

## Nutrigenomics Research Laboratory

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### **Background:**

Damage to the genome at the sequence, epigenetic and chromosome level is recognised as the most fundamental cause of infertility, developmental defects, neurodegenerative disease, cancer and accelerated ageing. We and others have shown that moderate deficiency or excess of certain micronutrients is associated with changes in level of DNA damage that are of a similar magnitude as those induced by pathological doses of common carcinogens and that these effects depend on genotype.

The emerging trend for individuals and health professionals to seek dietary strategies for disease prevention and the increased use of fortification, supplements and nutrient dense functional foods has accelerated the need to define more carefully the optimal doses of micronutrient intake and to develop DNA damage biomarkers to measure the bioefficacy and safety of the adopted dietary strategies in individuals.

Title and short description of project offered for 2009:

### **Detection of DNA damage in human buccal epithelial cells**

Genome damage caused by moderate micronutrient deficiency is of the same order of magnitude as the genome damage levels caused by exposure to significant doses of environmental genotoxins such as chemical carcinogens, ultra-violet radiation and ionising radiation. An example from our laboratory is the observation that chromosomal damage in cultured human lymphocytes caused by reducing folate concentration (within the normal physiological range) from 120 nM to 12 nM is equivalent to that induced by an acute exposure to ionising radiation (e.g. X-rays), a dose of radiation which is approximately ten times greater than the annual allowed safety limit of exposure for

radiation workers. Since moderate deficiency in just one micronutrient can cause significant DNA damage it is reasonable to be concerned about the possibility of additive or synergistic effects of multiple moderate deficiencies on genome stability.

This project will focus on detecting radiation-induced DNA damage in buccal cells *ex vivo* by using appropriate markers of DNA damage such as histone protein ( $\gamma$ -H2AX). The results of this project will have relevance in radiation biology (including radiation accidents & exposure of cosmic radiation in astronauts) as well as radiotherapy and oral mucositis patients and for determining nutritional status.

Key references:

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4. Beetstra S, Thomas P, Salisbury C, Turner J, Fenech M. Folic acid deficiency increases chromosomal instability, chromosome 21 aneuploidy and sensitivity to radiation-induced micronuclei. *Mutation Research*. 2005 578(1-2):317-26.