PERSONALISED NUTRITION FOR PREVENTION OF DNA DAMAGE

GENOME HEALTH NUTRIGENOMICS

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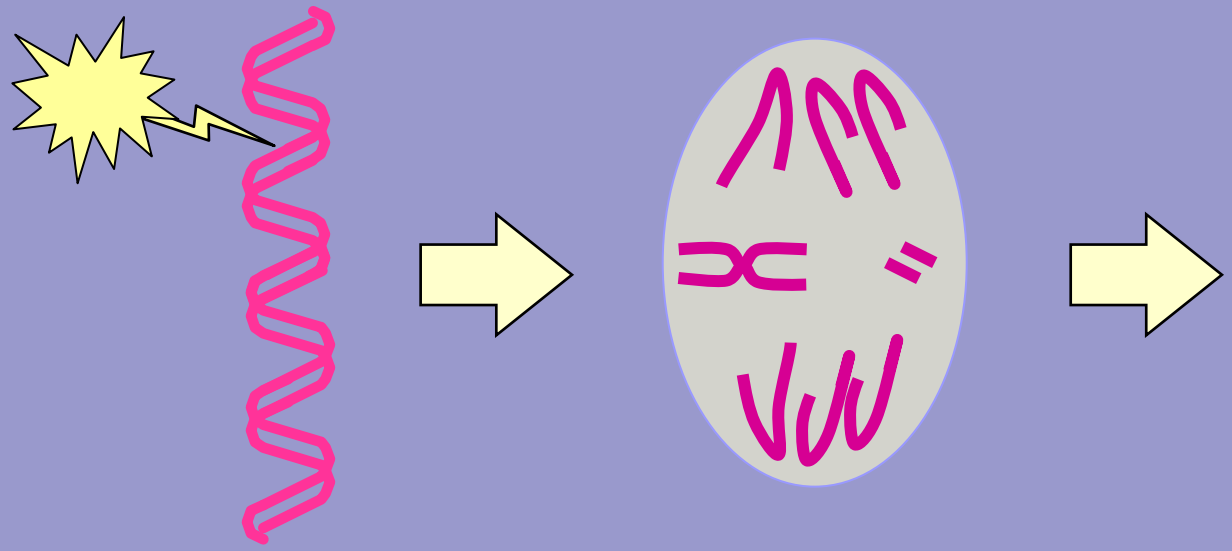
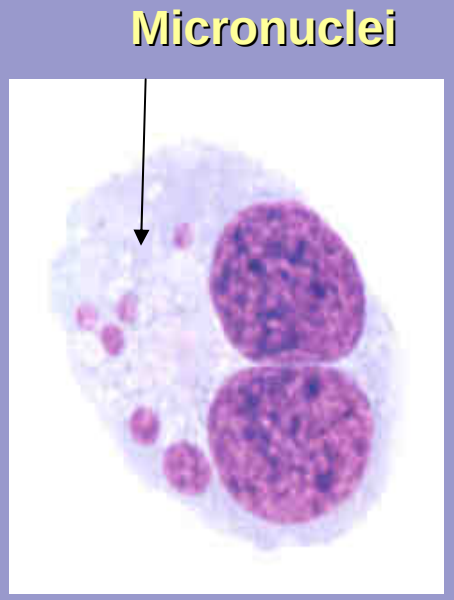
Genome damage





CYTOKINESIS-BLOCK MICRONUCLEUS (CBMN) ASSAY

- Oxidative stress
- Nutrient deficiency
- Excess calories

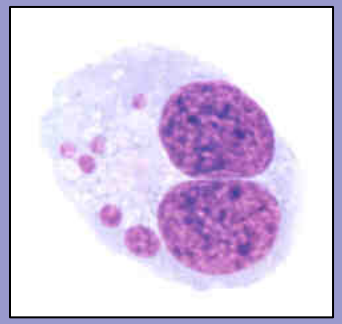
→

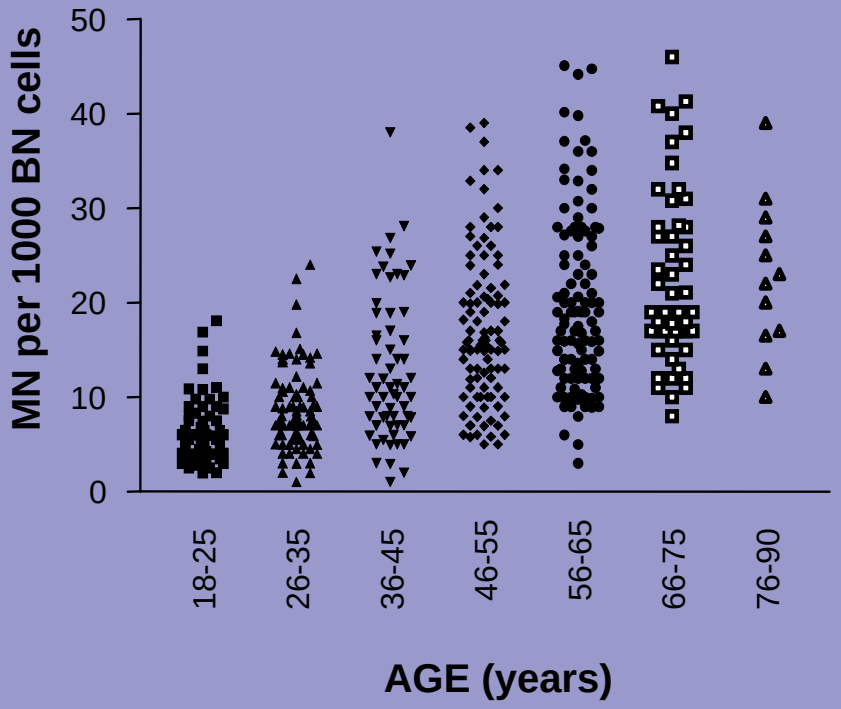
- Strand breaks in DNA
- Chromosome malsegregation
- DNA hypomethylation
- Telomere shortening

