



SYDNEY
ADVENTIST
HOSPITAL



Australasian
Research Institute

ARI Research laboratory

Purpose and Scope
2010





Australasian
Research Institute

Our Vision

The ARI will be a nationally recognised research leader in integrated multidisciplinary research into the cause and treatment of lifestyle and degenerative disease



Australasian
Research Institute

Our Aim

The ARI aims to be a multidisciplinary centre linking research in the basic, nutritional and medical sciences with clinical and community health practices to better understand and treat the causes of human lifestyle and degenerative disease



To satisfy its charter the ARI has 2 key areas of responsibility

- 1) Conduct innovative high quality research (both basic and clinical) targeted at human health and disease.

- 2) To provide *assistance and support* to SAH clinical staff, specialists and trainees and Avondale staff and students:
 - development of the research question and study plan and the most appropriate way to collect and collate data.
 - statistical review of gathered data
 - writing for publication
 - preparation of project material for GRANT application

Perspective - Cause of disease



Australasian
Research Institute

1° contributors to disease

Environmental

Psychosocial stress
(HPA activation)
Microbial Infection
Physical damage
Chemical toxin(s)
Radiation toxin(s)

Lifestyle choices

↓Exercise/physical activity
↑Exercise/physical activity
↓Nutrition
↑Nutrition
↓Sleep

Inheritance/genetic

Multiple loci
Degenerative (4000/pers)

2° biochemical/physiological dysregulation

↑ Immune activation Oxidative (free radical) stress other

3° biological changes

DNA damage Cell degeneration Physiological dysfunction

4° disease (top 5 killers)

Cancer (32%)

Circulatory diseases (32%)

COPD (4%)

Dementia (3%)

Diabetes 1&2 (3%)

Circulatory diseases (37%)

Cancer (26%)

Dementia (7%)

COPD (3%)

Diabetes 1&2 (3%)

Perspective - Cause of disease



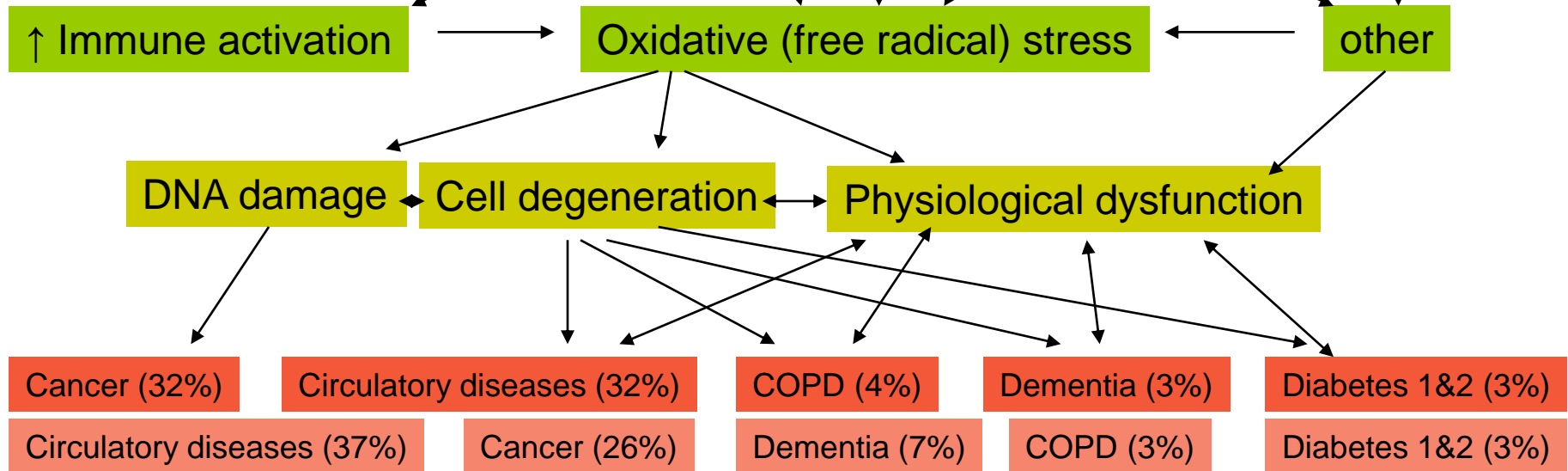
Environmental

Psychosocial stress
(HPA activation)
Microbial Infection
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↓ Exercise/physical activity
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↓ Nutrition
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↓ Sleep

Inheritance/genetic





Environmental

Psychosocial stress
(HPA activation)
Microbial Infection
Physical damage
Chemical toxin(s)
Radiation toxin(s)

Lifestyle choices

↓ Exercise/physical activity
↑ Exercise/physical activity
↓ Nutrition
↑ Nutrition
↓ Sleep

Inheritance/genetic

↑ Immune activation

Oxidative (free radical) stress

other

DNA damage

Cell degeneration

Physiological dysfunction

Cancer (32%)

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Overall Goal:

- Our research aims to understand the impact of nutrition and lifestyle on performance and health throughout all stages of life.

Our specific objectives are to:

- characterise the impact of nutrition and lifestyle on the body's level of oxidative stress.
- study issues of diet and lifestyle in communities with identified health needs.
- identify and/or develop nutritional therapies (incl. herbal) that promote human performance (mental or physical) or alleviate disease.



