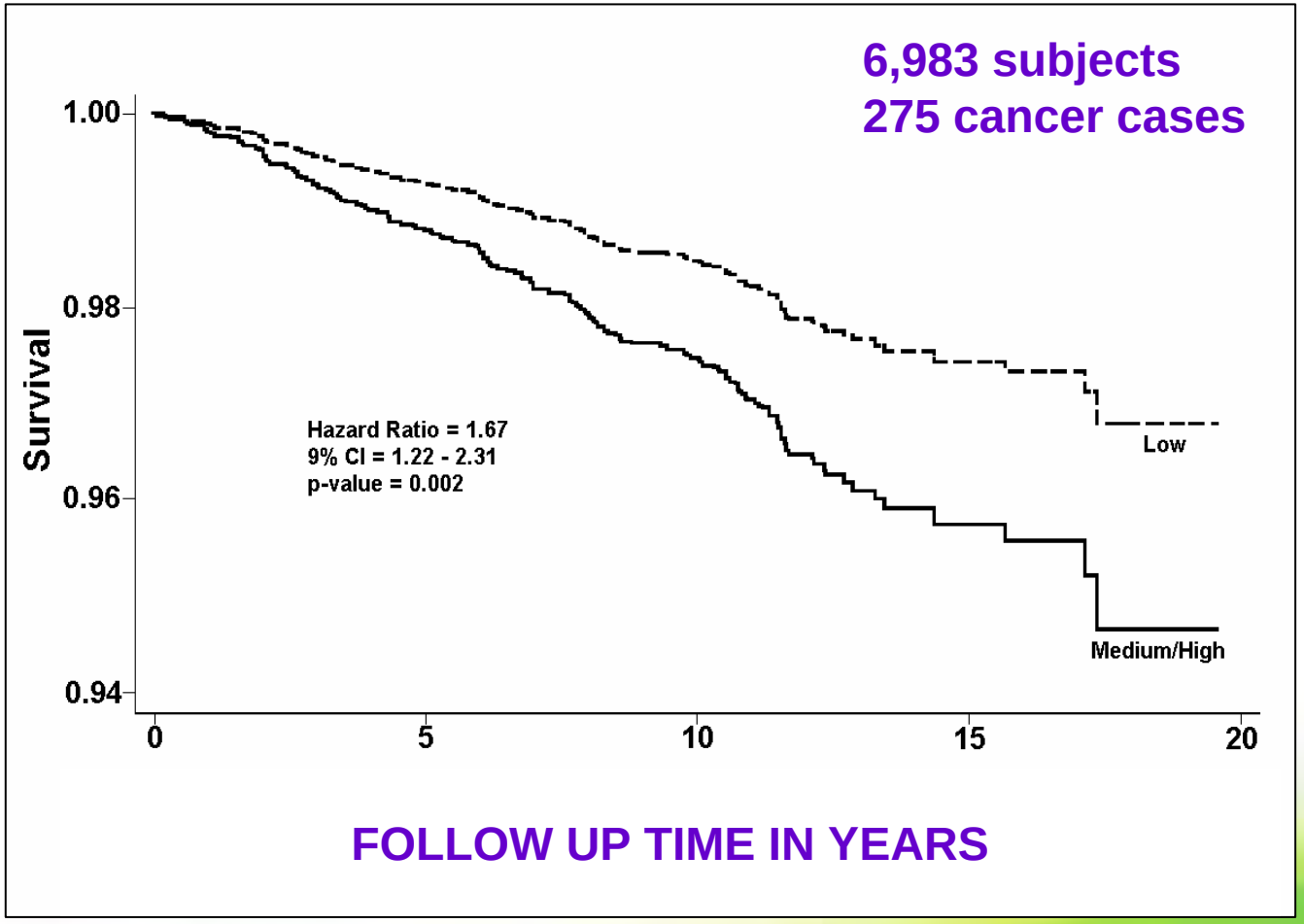
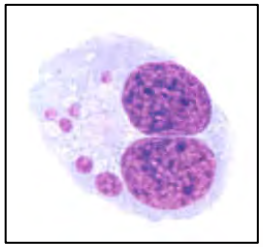
PROBABILITY OF SURVIVING WITHOUT CANCER

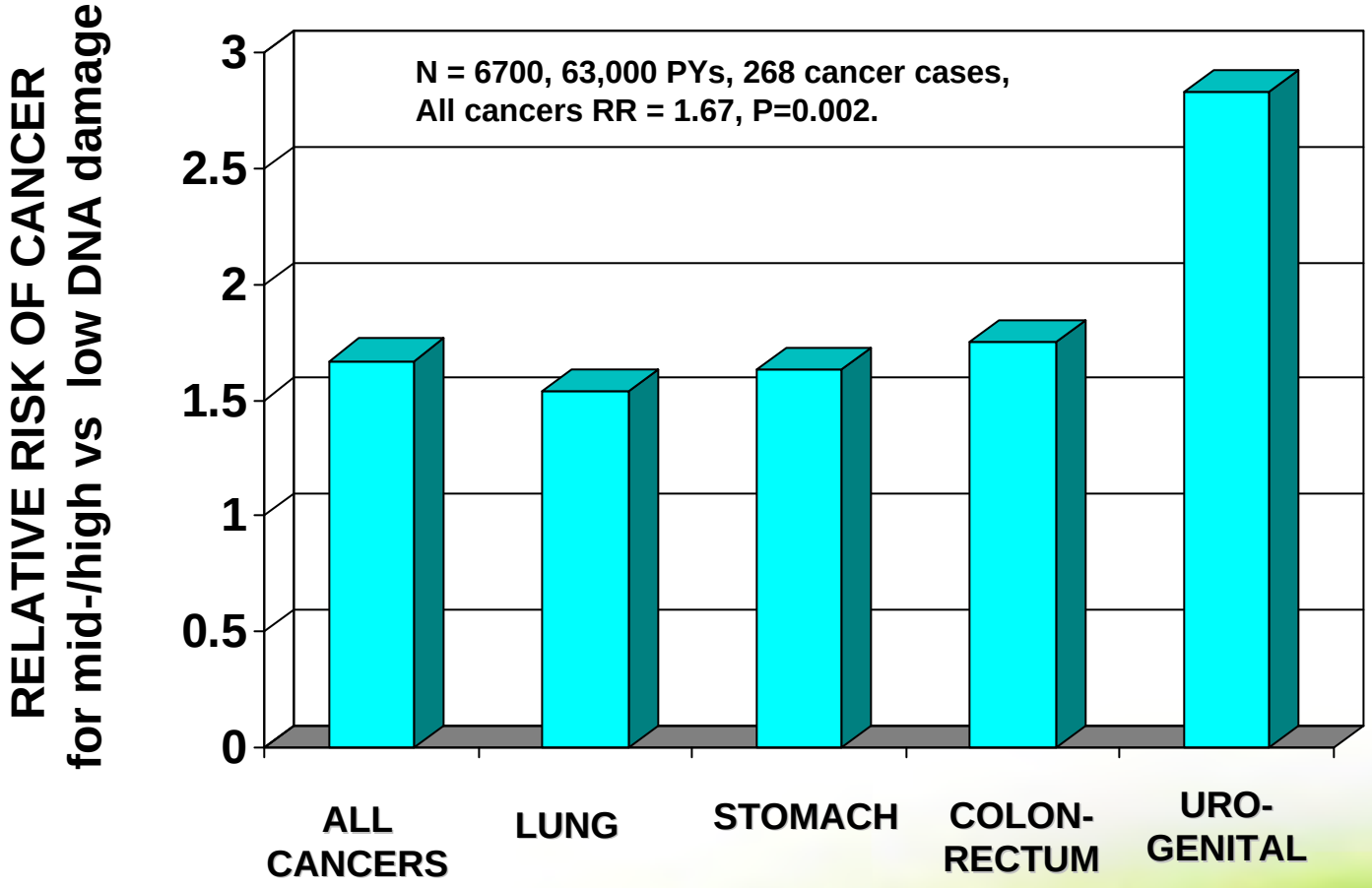




HUMN project (www.humn.org)

Bonassi et al (Carcinogenesis 2007)