→

Human cells with damaged & unstable genomes

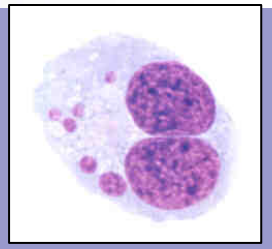
Genome damage increases with age



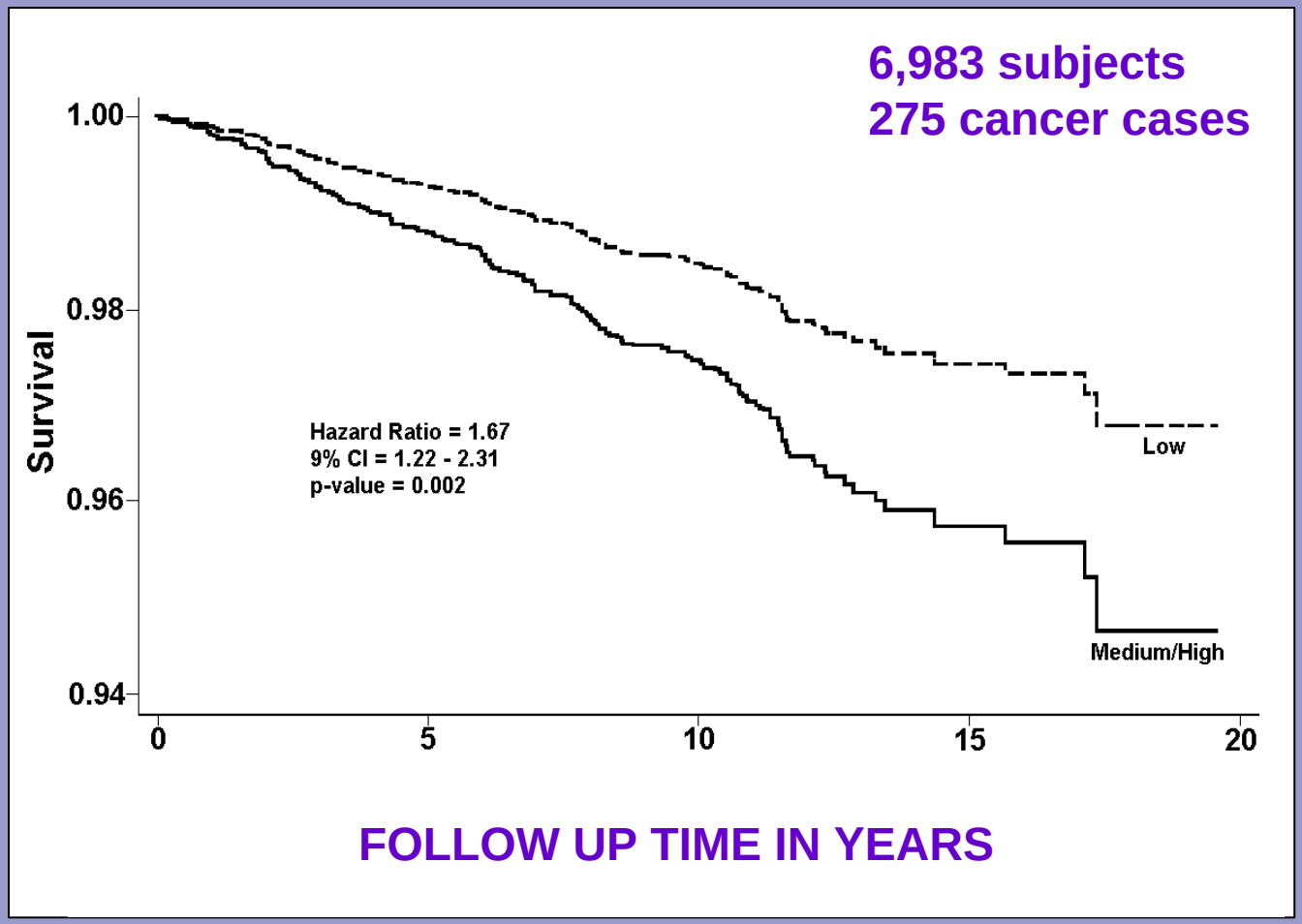


Fenech et al. 2000

Risk of cancer increases with higher MN frequency

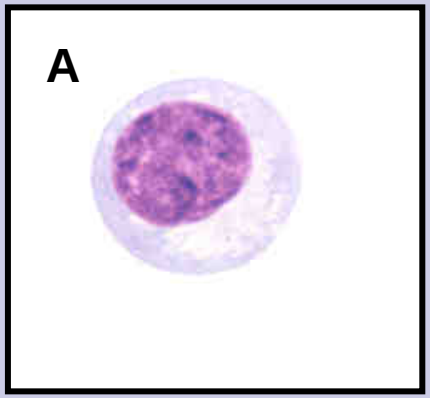


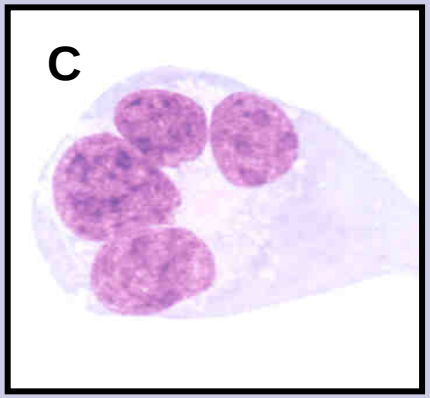
PROBABILITY OF SURVIVING WITHOUT CANCER



HUMN *project (www.humn.org)*

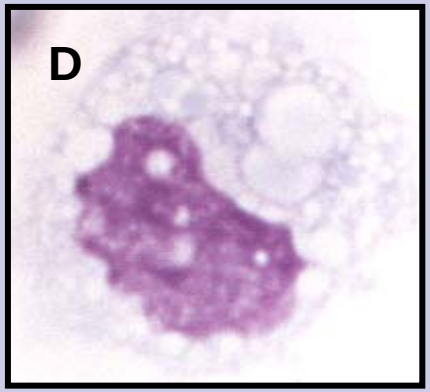
Bonassi et al (Carcinogenesis 2007)





A ,B, C

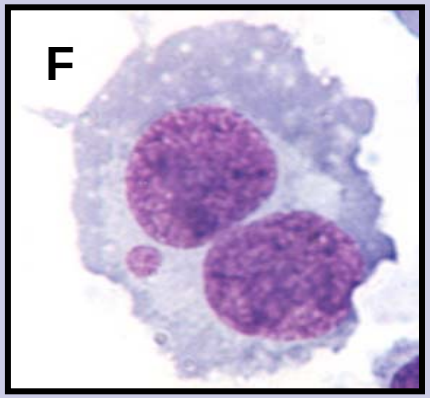
NUCLEAR DIVISION INDEX

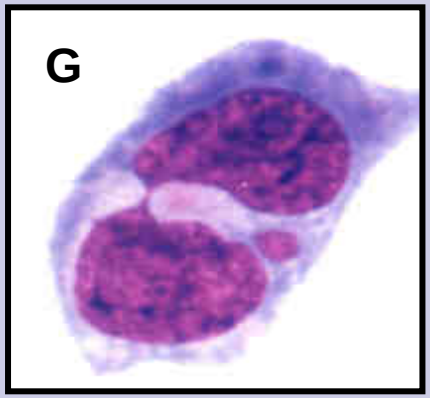


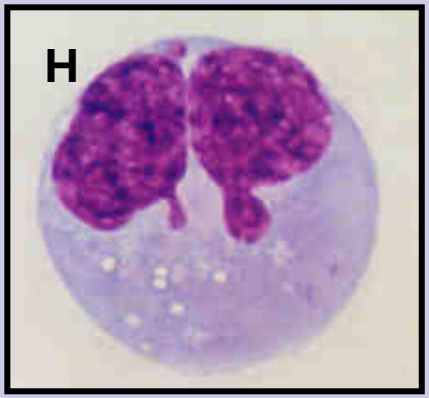
CBMN CYTOME ASSAY

D,E

CELL DEATH







F, G, H

DNA DAMAGE

CORRELATION OF PLASMA MICRONUTRIENTS WITH CBMN CYTOME ASSAY BIOMARKERS IN LYMPHOCYTES

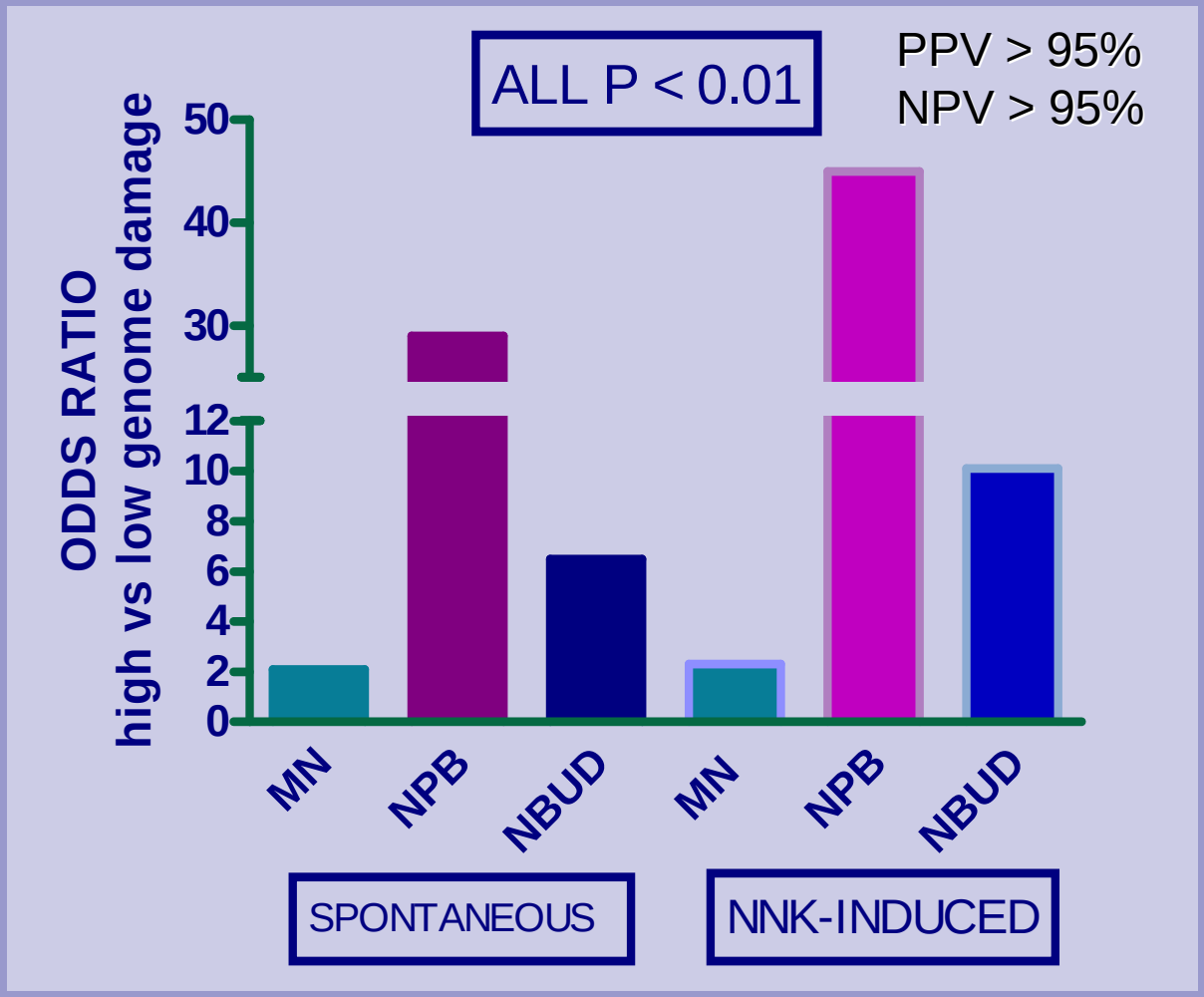
overweight/obese men (BMI>25kg/m2)