The Australian National Research Priorities (NRP's)

The Australian government's department of Innovation Industry Science and Research in its June 2009 update identified Australia's NRP's as:

- An environmentally sustainable Australia
- Promoting and maintaining good health**
- Frontier technologies and transforming Australian industries
- Safeguarding Australia

*The priority goals for: **Promoting and Maintaining Good Health** are:*

- A healthy start to life
- Ageing well, ageing productively
- Preventive healthcare
- Strengthening Australia's social and economic fabric



Pure air

Sunlight

Abstemiousness (*no tobacco,
coffee, tea or alcohol*)

Rest

Exercise

Proper diet (low calorie,
vegetable-rich)

Use of water

Trust in GOD

E.G. White MH 1905



The Australasian Research Institutes research laboratory

Will possess:

Spectrophotometry/fluorimetry

Protein electrophoresis

HPLC small molecule analysis

PCR (mRNA)

Respiratory gas analysis (metabolic cart)

GC-MS

These will enable the lab to:

1) Changes to body biochemistry based on diet/lifestyle factors

2) Assess impact of diet/lifestyle on oxidative stress markers

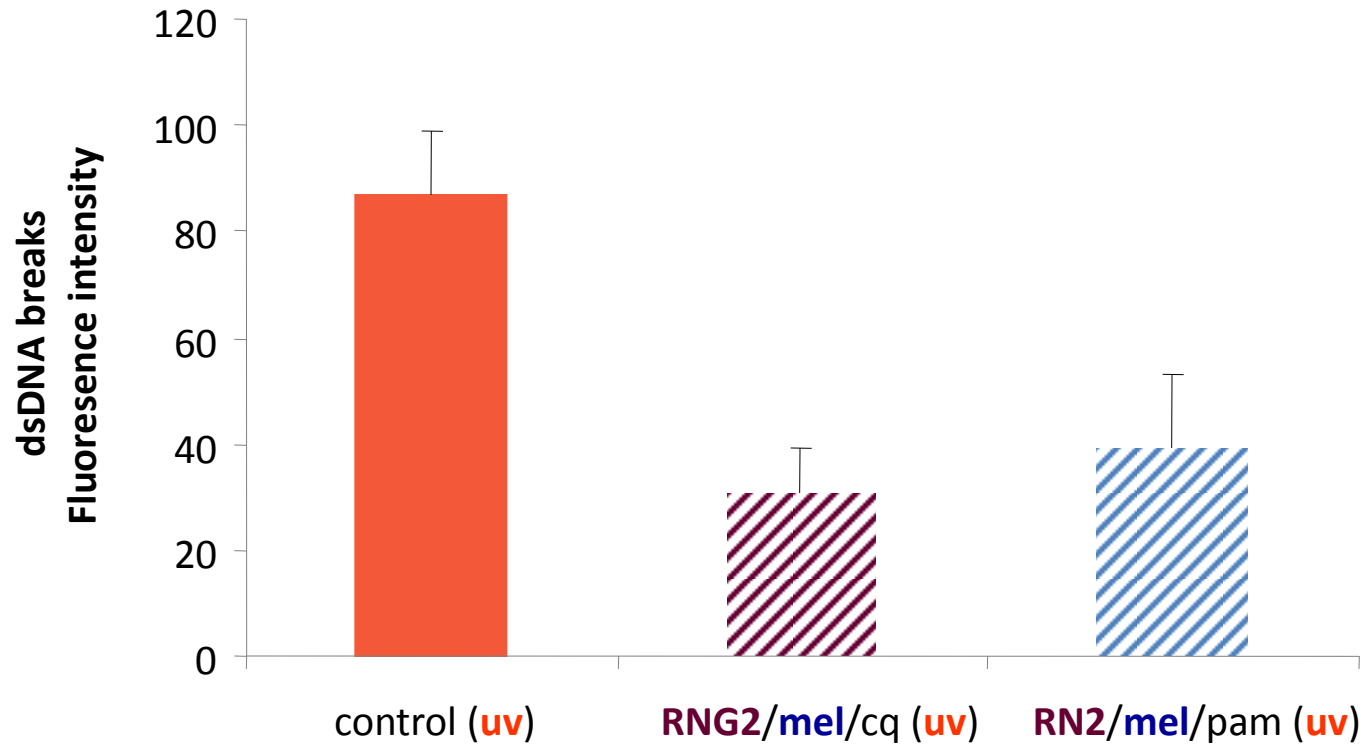
2) Human tissue culture; biochemical characterization of specific