A Medium or High level DNA damage predicts an elevated risk of cancer



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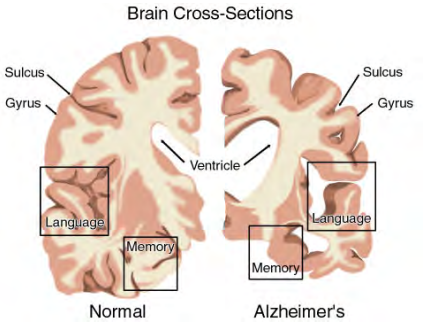
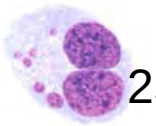
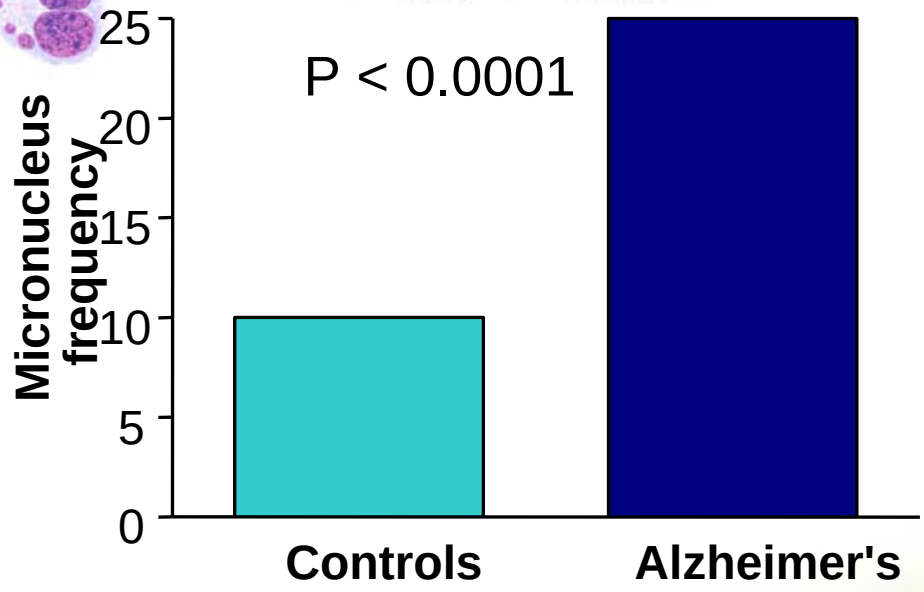
HUMN project

Bonassi et al Carcinogenesis (2007)

Increased DNA damage is associated with risk of Alzheimer's disease, Parkinson's disease, diabetes, osteoporosis, hair greying and loss