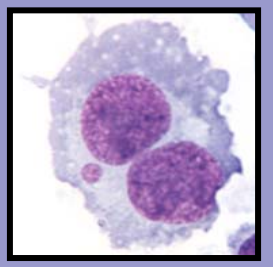
	PL Zn	PL Mg	PL Se	PL B12	PL FOL
APOP	NS	NS	NS	NS	NS
NECRO	**-0.41***	NS	NS	NS	NS
NDI	**0.34***	**0.40***	**0.34***	NS	**0.49***
MN	NS	NS	NS	**-0.32***	**-0.33***
NPB	NS	NS	**-0.46***	NS	NS
NBUD	NS	NS	NS	NS	NS

	Pl Zn ug/ml	Pl Mg ug/ml	Pl Se ug/ml	Pl B12 pmol/L	Pl Fol nmol/L
N	40	40	40	40	40
Minimum	0.66	17	71.3	99	5.5
25% Percentile	0.835	18.05	91.2	184	9.9
Median	0.905	18.75	95.5	245.5	13.6
75% Percentile	1.04	20.1	104.9	303	17
Maximum	1.515	22.2	118.4	434	26.8

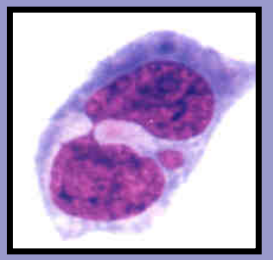
LUNG CANCER RISK IN SMOKERS ASSOCIATED WITH CBMN ASSAY BIOMARKERS IN LYMPHOCYTES

139 cases & 130 controls matched for age, gender & smoking history

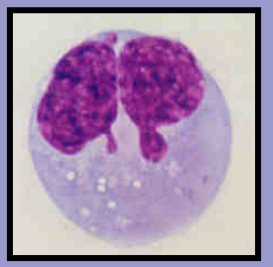




MN
Chromosome Breakage or loss



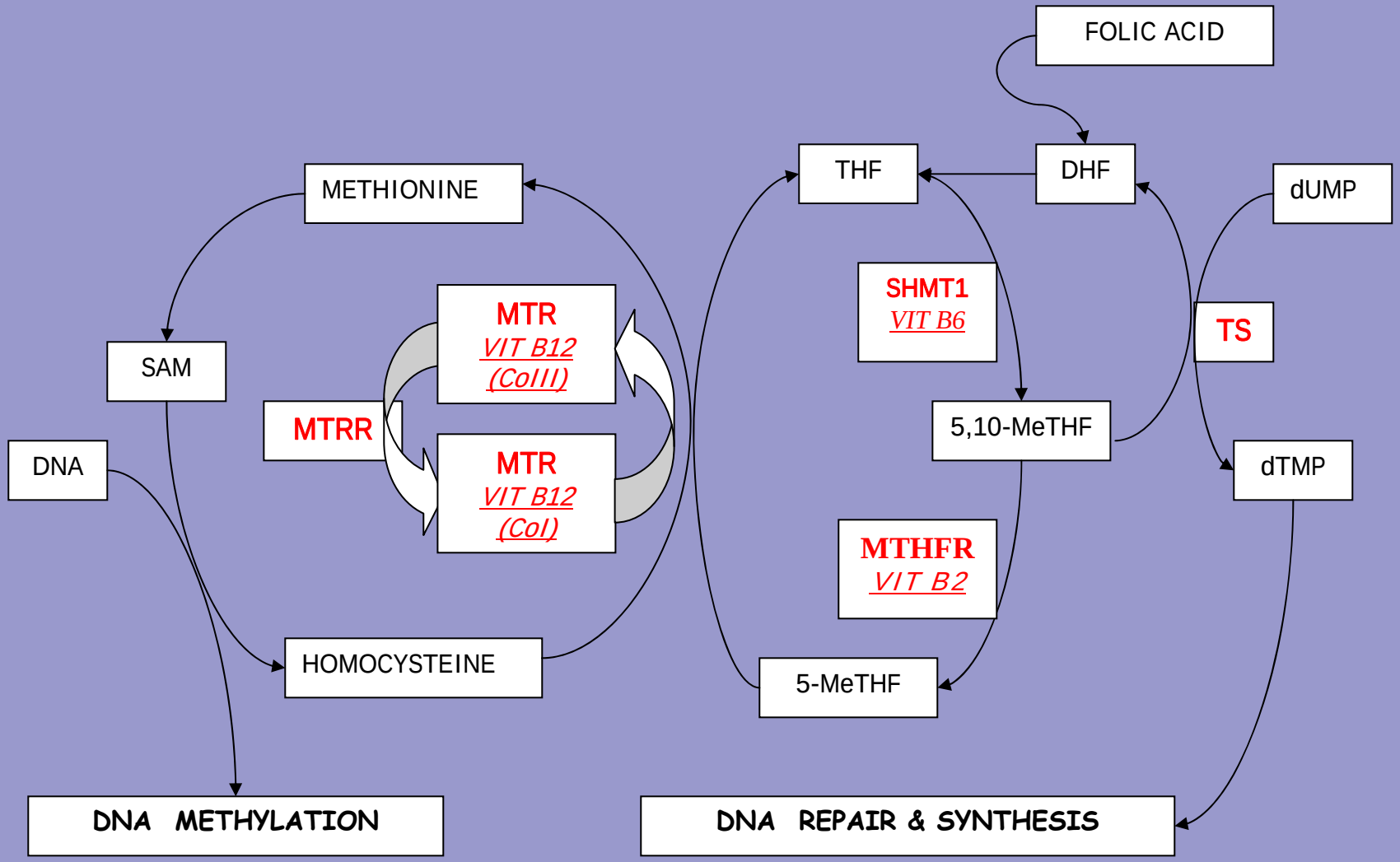
NPB :
DNA Misrepair or Telomere dysfunction