Tissues enabling development of pharmacological testing of nutritional

Therapeutics (e.g. polyphenols to improve DNA repair in UV damaged skin

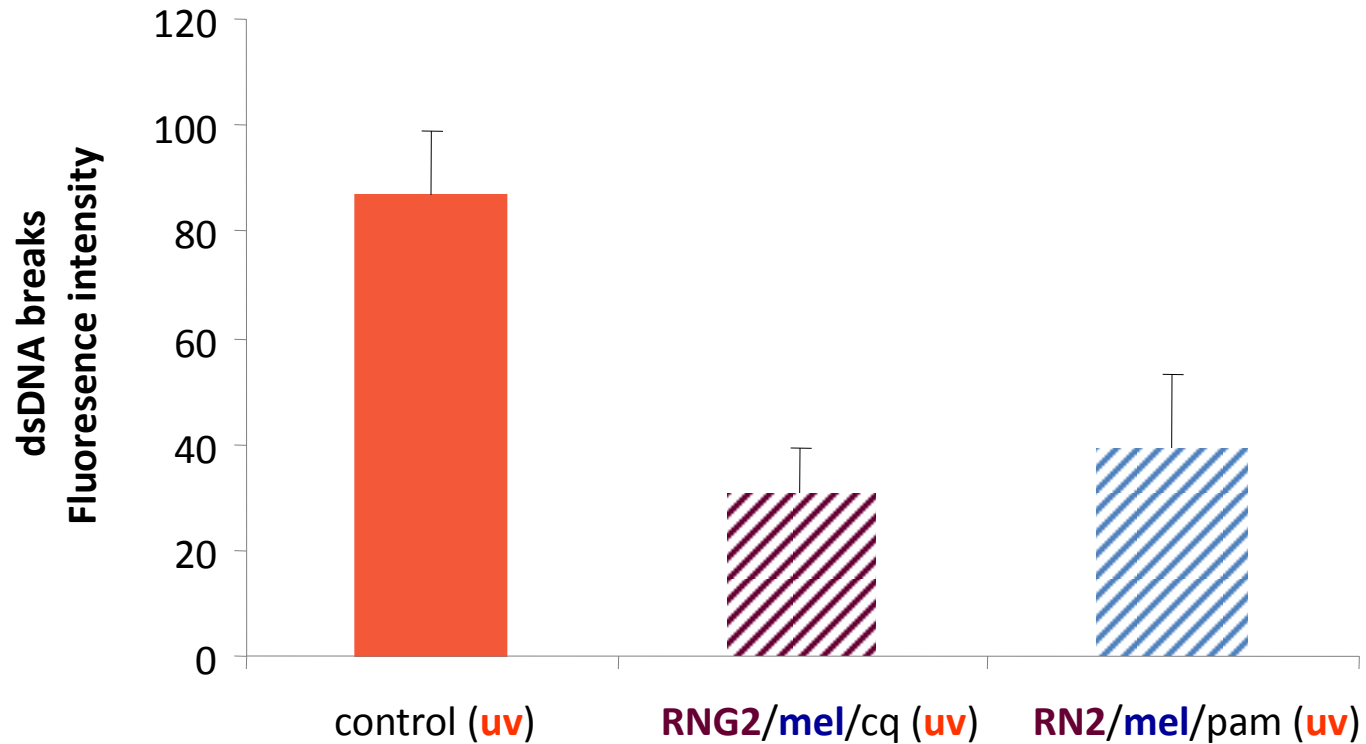
Research Highlights (selected)