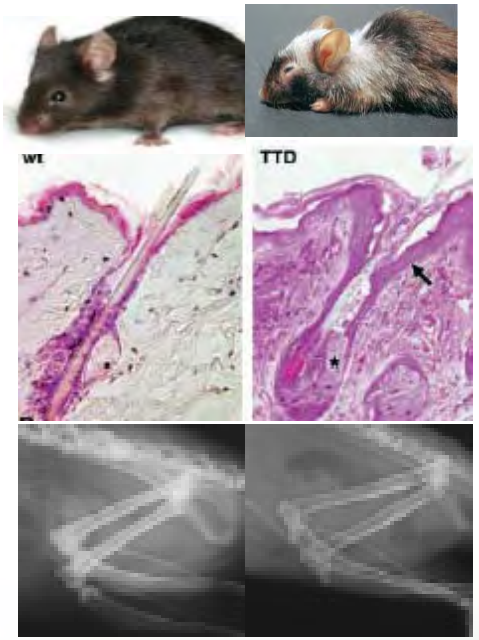






Migliore et al (1999) Cytogenetics Cell Genetics

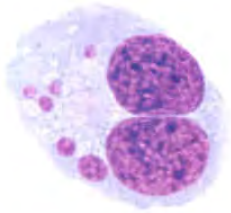
WT **TTD**

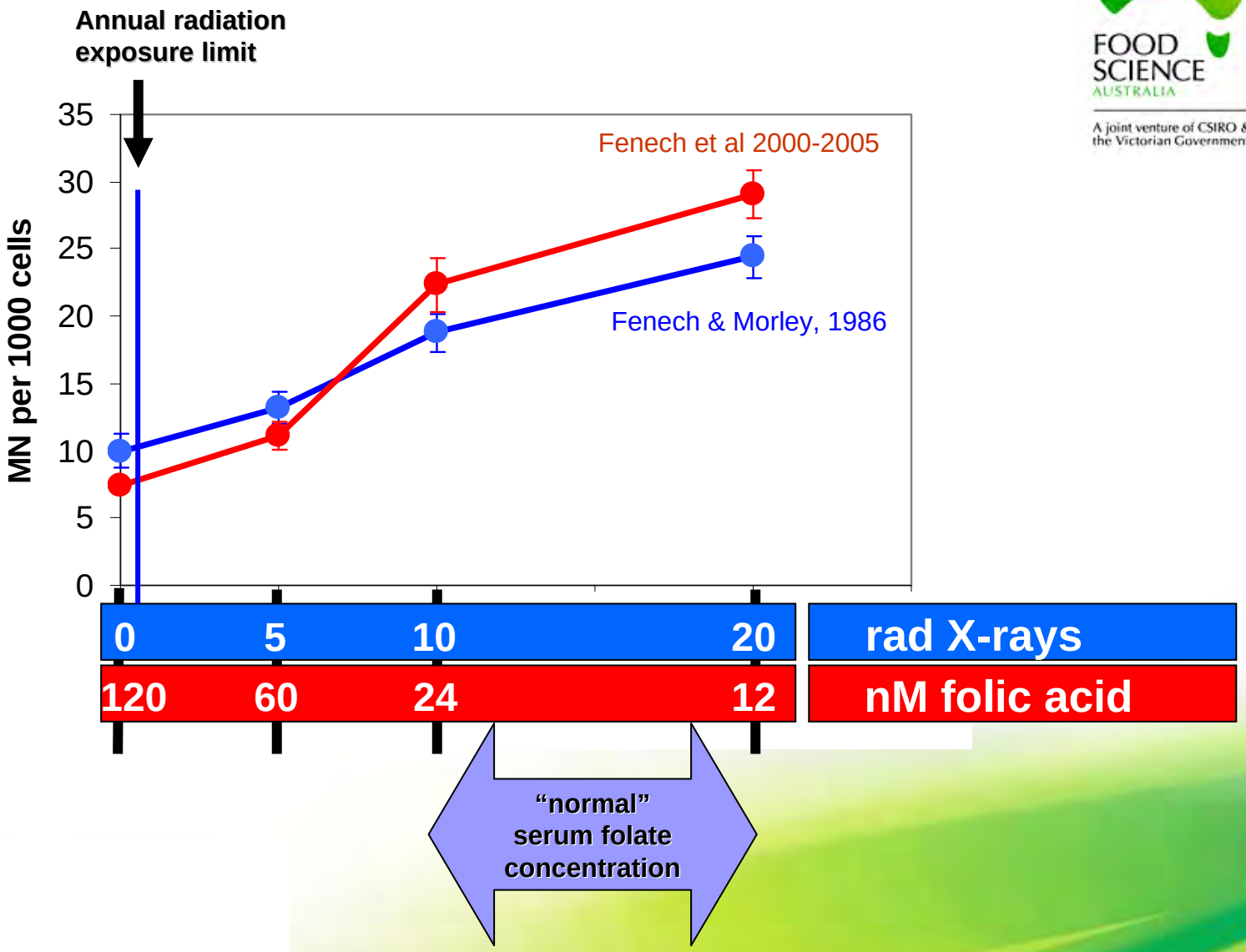


Premature aging in mice deficient in DNA Repair and transcription

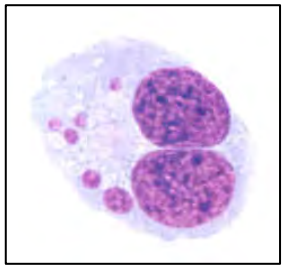
deBoer et al. Science 2002

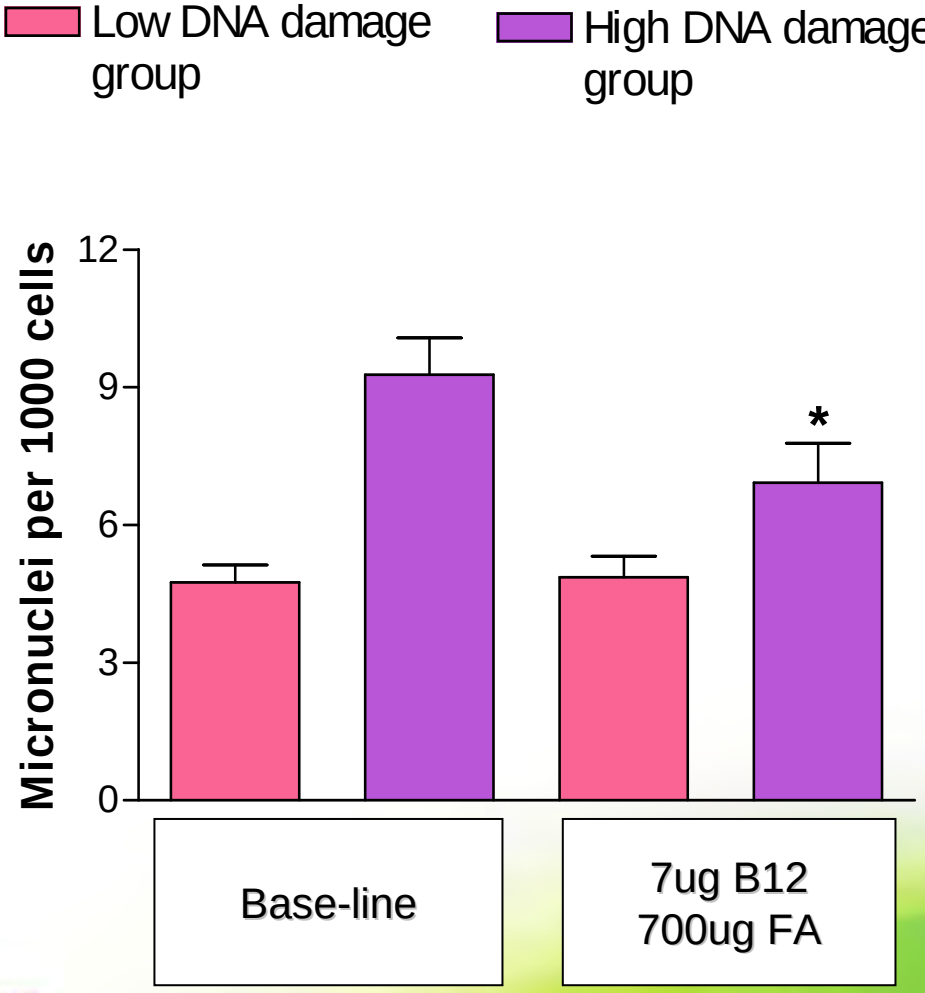
Moderate folate deficiency causes as much DNA damage as radiation





Supplementation with folic acid & vit B12 in cereal reduces DNA damage in young Australians (18-32 y)