NBUD:
Gene amplification

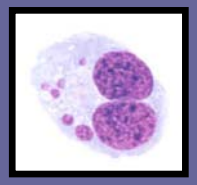
El-Zein et al Cancer Res 2006

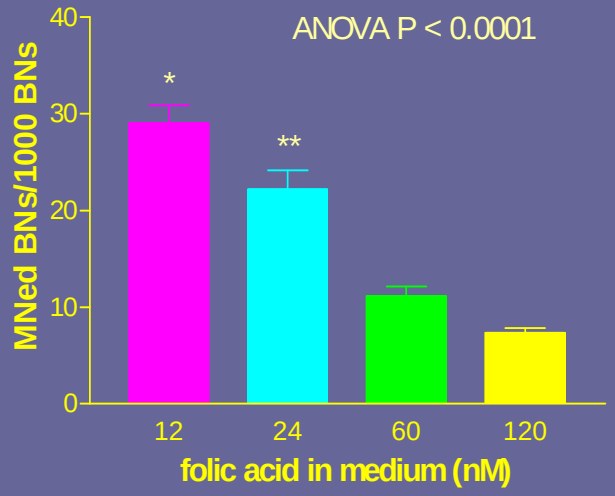
Folate, B12, B6 and B2 and genome maintenance



[A]

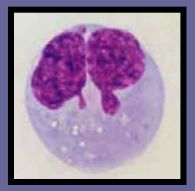
MICRONUCLEATED CELLS

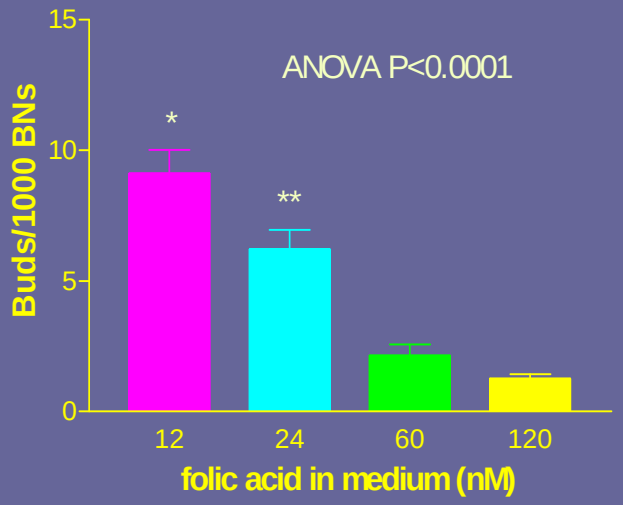




[B]

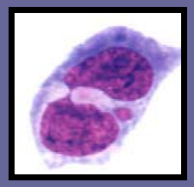
NUCLEAR BUDS

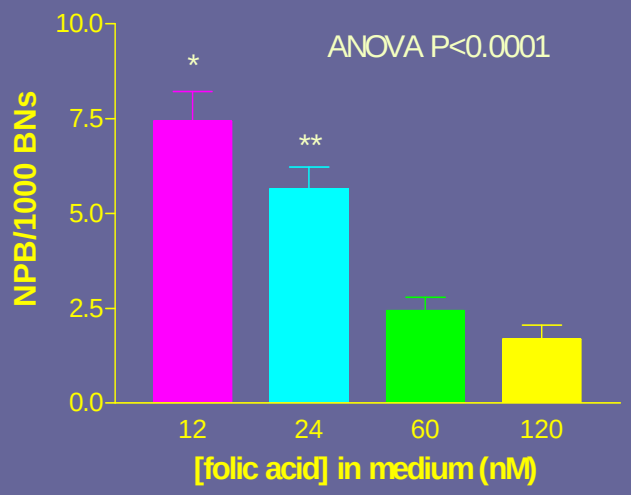




[C]

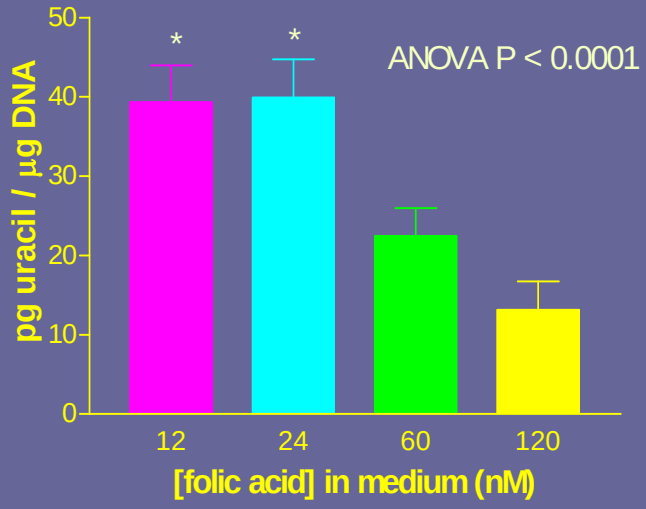
NUCLEOPLASMIC BRIDGES





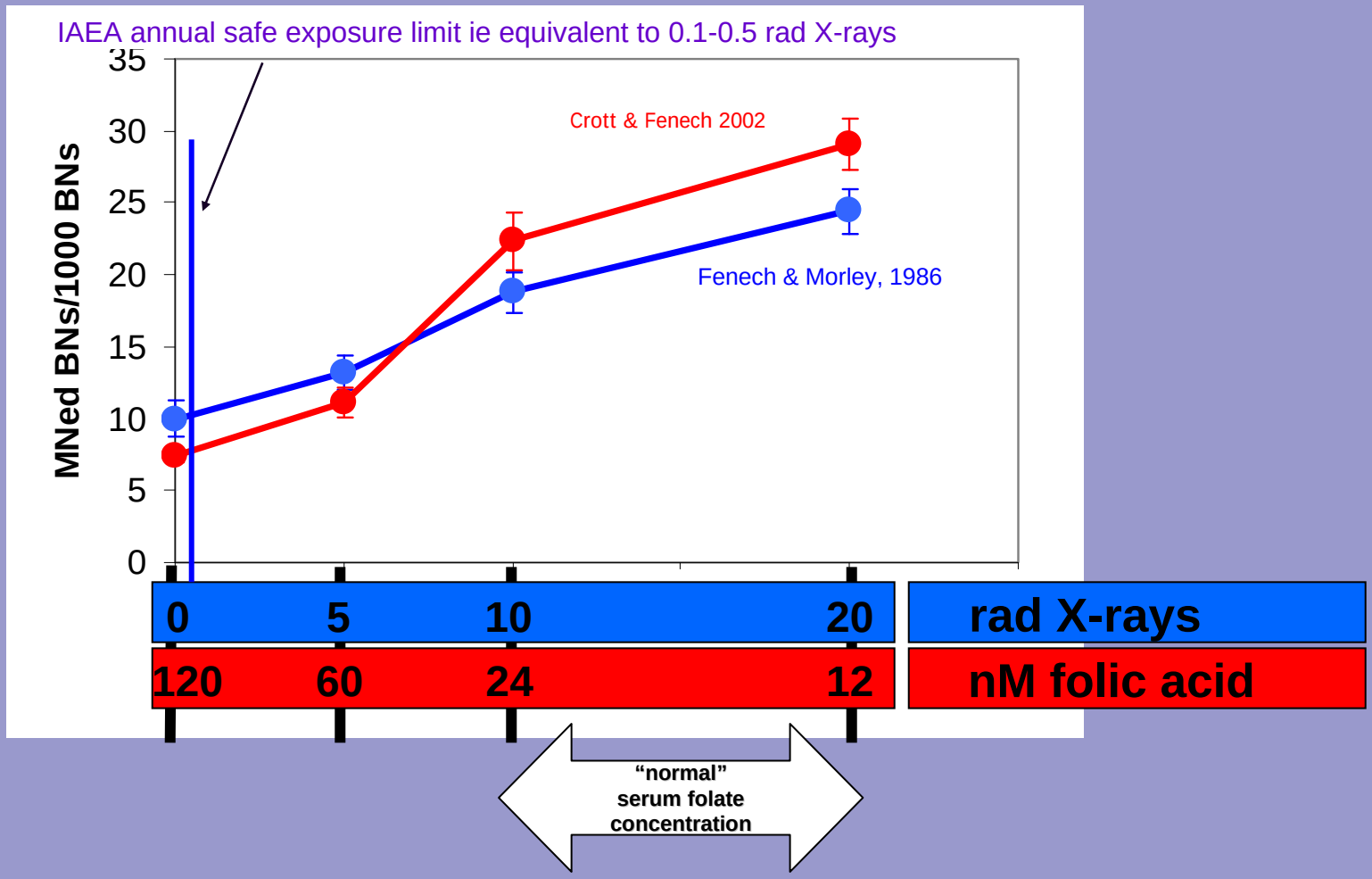
[D]