1. Skin repair (after UV damage)

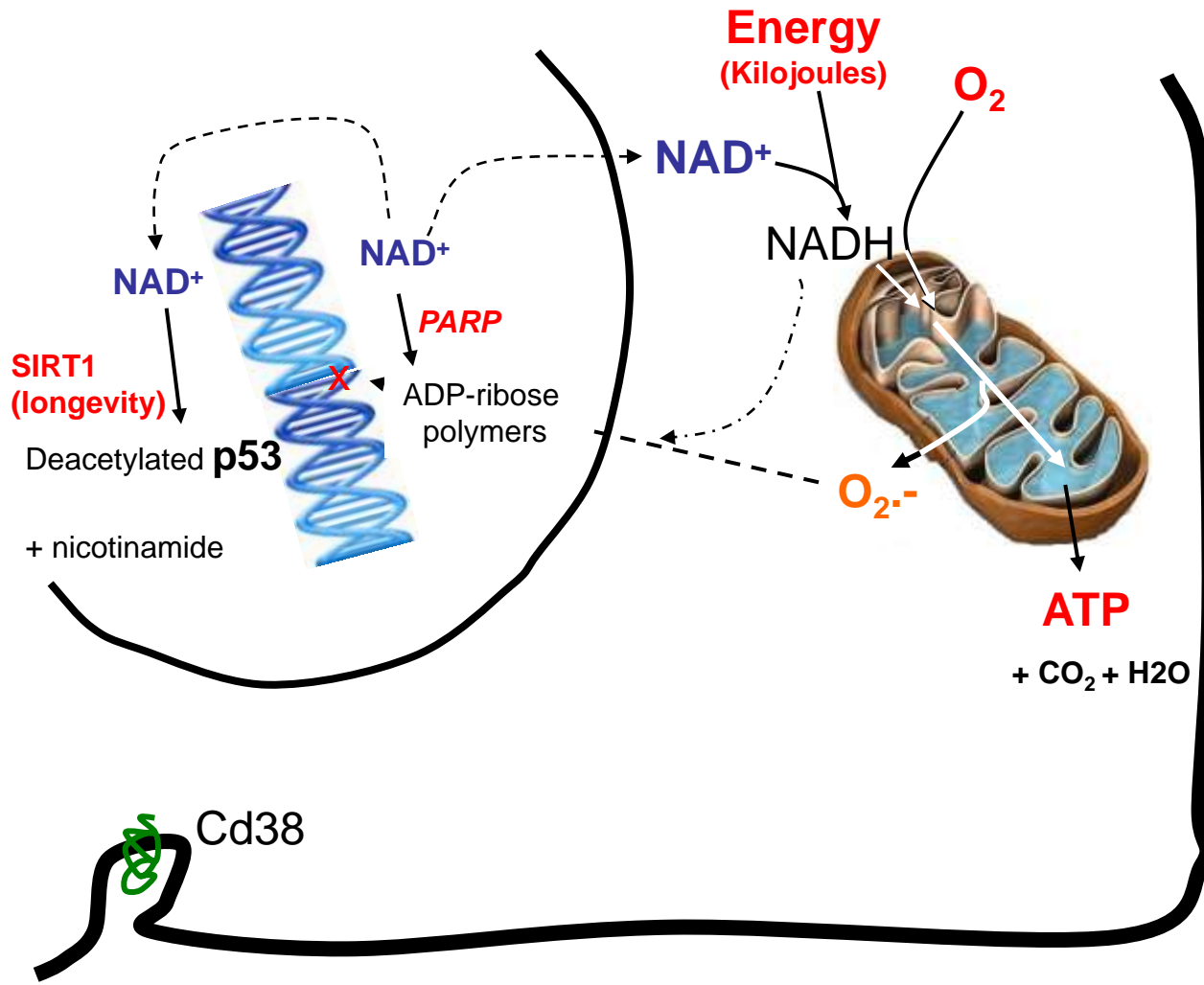


Research Highlights (selected)

1. Skin repair (after UV damage)



Background: Importance of NAD⁺



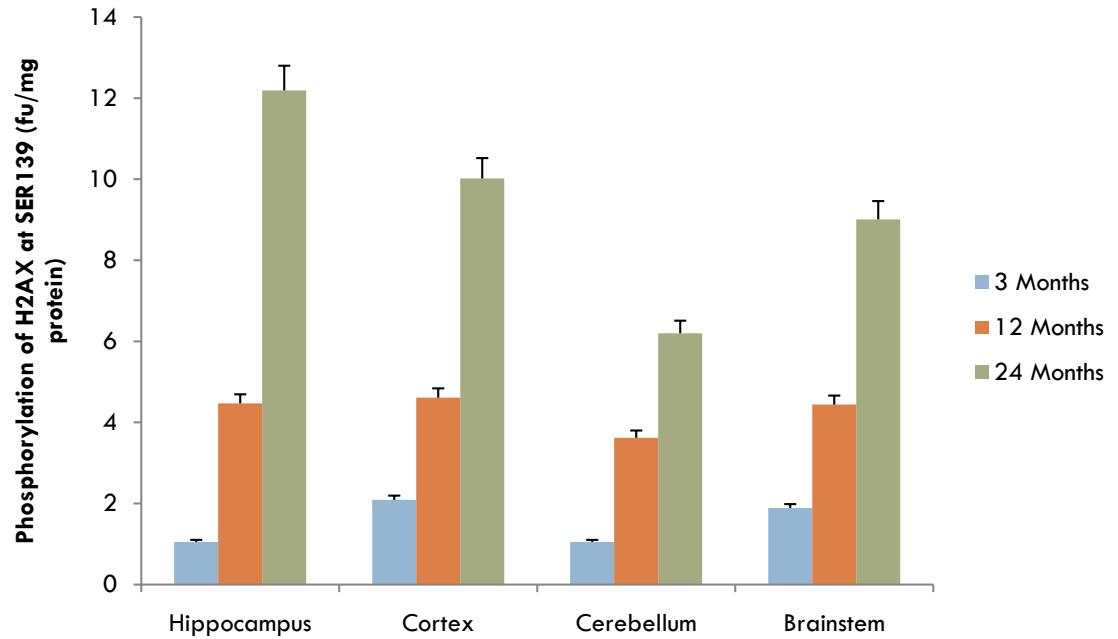
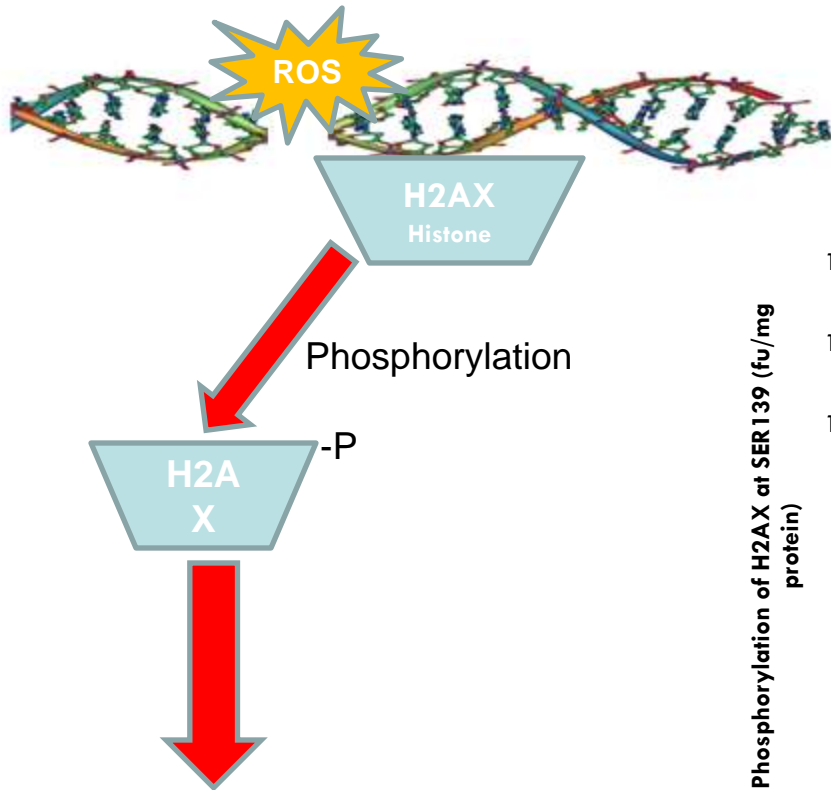
NAD as a **cofactor** for