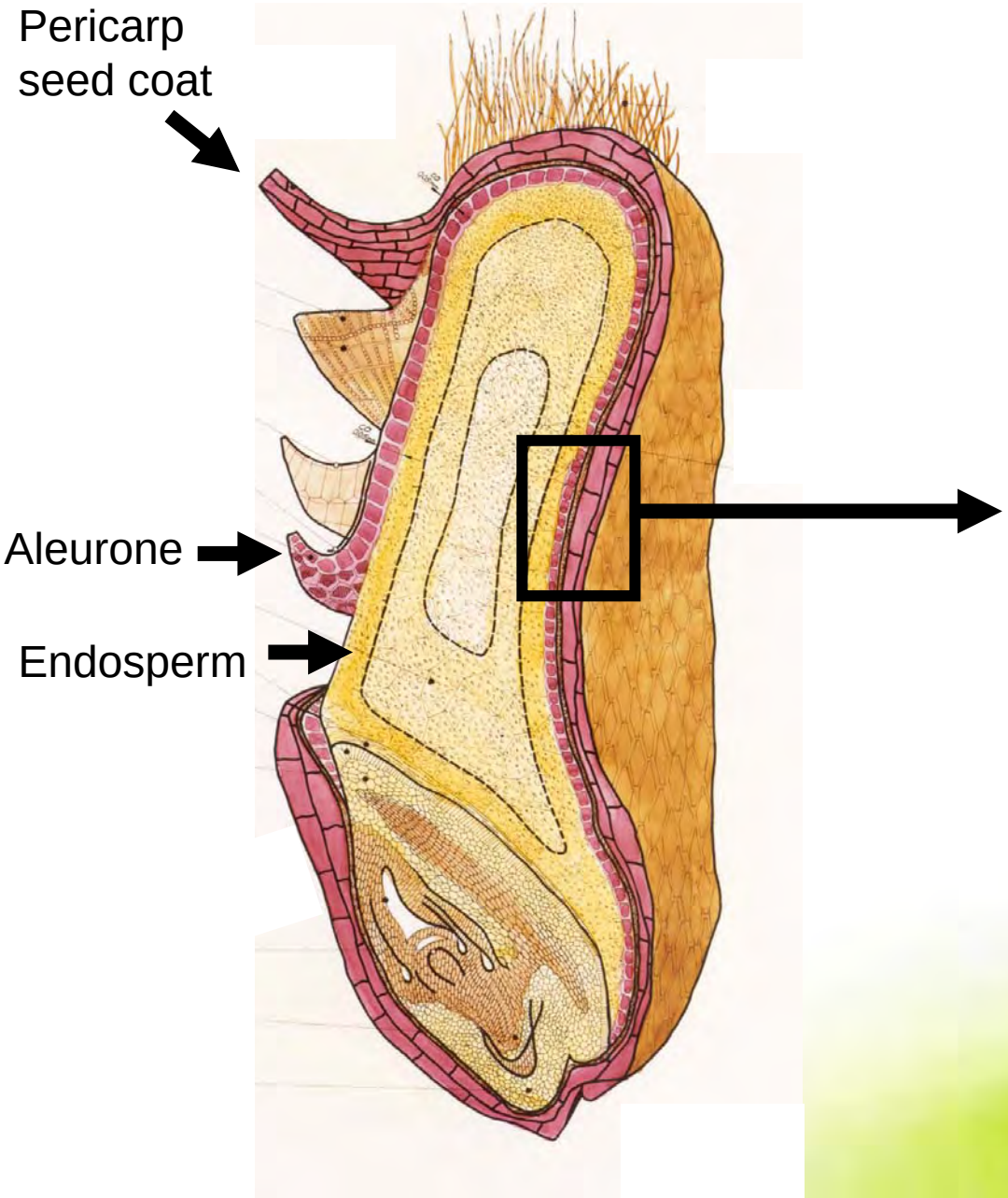


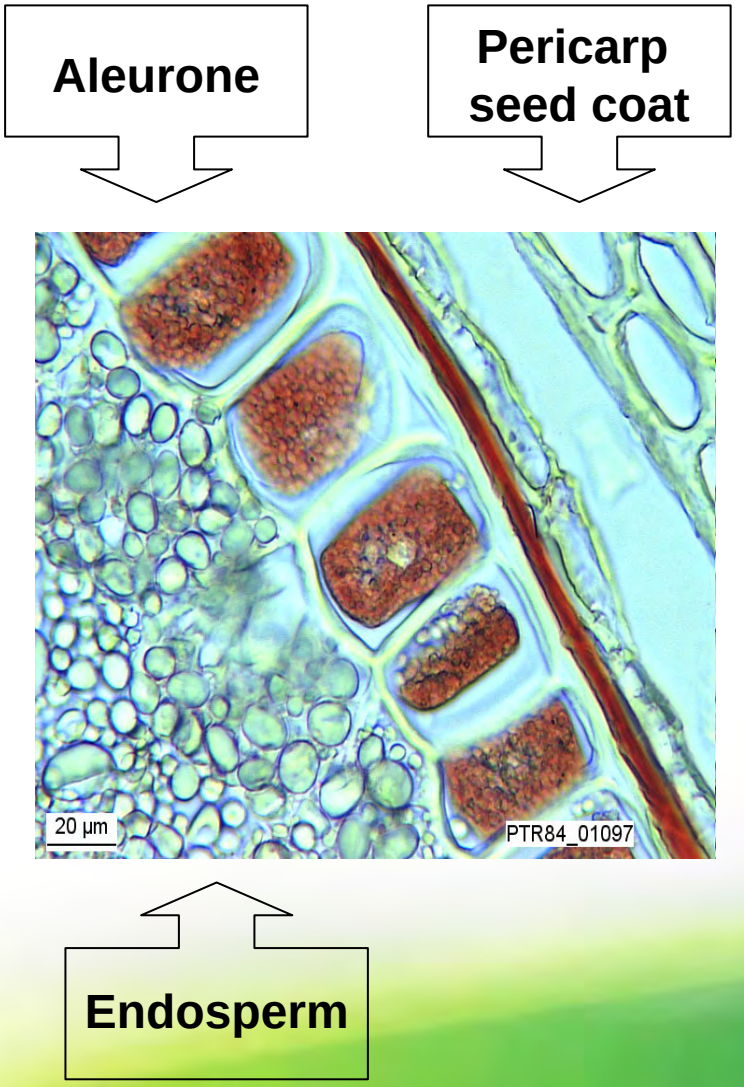


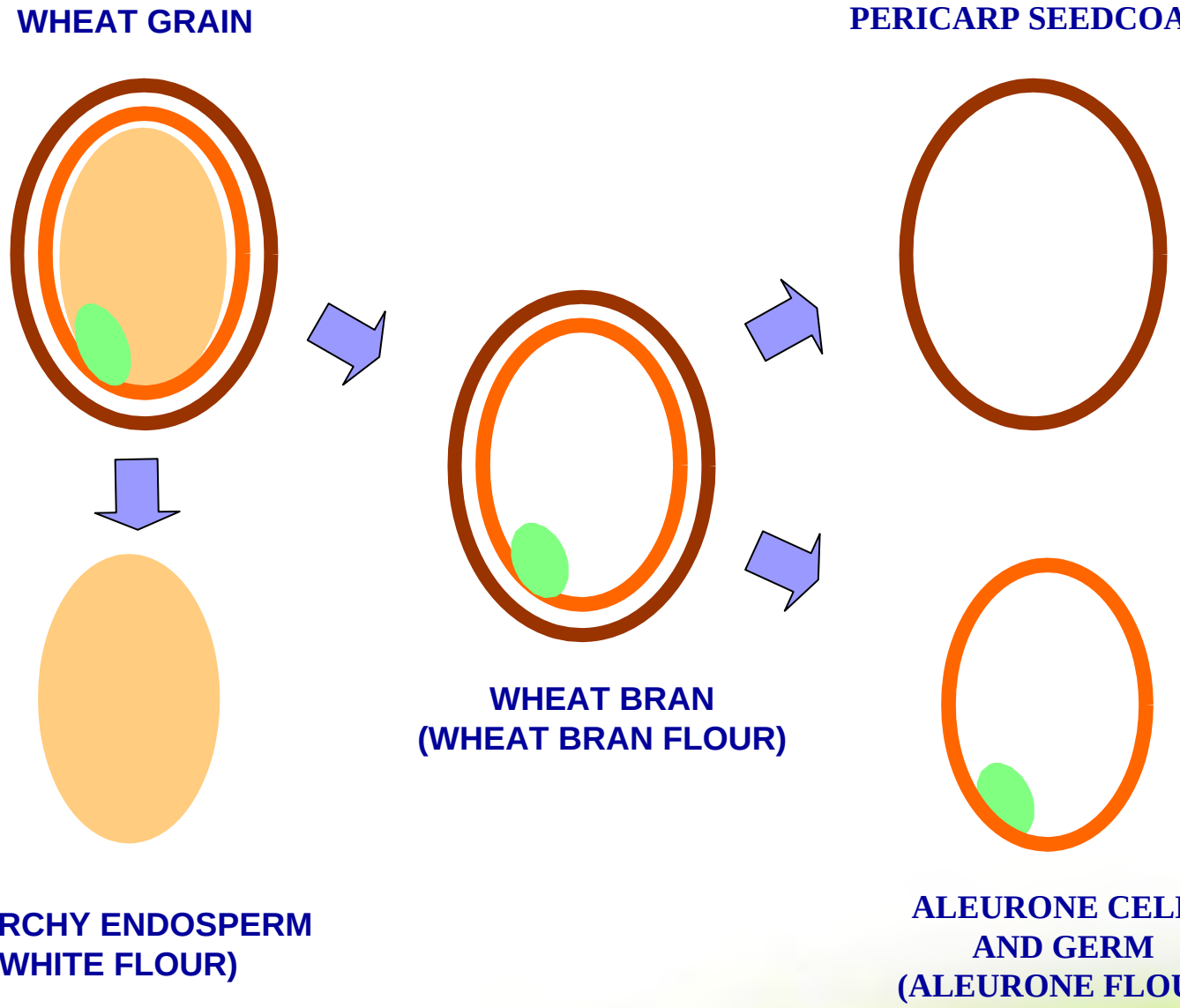
*** P<0.01**

Fenech et al. 1998 Carcinogenesis

Fenech et al 1998 Carcinogenesis


Pericarp
seed coat
Aleurone
Endosperm


Aleurone
Pericarp
seed coat
20 µm
PTR84_01097
Endosperm



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Key steps in isolation of wheat bran and aleurone flour

RANDOMISED SHORT TERM INTERVENTION WITH A CROSS-OVER

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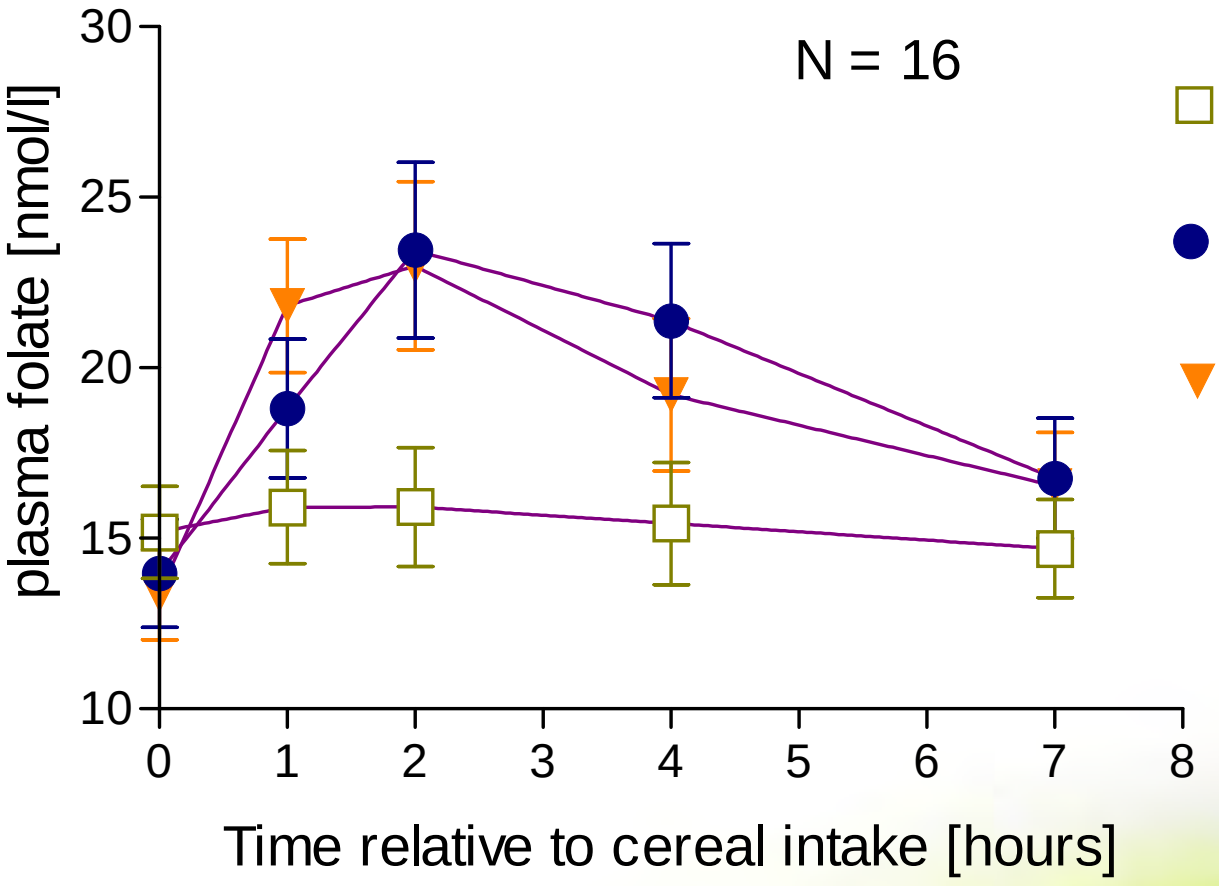
8 males and 8 females aged 20-45 years