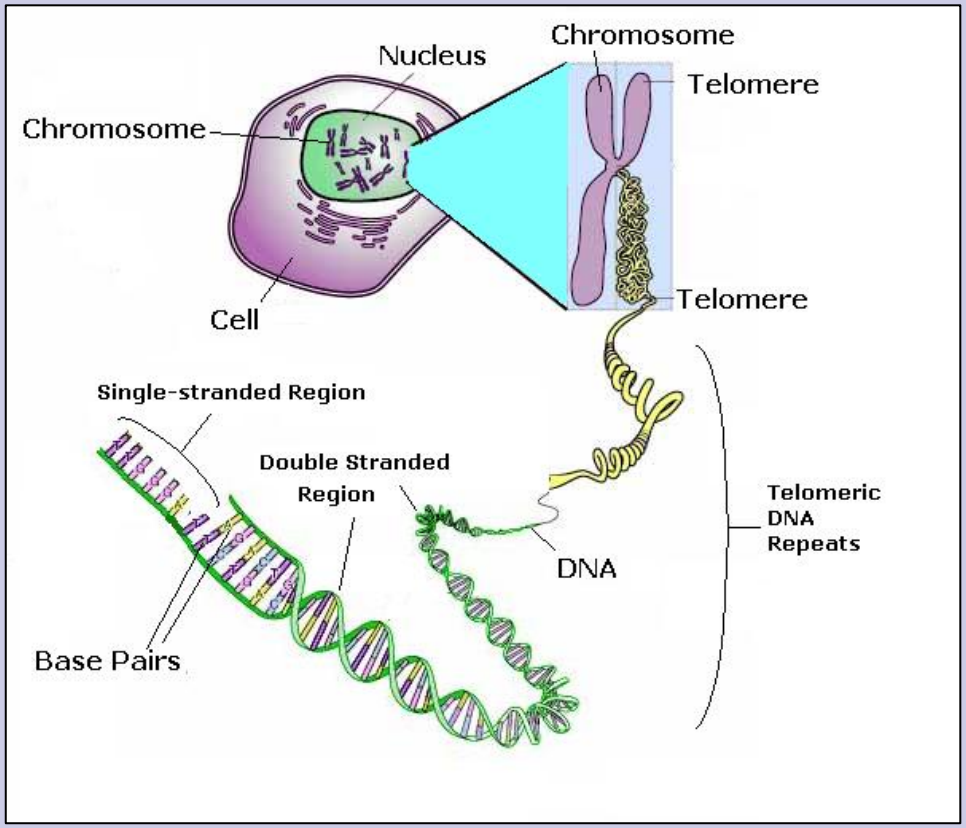
URACIL



Crott et al. Carcinogenesis 2001

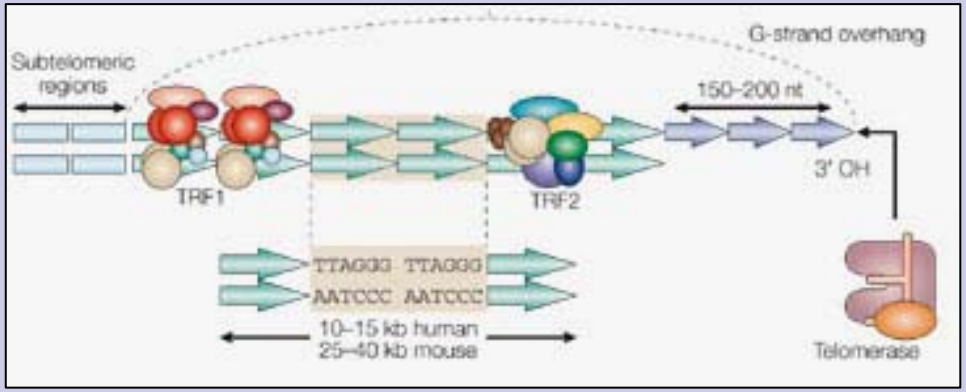
Genome damage induction by Folic acid deficiency is as important as that induced by unsafe doses of ionising radiation