- ATP production
- dehydrogenase reactions

NAD as a **substrate** for

- DNA repair enzyme poly(ADP-ribose) polymerase (PARP)
- transcriptional regulation (Sirtins)
- Secondary messenger signaling (CD38)

DNA Damage increases with age (Rat)

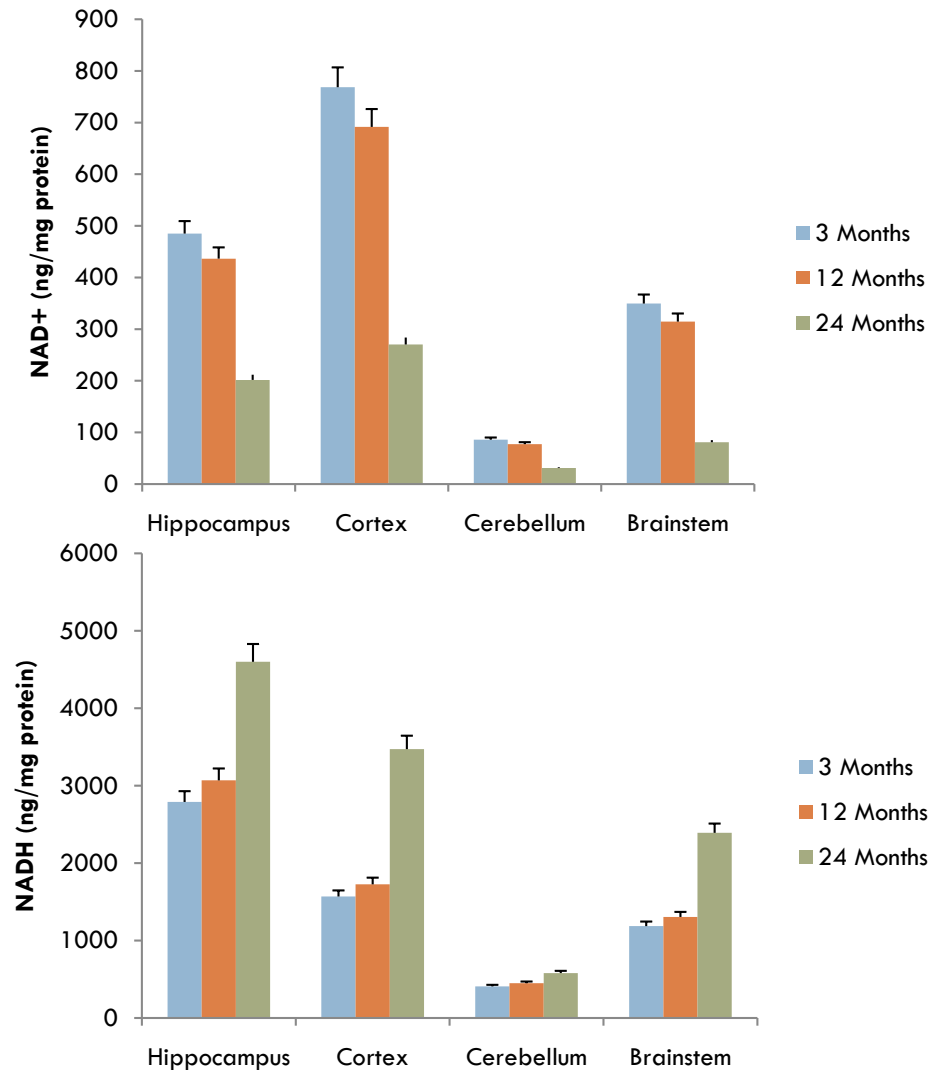
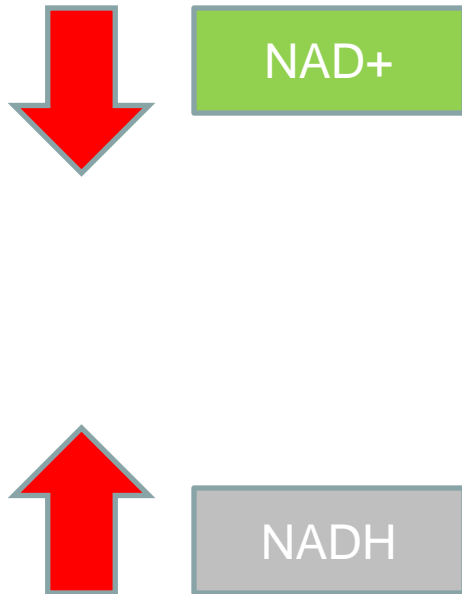


•Delayed Cell Proliferation

•Repair of Damaged DNA

NAD⁺ levels decrease with Age (rat)