* 100 g cereal was eaten at each round with 100ml milk
* each tablet contained 500ug free folic acid
* 7 days between each round

Change in plasma folate following intake of ALF cereal



WB cereal
ANOVA P = 0.1139

ALF cereal
ANOVA P < 0.0001

0.5mg folic acid tablet + WB cereal
ANOVA P < 0.0001

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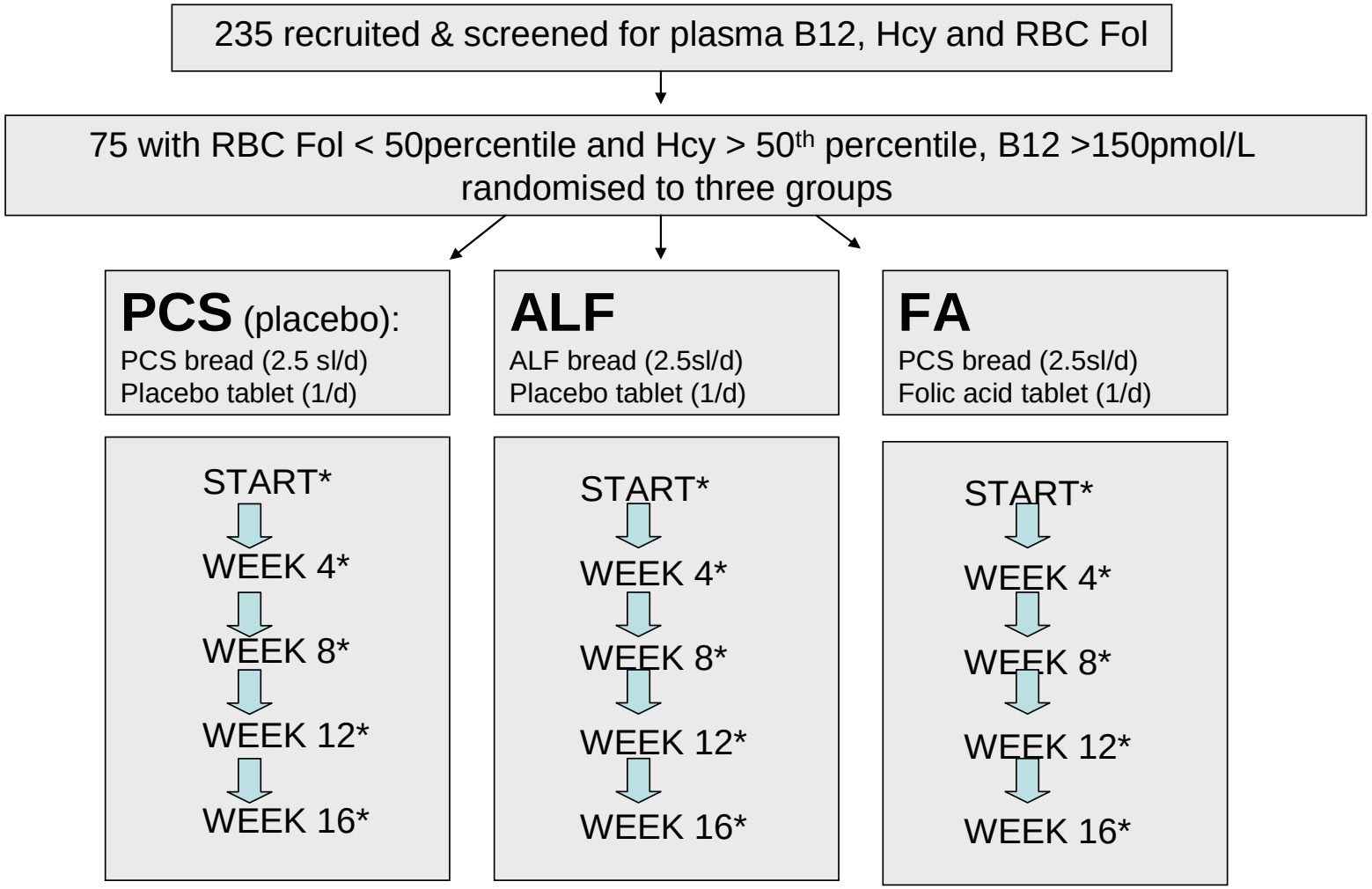
Results for today Ideas for tomorrow

Fenech et al J. Nutr 1999

Aleurone Trial Design



* Blood samples; dietary questionnaire at beginning and end of intervention only.

% CHANGE AT 16 WEEKS RELATIVE TO BASE-LINE

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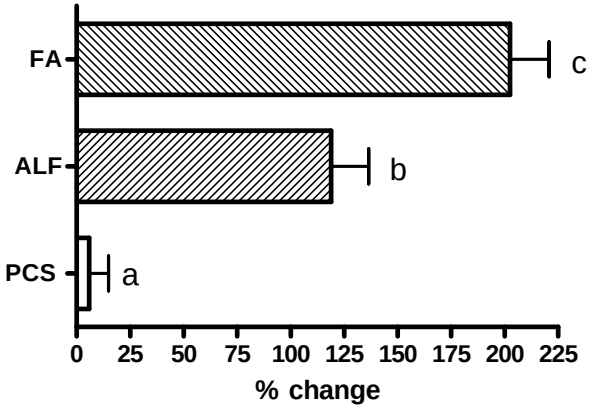
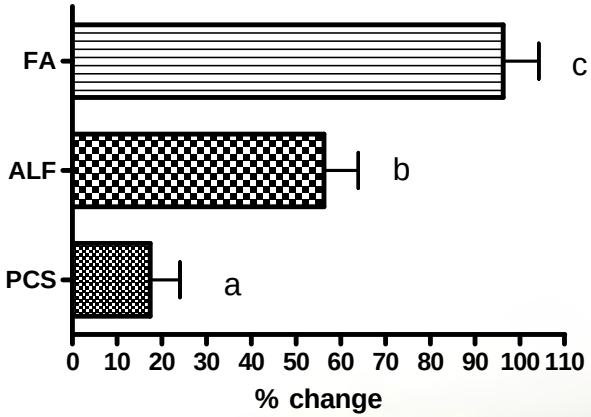
% change in plasma folate at 16 weeks (adjusted for base-line)

ANOVA P < 0.0001



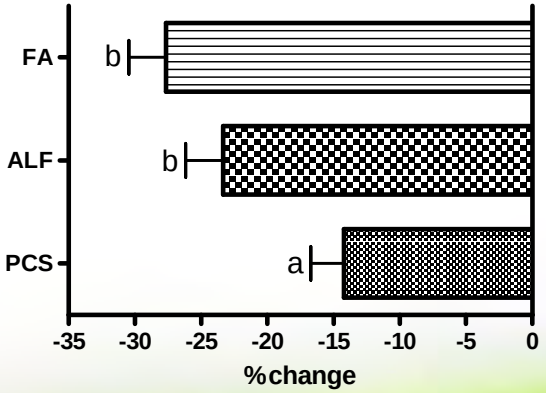
%change in RBC folate at 16w (adj for base-line) rel to baseline