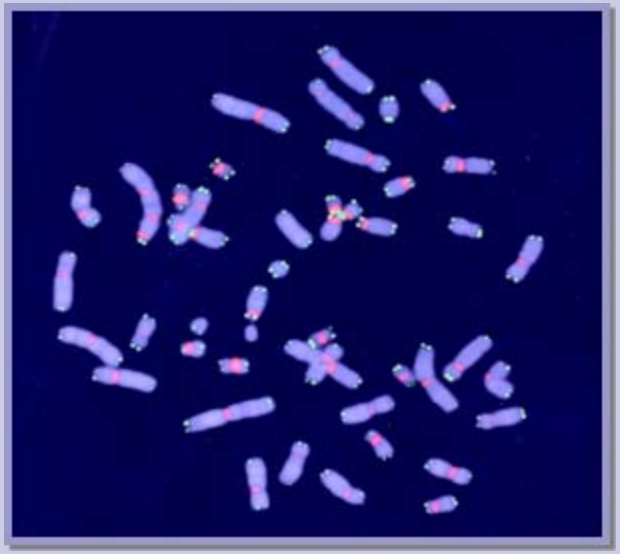


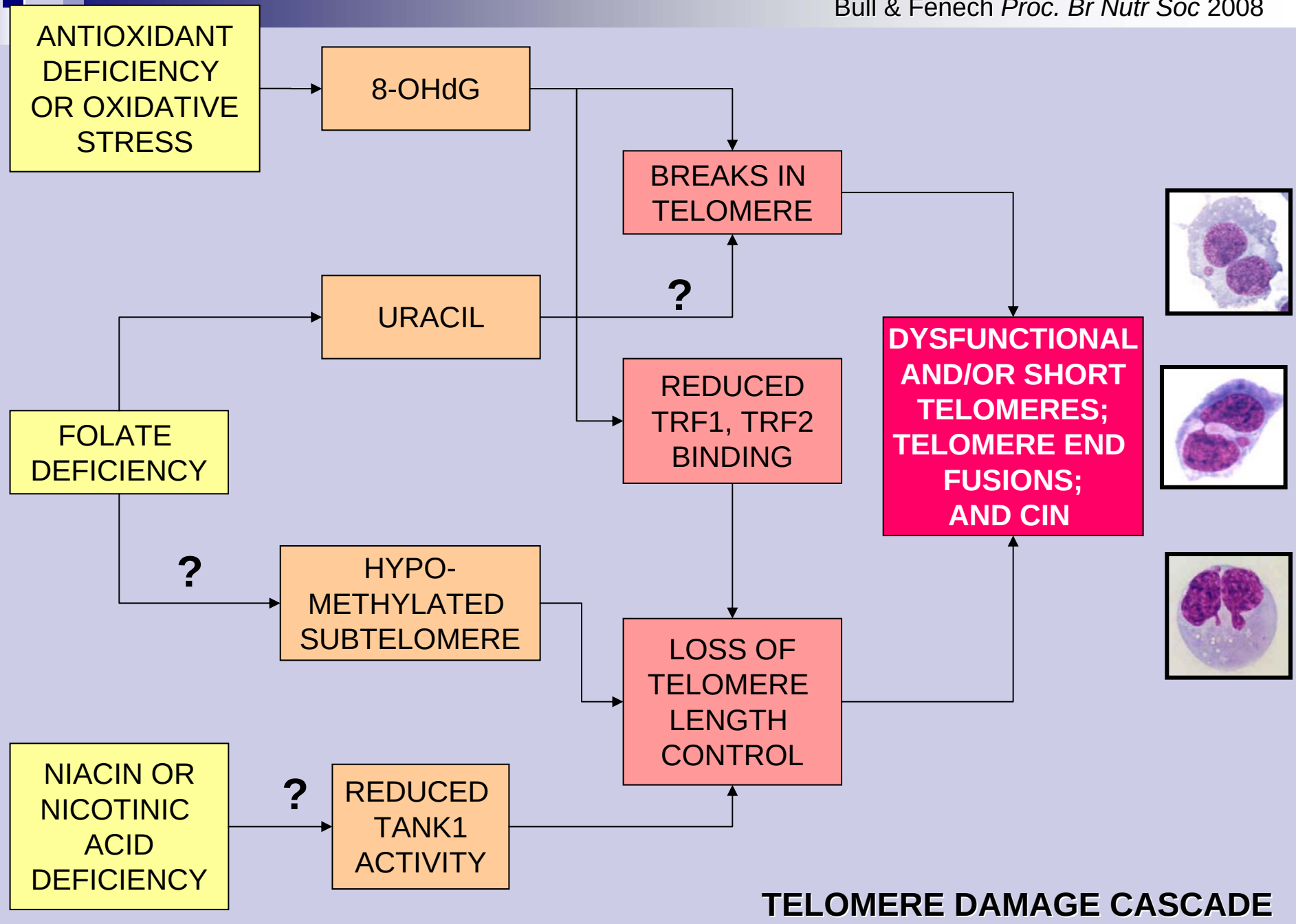


TELOMERES ARE ESSENTIAL FOR CHROMOSOME STABILITY

TELOMERE SHORTENING OR DYSFUNCTION INCREASES RISK FOR CANCER AND ACCELERATES AGEING

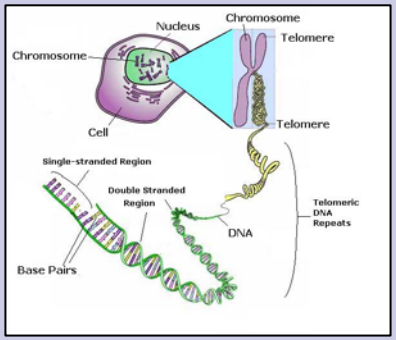


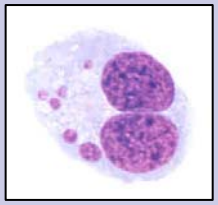


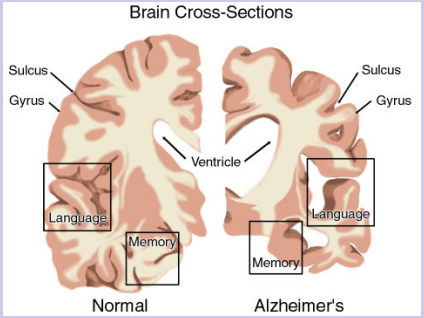


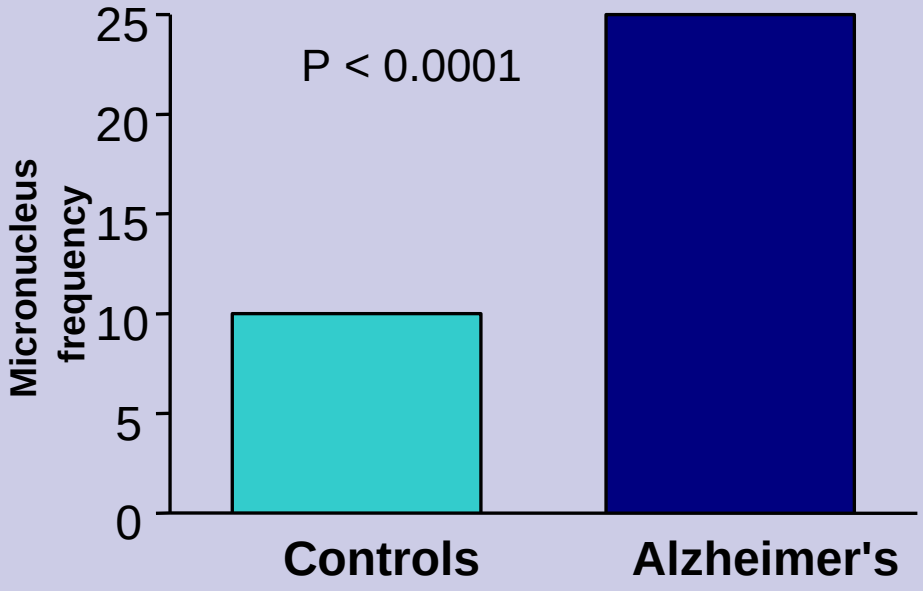
TELOMERE DAMAGE CASCADE

Increased lymphocyte DNA damage is associated with Alzheimer's disease



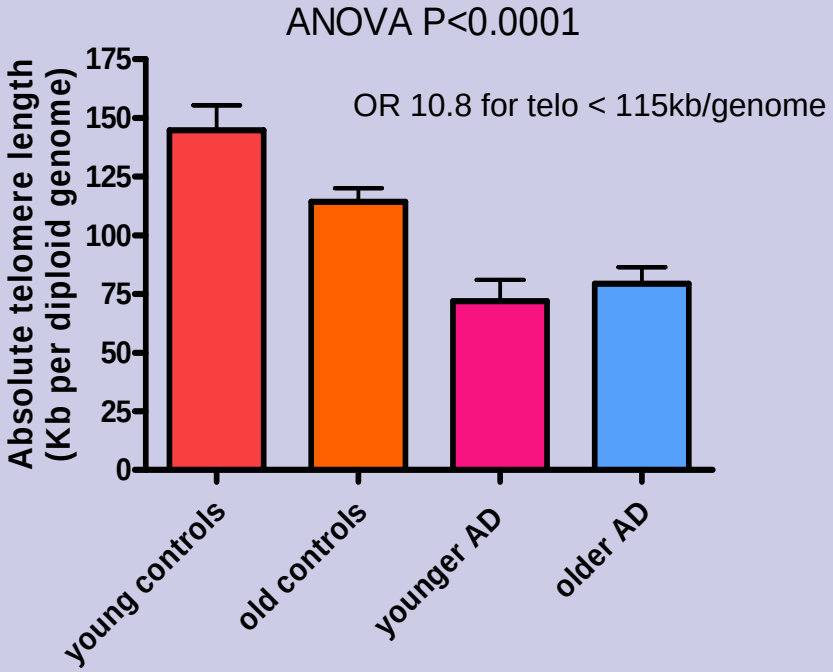






Migliore et al (1999) Cytogenetics Cell Genetics

LYMPHOCYTE TELOMERE LENGTH
IS REDUCED IN ALZHEIMER DISEASE



Thomas et al 2008 Mech Age. Dev.

Dietary factors associated with reduced risk of **Alzheimer disease**

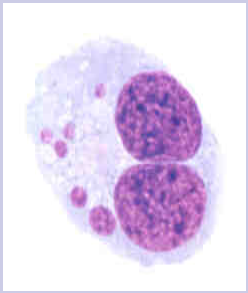
- Vitamin E (from foods)
- Folate and Vitamin B12 (from foods and supplements)
- Niacin
- Fish at least once per week
- Moderate intake of wine (1-6 drinks/week)
- Less calories and less saturated fat