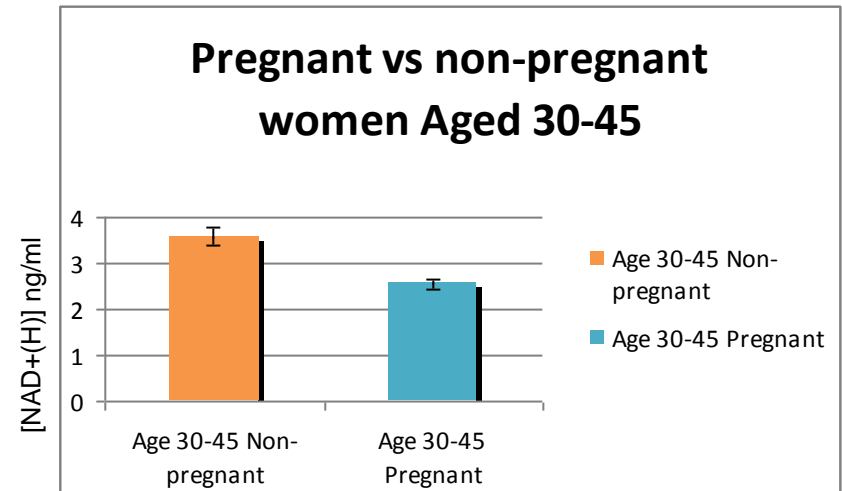
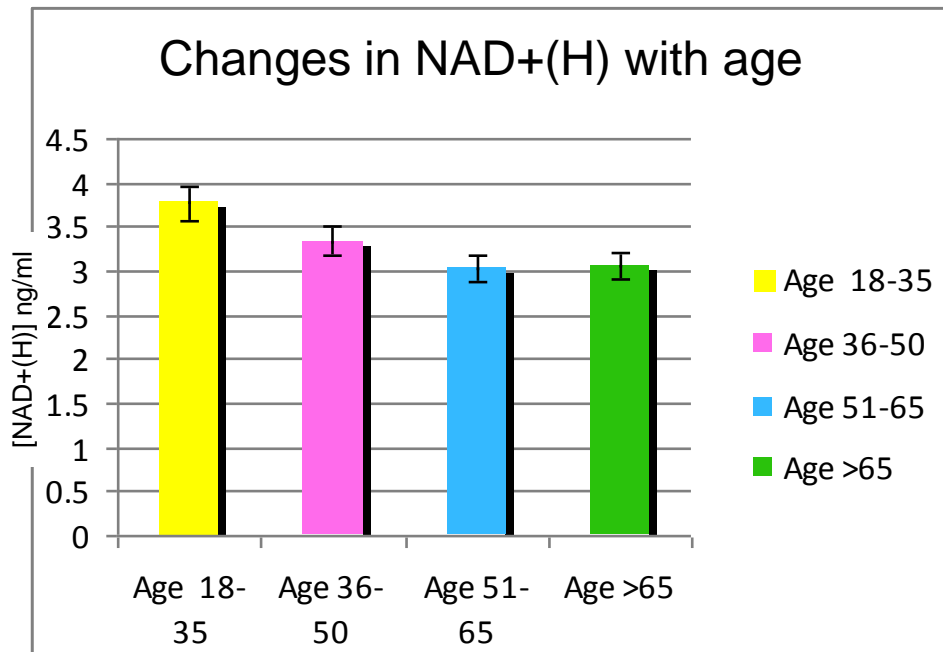
(as predicted)



Prelim...Results

Changes in NAD+(H) with age (Human serum)

Y. Chua (Hon student U.Syd)





Age related Changes in NAD+ Metabolism Oxidative stress and Sirt1 activity in human muscle.

Quantitation of key markers of oxidative stress and inflammation in human cerebrospinal fluid and correlation with diet, lifestyle and psychosocial factors.

Quantitation of NAD+(H) levels in normal human plasma: correlation with age and oxidative stress.

Cord Blood Banking – An Australian Experience Identification of Factors that affect Post Thaw Stem Cell Viability and Recovery

Pilot study to assess the incidence and efficacy of treatment of H.pylori infection in a representative population from the Gyuto Monastery in Northern India.

Characterisation of the effect of polyphenol fortified red grape juice on markers of oxidative stress and redox potential in healthy human subjects.

Insulin resistance and childhood diabetes (Healthy under the skin you're in).

Comparison of adipocytokine levels in age, sex and BMI matched vegetarian versus non-vegetarian adults

Involvement of the kynurenine pathway in the persistence of childhood and adult brain tumours

Assessment of the impact of massage therapy (Bowen Therapy) on the experience of pain, anxiety, nausea and fatigue in cancer patients

Survey of Caffeine (+ energy drink) intakes in Australian adolescents

PhD students

Investigation of the efficacy of community-based lifestyle education programs in reducing metabolic risk factors in adults.



- 1. Age related Changes in NAD⁺ Metabolism Oxidative stress and Sirt1 activity in human muscle.**
- 2. Quantitation of key markers of oxidative stress and inflammation in human cerebrospinal fluid and correlation with diet, lifestyle and psychosocial factors.**
- 3. Quantitation of NAD⁺(H) levels in normal human plasma: correlation with age and oxidative stress.**
- 4. Cord Blood Banking – An Australian Experience Identification of Factors that affect Post Thaw Stem Cell Viability and Recovery**
- 5. Pilot study to assess the incidence and efficacy of treatment of H.pylori infection in a representative population from the Gyuto Monastery in Northern India.**
- 6. Characterisation of the effect of polyphenol fortified red grape juice on markers of oxidative stress and redox potential in healthy human subjects.**
- 7. Insulin resistance and childhood diabetes (Healthy under the skin you're in).**
- 8. Brain Biology Food and Mood: Adolescent health study**
- 9. Involvement of the kynurenine pathway in the persistence of childhood and adult brain tumours**
- 10. Assessment of the impact of massage therapy (Bowen Therapy) on the experience of pain, anxiety, nausea and fatigue in cancer patients**
- 11. Survey of Caffeine (+ energy drink) intakes in Australian adolescents (Avondale)**
- 12. Investigation of the efficacy of community-based lifestyle education programs in reducing metabolic risk factors in adults. P. Rankin (PhD candidate-Avondale)**