ANOVA P < 0.0001



%change in plasma homocyst(e)ine at 16 weeks (adj for baseline) relative to baseline

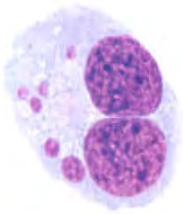
ANOVA P = 0.0034



18% reduced risk for stroke
Wang et al Lancet 2007

Fenech et al. Br. J. Nutr. 2004

Results for today Ideas for tomorrow



EFFECT ON GENOME DAMAGE

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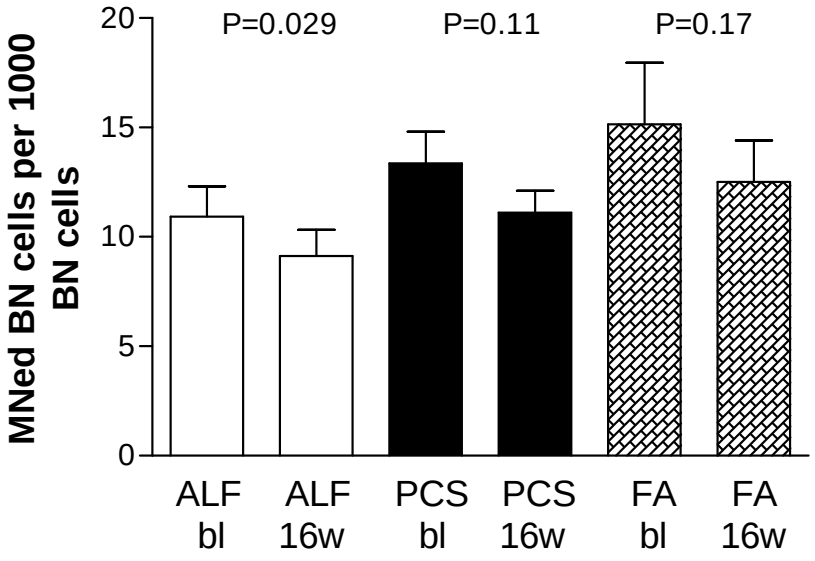

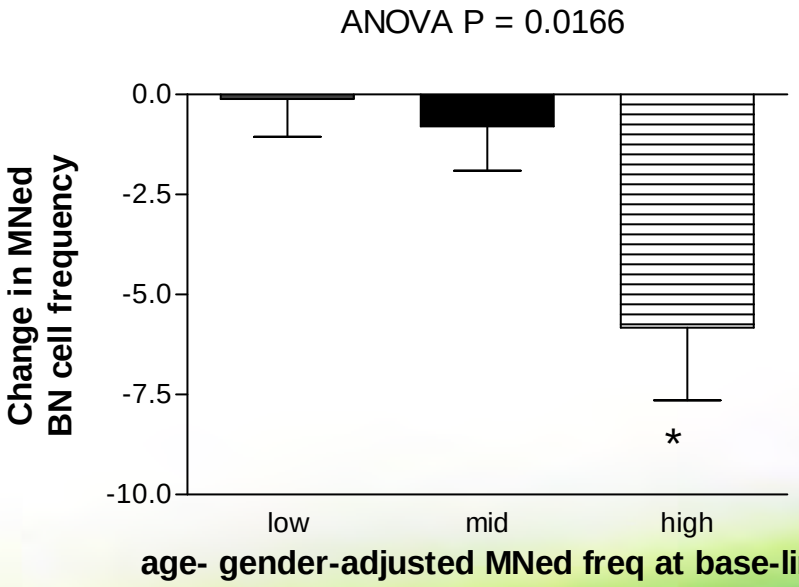

Caloric Restriction and Aging

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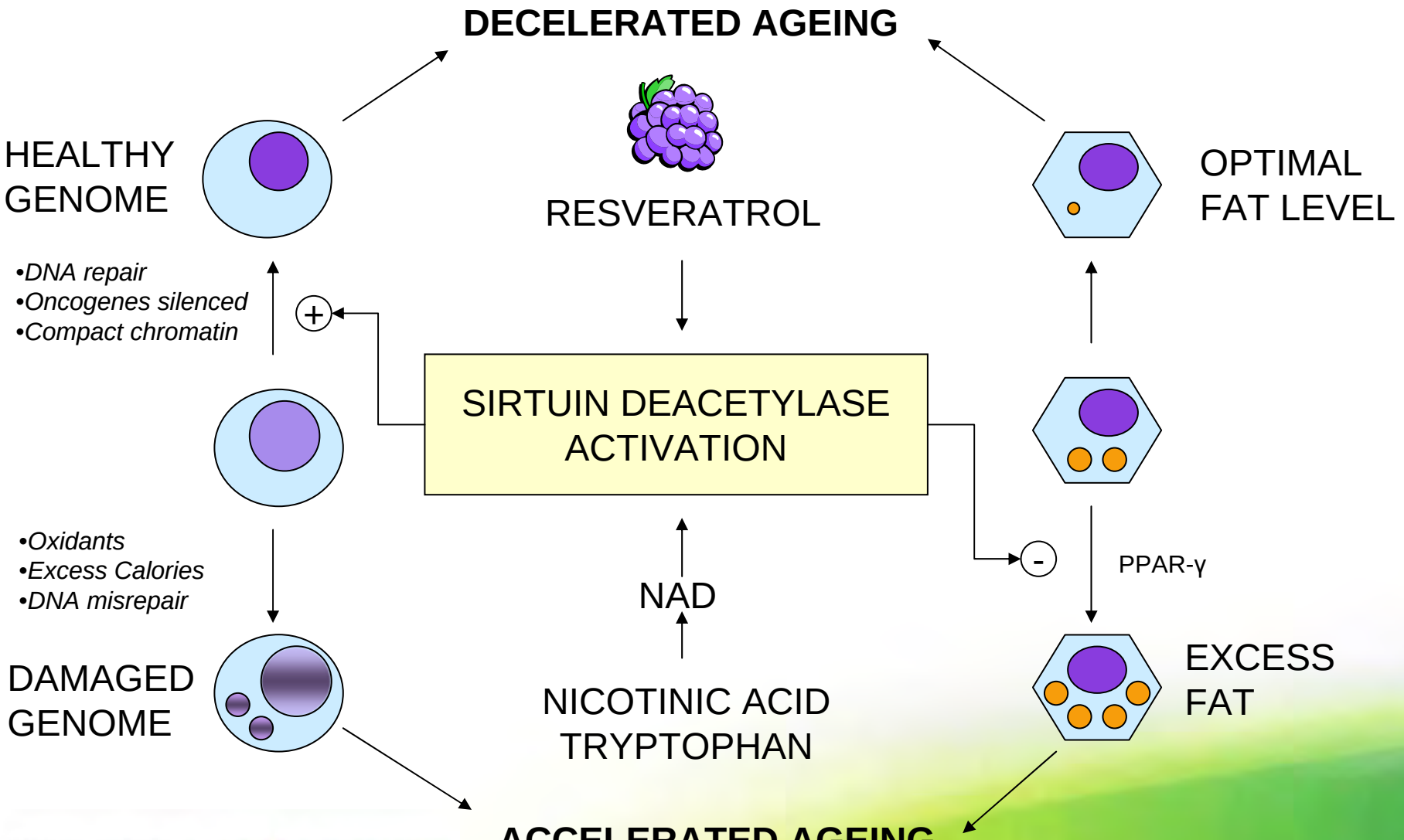
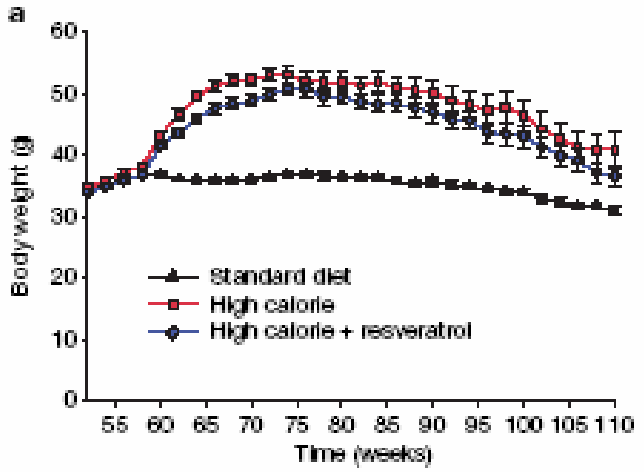
DISCOVERY OF CALORIC RESTRICTION MIMETICS