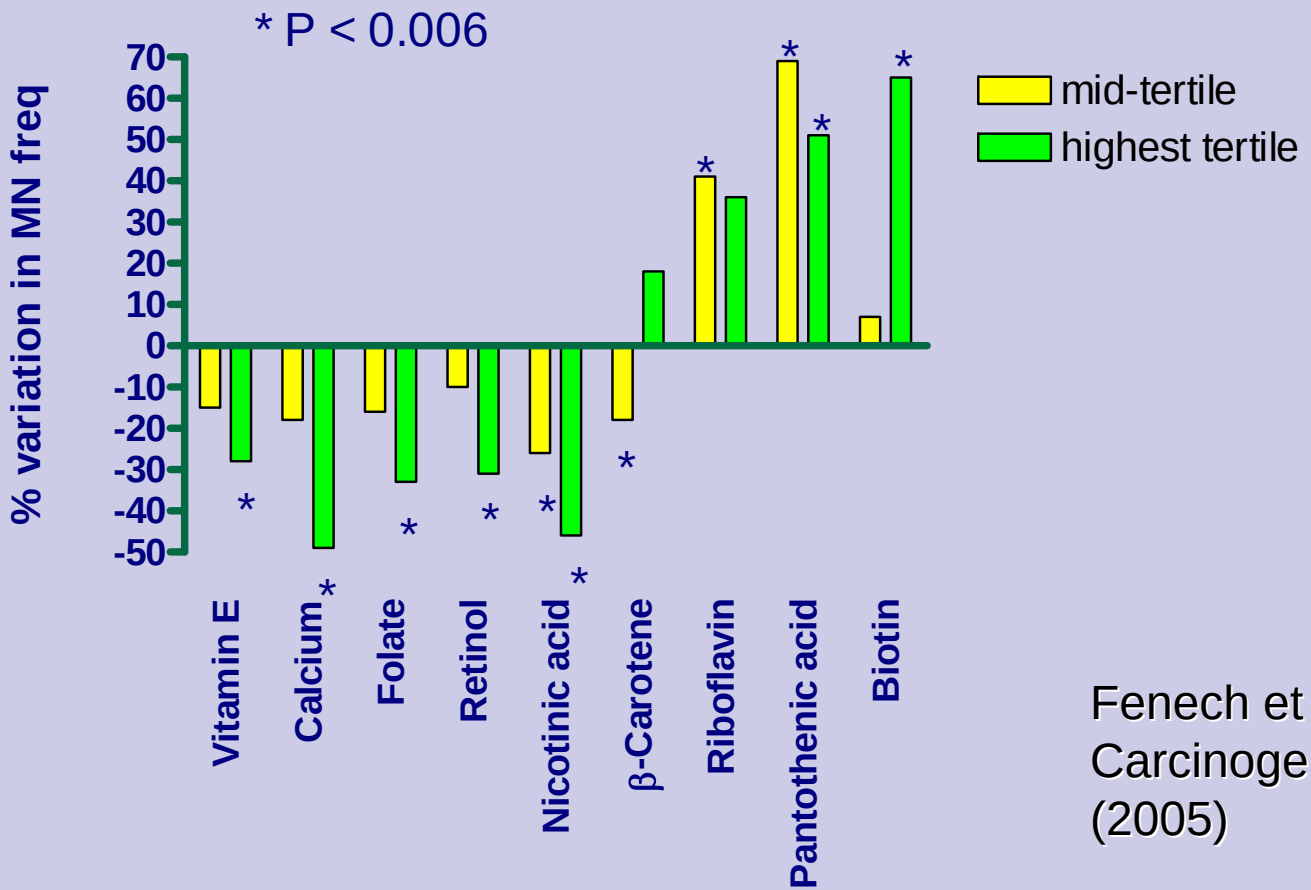
Morris MC et al. J. Neurol Neurosurg Psychiatry 2004; Luchsinger and Mayeux, The LANCET Neurology 2004

MICRONUTRIENTS AND GENOME DAMAGE

RESULTS OF ANALYSIS OF FOOD FREQUENCY QUESTIONNAIRE AND GENOME DAMAGE DATABASE

% variation in genome damage with increased intake relative to lowest tertile of intake

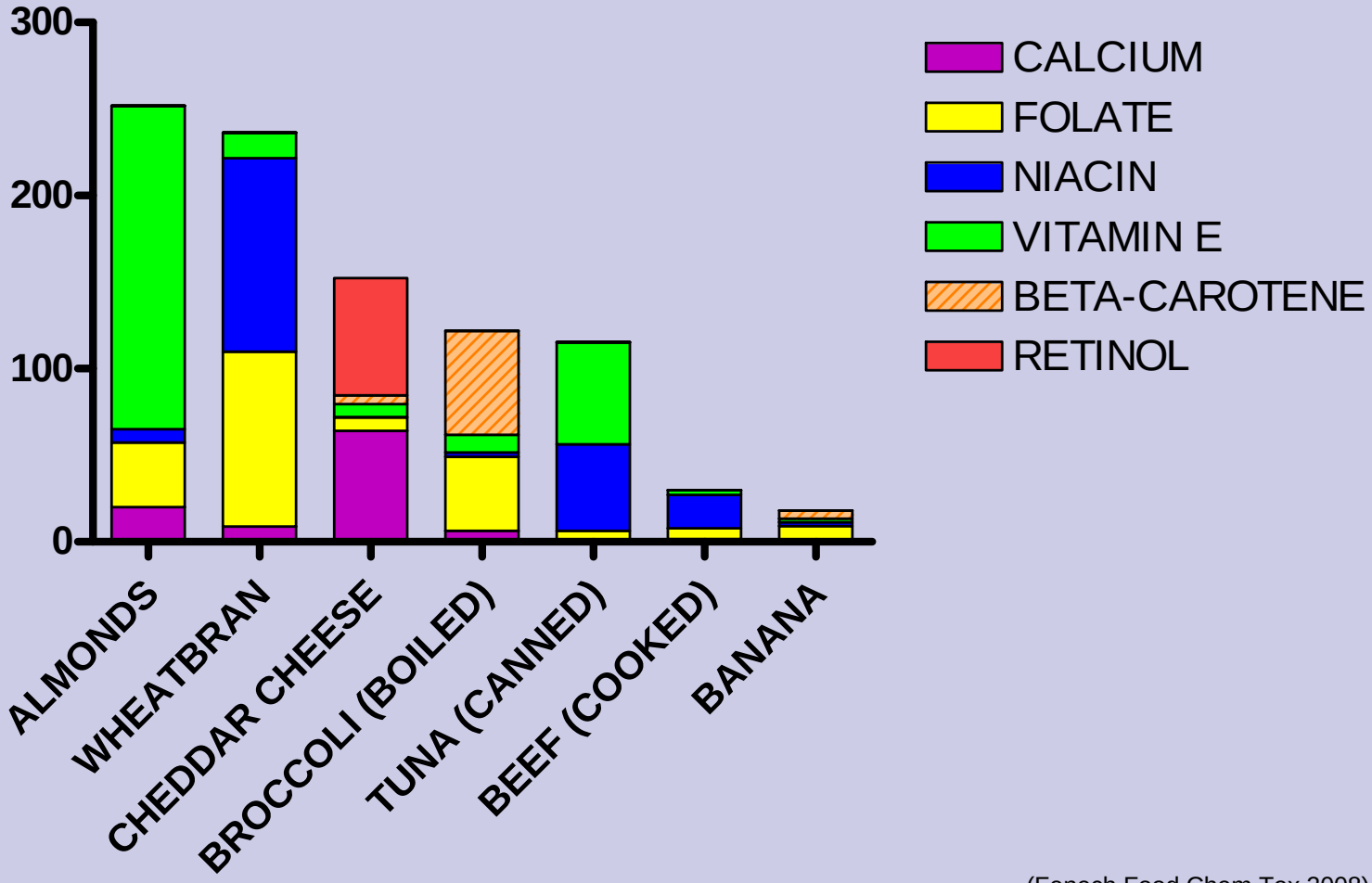




Fenech et al. Carcinogenesis (2005)