1 Full papers (submitted)

- Braidy N, Guillemin G, Mansour H, Chan-Ling T, Poljak A; Grant R. Age related Changes in NAD⁺ Metabolism Oxidative stress and Sirt1 activity in Wistar Rats. *PLoS One* (Sept 2010)
- Braidy N, Guillemin G, Mansour H, Chan-Ling T, Poljak A; Grant R. Age related Changes in NAD⁺ Metabolism Oxidative stress and Sirt1 activity in the Brain of Wistar Rats. *J. Neuroscience* (Sept 2010)
- Braidy N, Guillemin G, Mansour H, Chan-Ling T, Poljak A; Grant R. Changes in Kynurenine Pathway Metabolism During Aging. *Aging cell* (Sept 2010)
- Pope B, Hokin B, Grant R. Umbilical Cord Blood Stem Cells: Factors that Affect Viability before, During and After Freezing. *Stem Cells and Development* (Sept 2010)

3.2 Full papers (published)

- Guest J, Bilgin A, Pearce R, Baines S, Zeuschner C, Morris M, Grant C, Grant R. Evidence for Under Nutrition in Adolescent Females using Routine Dieting Practices: *Asia Pac J Clin Nutr* (In press June, 2010)
- Grant R, Nguyen S, Guillemin G. Kynurenine pathway metabolism is involved in the maintenance of the intracellular NAD⁺ concentration in human primary astrocytes. *Int. J. Tryp. Res.* 3:151–156 2010
- Mach J, Midgley A, Dank S, Grant R, Bentley D., The Effect of Antioxidant Supplementation on Fatigue during Exercise: Potential Role for NAD⁺(H). *Nutrients*, 2: 319-329 2010
- Braidy N, Grant R, Adams S, Guillemin G. Neuroprotective Effects of Naturally Occurring Polyphenols on Quinolinic Acid-Induced Excitotoxicity in Human Neurons. *FEBS J.* 277(2):368-82. 2010
- Watson B and Heise S. Breaking the silence: Napali women, uterine prolapse and hysterectomy. *Social Devel. Issues* 31(3):68-79. 2009
- Anderson MI, Simpson GK, Morey PJ, Mok MC, Gosling TJ, Gillett LE. Differential pathways of psychological distress in spouses versus parents of people with severe traumatic brain injury (TBI): Multigroup analysis. *Brain Injury*; 23(12): 931–943 2009
- Yiquan Chen, Roger Stankovic, Karen Cullen, Vincent Meininger, Brett Garner, Sarah Coggan, Ross Grant, Bruce J. Brew, and Gilles J. Guillemin The Kynurenine Pathway and Inflammation in Amyotrophic Lateral Sclerosis. *Neurotox Res.* Nov 18. [Epub ahead of print] 2009
- Brady N, Grant R, Guillemin G. Mechanism for Quinolinic Acid Cytotoxicity in Human Astrocytes and Neurons. *Neurotox Res* 16(1):77-86 2009
- Grant RS, Coggan S, Smythe GA. The Physiological action of Picolinic Acid in the Human Brain. (invited Review). *Int. J. Tryp. Res.* 2:71-79 2009
- Braidy N Grant R, Brew BJ, Adams S, Jayasena T, Guillemin G. Effects of Kynurenine Pathway Metabolites on Intracellular NAD⁺ synthesis and Cell Death in Human Primary Astrocytes and Neurons. *Int J. Tryp. Res.* 2:61-69 2009
- Coggan S, Smythe G, Bilgin A, Grant R Ψ. Age and Circadian Influences on Picolinic acid concentrations in human Cerebrospinal Fluid. *J. Neurochem.* 108:1220-1225 2009
- Grant R, Bilgin A, Zeuschner C, Guy T, Pearce R, Hokin B, Ashton J. The Relative Impact of a Vegetable-Rich Diet On Key Markers Of Health In A Cohort Of Australian Adolescents. *Asia Pac J Clin Nutr* 2008;17 (1):107-115
- Braidy N, Guillemin G, Grant R Ψ. Promotion of Cellular NAD⁺ Anabolism: Therapeutic Potential for Oxidative Stress in Ageing and Alzheimer's Disease. (Review) *Neurotox. Res.* 2008; 13 (4):1-12

3.3. Conference abstracts (Cumulative)

Grant R, Braidly N, Guillemain G. Polyphenol combination therapy enhances NAD⁺ levels and improves DNA repair after UVB damage in primary human keratinocytes. *Australian Health and Medical Research Congress* Nov **2010**

Guest J, Bilgin A, Pearce R, Garg M, Morris M, Grant R. Ω -3 & Ω -6 Polyunsaturated Fatty Acids levels in a cohort of Australian Adolescents. *Australian Health and Medical Research Congress* Nov **2010**

Guest J, Bilgin A, Pearce R, Baines S, Zeuschner C, Grant C, Morris MJ, **Grant R.** Adolescent females using common weight control techniques show biochemical evidence of reduced nutrition. *Macquarie university, Fat Studies: A Critical Dialogue interdisciplinary conference* Sydney, Sept 10-11, **2010**