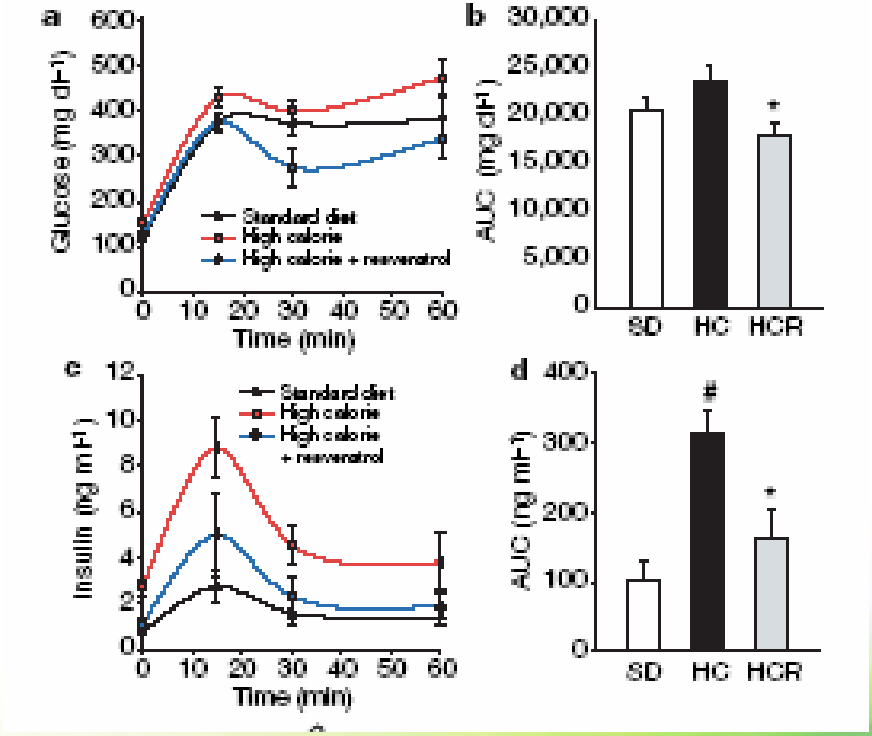


Results for today Ideas for tomorrow

Howitz et al Nature 2004

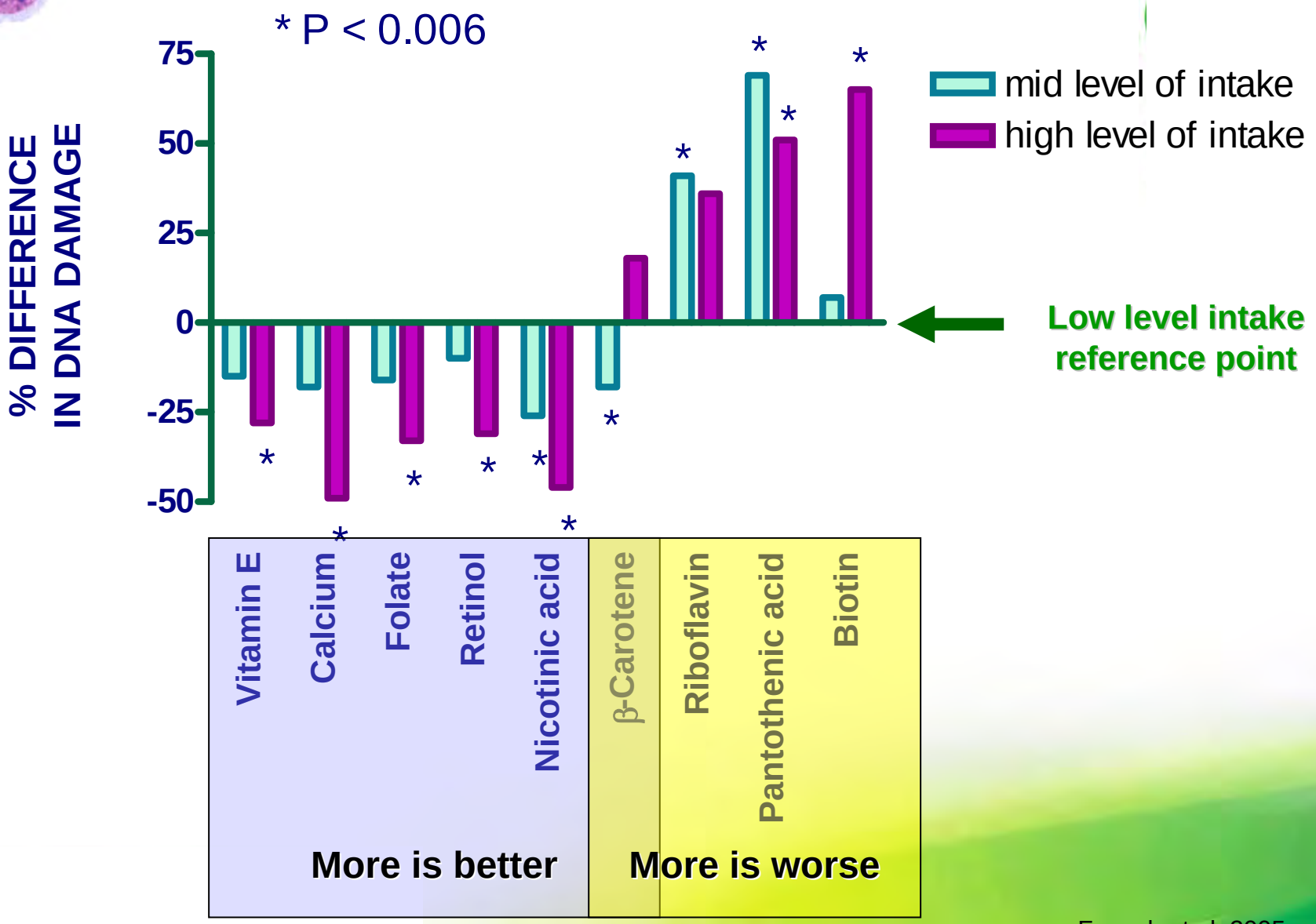
Resveratrol improves health and survival of mice on a high-calorie diet