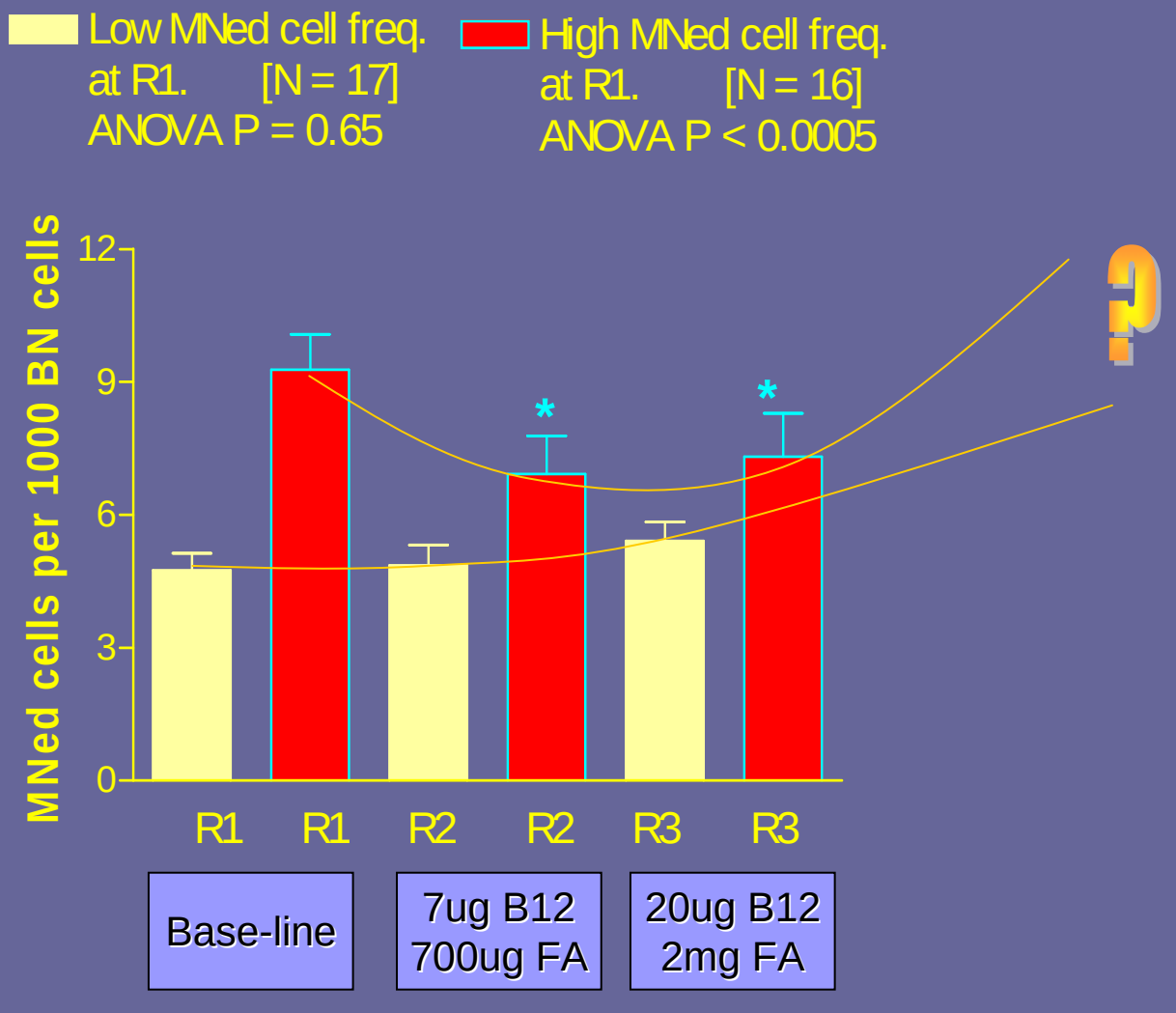
Q. Which dietary pattern will work for your genotype ?

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



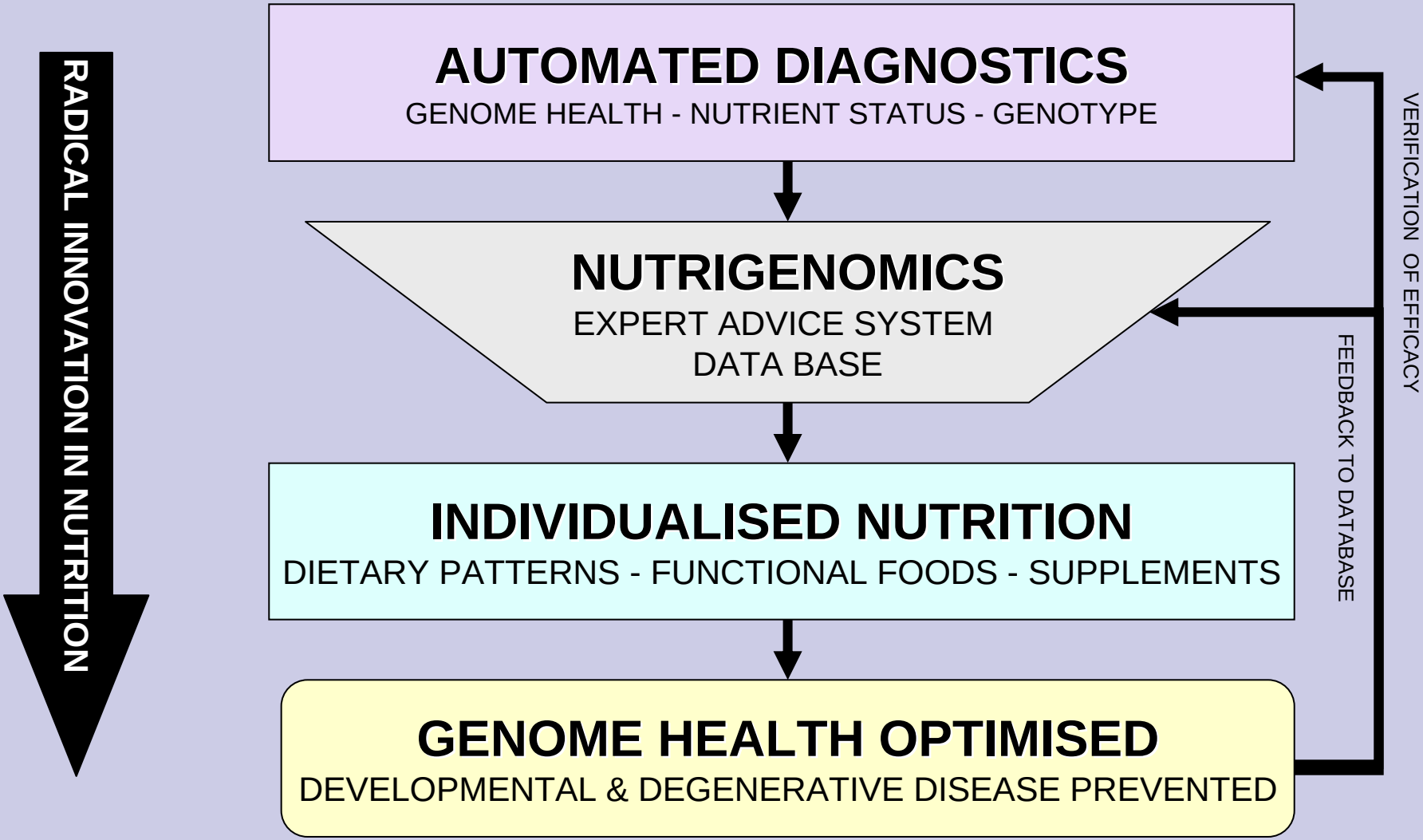
(Fenech Food Chem Tox 2008)

Supplementation with 3.5 times RDI folic acid & vit B12 reduces micronucleus index by 25 % in subjects with above average chromosome instability



Fenech et al. 1998 Carcinogenesis

GENOME HEALTH CLINIC



Funding: Reach 100, NCEFF

Fenech M (2005) Mutagenesis 20: 225-269

ABC Catalyst, DNA Doctor Story

Reach 100
PREVENTION FOR LIFE

www.reach100.com.au

Launched by
Minister of Community Health
& Ageing on2nd July 2007

REACH100 DOCTORS

•INTERACT WITH CLIENTS TO EXPLAIN GENOME HEALTH TEST RESULTS
• PROVIDE NUTRITIONAL AND LIFE-STYLE ADVICE
•VERIFY WITH SECOND TEST THAT DNA DAMAGE IS ACTUALLY DECREASED
•IF NOT, FURTHER ADJUSTMENTS TO RECCOMMENDATIONS ARE MADE

CSIRO GENOME HEALTH NUTRIGENOMICS LABORATORY

•PERFORMS CBMN ASSAY TEST,
•INTERPRETS RESULT FOR REACH100 DOCTORS
•PROVIDES SCIENTIFIC UPDATES ON DIETARY, LIFE-STYLE AND GENETIC VARIABLES AFFECTING DNA DAMAGE
•BUILDS DE-IDENTIFIED GENOME HEALTH NUTRIGENOMICS DATA BASE

Acknowledgements

**Kellogs Pty Ltd, MLA, NCEFF,
Blackmores, Nutrilite/Amway
NHMRC, Cancer Council SA, NIH/NIAID
EU CancerRiskBiomarkers Prog.**