Grant, R. Resveratrol Increases Intracellular NAD⁺ Levels through Up regulation of The NAD⁺ Synthetic Enzyme Nicotinamide Mononucleotide Adenylyltransferase. Available from *Nature Proceedings* <<http://hdl.handle.net/10101/npre.2010.4421.1>> **2010**

Grant R, Nguyen S, Guillemain G. Kynurenine pathway metabolism is involved in the maintenance of intracellular NAD⁺ concentrations in neurons and astrocytes. *Australian Neuroscience Society*, Sydney Feb **2010**

Adams S., Braidly, N., Grant, R. and Guillemain G. Characterisation of the kynurenine pathway in astroglomas *Australian Neuroscience Society*, Sydney Feb **2010**

Braidly N*, Guillemain G, Mansour M, Chan-Ling T, Grant R Age-related changes in NAD⁺ metabolism in the brain of aged female wistar rats. *Australian Neuroscience Society*, Sydney Feb **2010**

Mach J, Bentley D, Dank S, Karlsson C, Karlsson T, Bilgin A, Grant R. Characterisation of the effect of antioxidant supplementation on fatigue during exercise: Potential role for NAD⁺(H). *Australian Society for Clinical and Experimental Pharmacology* , Sydney, Dec **2009**.

Guest J, Bilgin A, Baines S, Zeuschner C, Le-Rossignol-Grant C, Morris M. Grant R. Adolescent females using common weight control techniques show biochemical evidence of reduced nutrition. *Nutrition Society of Australia*, national convention, Newcastle, Dec **2009**

Watson B., Heise S. Uterine Prolapse: The Self-reported knowledge and impacts of a uterine prolapse and hysterectomy on underprivileged Nepali women and families. *ICSD Conference, Mexico July 2009*

Grant R, Coggan S*, Bilgin A, Smythe G. Age and circadian influences on picolinic acid concentrations in human cerebrospinal, fluid *Australian Health and Medical Research Congress*, Brisbane, Nov **2008**

Braidly N*, Guillemain G, Adams S, Grant R. RNG2 increases NAD⁺ synthesis in Human Neurons and Astrocytes. *Australian Health and Medical Research Congress*, Brisbane, Nov **2008**

Pearce R, Grant R, Low A, Bilgin A, Baines S, Morris M. Intake of selected foods by vegetarians and omnivores in the adult adipocytokine study. *Nutrition Society of Australia 32nd annual Scientific meeting* Adelaide Nov **2008**

Matuszek M, Grant R. No effect of statins or ezetimibe on fat metabolism during aerobic exercise in dyslipidaemic individuals *Australian Physiological Society*, Melbourne, Dec. **2008**

Grant R, Bilgin A, Zeuschner C, Guy T, Ashton J, Brown S. Impact of a vegetarian diet on key markers of metabolic syndrome in a selected group of Australian children. *5th Int. Congress on vegetarian Nutrition (ICVN)* Loma Linda University, California, March **2008**

Hokin B, Grant R, Bilgin A, Zeuschner C, Guy T, Ashton A. Vitamin B12 and homocysteine status in vegetarian and non vegetarian Australian adolescents. *5th Int. Congress on vegetarian Nutrition (ICVN)* Loma Linda University, California, March **2008**

Braidly N*, Guillemain G, Grant R. A Mechanism For Quinolinic Acid Induced Cytotoxicity In Human Primary Astrocytes. *Proc.Aust.Neurosc.Soc.* Hobart, Australia. **2008**

Braidly N*, Guillemain G, Grant R Effect Of Kynurenine Pathway Inhibition On NAD Metabolism And PARP Activity In Human Brain Cells. *Proc.Aust.Neurosc.Soc.* Hobart, Australia. **2008**



3.3. Conference abstracts (Cumulative)

Brady N, Guillemin G, Grant R. Quinolinic acid induced cytotoxicity in human astrocytes: an NMDA mediated mechanism. *Proc.Syd. Tryptophan and kynurenine pathway, biannual symposium*, Dec **2007**

Brady N, Grant R, Guillemin G. Effect of Kynurenine Pathway Inhibition on NAD Metabolism & PARP Activity in Human Brain Cells. *St Vincent's Hospital Symposium*, **2007**

Grant R., Bilgin A., Zeuschner C., Guy T., Pearce R., Hokin B., Ashton J. Regular Nut Consumption Linked To Lower BMI in a Cohort of Australian Adolescents. *International Life Science Institute*, 2nd Functional Foods Conference, K.L. Malaysia, **2007**

Fedorow H, Grant R, Kapoor V, Naif H, Tryptophan Metabolism In Human Macrophages Infected By Selected Strains Of Hiv-1: Implications For Aids Dementia, International Brain Research Organisation (IBRO), *Neurobiology of Neglected African Diseases, Satellite Meeting of the 7th IBRO World Congress*. **2007**

Pearce R, Grant R, Greive C, Morey P. Brain Power Supplements: Self-reported Use by Adolescents in the 2005 Teen Nutrition and Cognitive Function Study, *Nutr & Dietetics 64(spl. 1): s32*, **2007**

Pearce R, Grant R, Greive C, Morey P. Brain Power Supplements: Comparison of Self-reported Use by Vegetarian and Non-vegetarian Adolescents in the 2005 Teen Nutrition and Cognitive Function Study. *Diatet. Assoc. Austr.*, **2007**

Kim Godbout. Adult perceptions of their role in developing resilience in young people. *MSc thesis, Macquarie University, March (2006)*