Baur et al Nature 2006

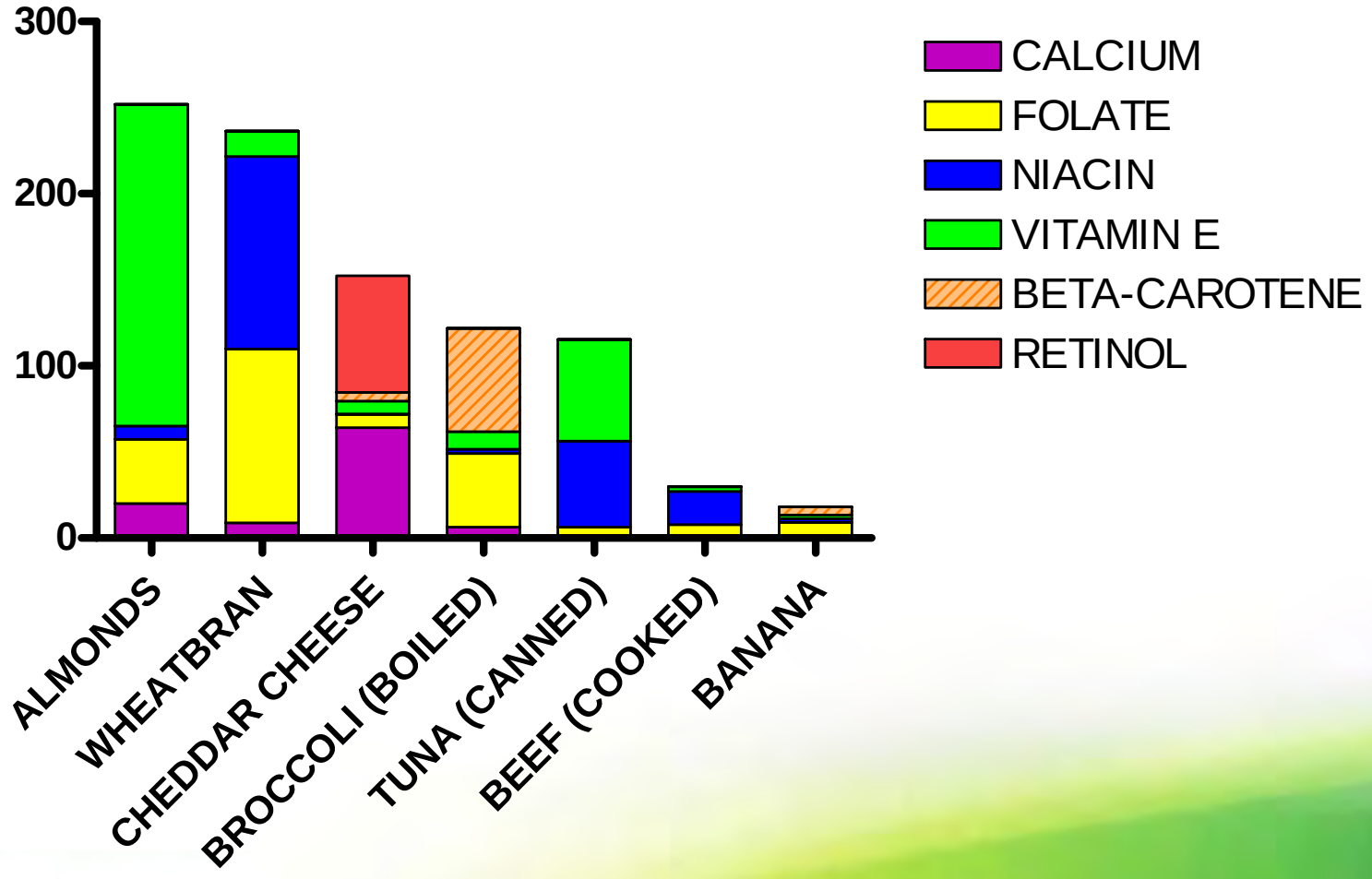
Micronutrient intake determines DNA Damage rate



Fenech et al. 2005

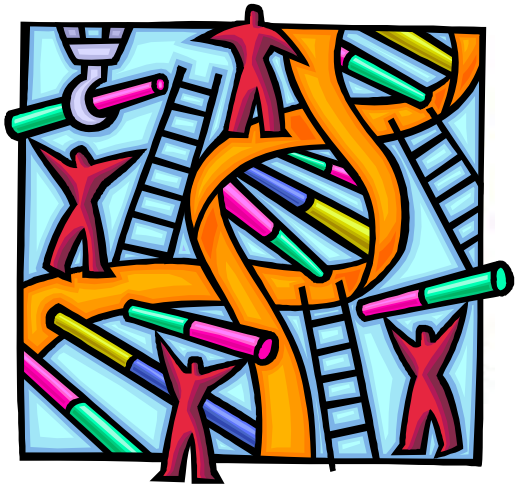
Q. Which dietary pattern will work for your genotype ?

A. It depends on the “nutriome” of the foods you prefer to eat



(Fenech in preparation)

GENOME DAMAGE



- MOST FUNDAMENTAL DISEASE

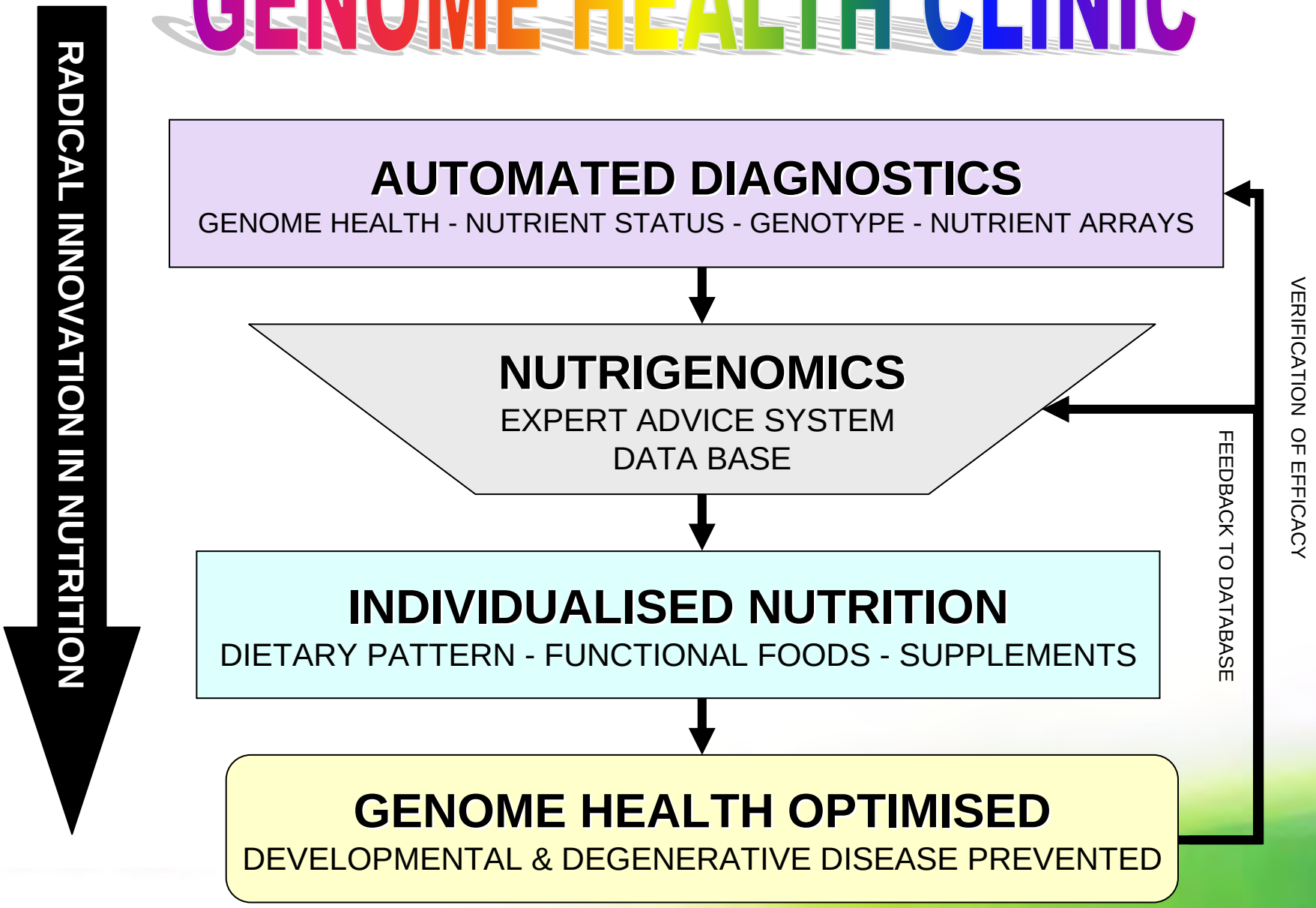
- CAN BE DIAGNOSED

- CAN BE TREATED NUTRITIONALLY*

* 25% reduction in micronucleus freq with 700ug folic acid + 7 ug vit B12 (Fenech et al. 1998)

*13% reduction in micronucleus frequency with ACEZn Supplement (Fenech et al. 2005)

GENOME HEALTH CLINIC



Funding: Reach 100, NCEFF

Fenech M (2005) Mutagenesis 20: 225-269

ABC Catalyst, DNA Doctor Story

Opportunities for the Food and Health Industry

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- Low Calorie Nutrient Dense Foods
- Foods Certified for Nutritional Composition
- Foods and Food Combinations that deliver nutritional requirements for Genome Health
- Individualisation and Biomarkers

FUTURE FOOD AND FUTURE HEALTH DIETS IN PRACTICE

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