# Individual differences in DNA damage and repair: what do they mean?

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Human biomonitoring studies make great use of the comet assay to measure DNA damage (strand breaks and altered bases), antioxidant status, and DNA repair activity, generally in lymphocytes isolated from venous blood. The involvement of DNA damage as the initiating event in carcinogenesis is evident, and yet almost all damage is repaired before it can cause mutations; DNA damage is therefore best seen as a marker of exposure to genotoxins. DNA repair is regarded as a marker of susceptibility; a high intrinsic repair rate should protect against mutations and cancer. However, rather little is known of the regulation of repair. Inter-individual variation – in both base BER and NER (base and nucleotide excision repair) activities – is far greater than can be explained by genetic polymorphisms, and environmental and/or intrinsic factors are clearly involved. There is evidence for induction of repair by exposure to certain genotoxins, and dietary factors have been shown to modulate both BER and NER. The mechanism of regulation, which seems to be at a post-transcriptional level, is not yet understood, but we assume that the various factors interact with a common cell signalling pathway.

I will describe some recent and on-going studies. The NewGeneris project aimed to investigate the influence of maternal exposure and nutrition on health of newborns, using a range of biomarkers including the comet assay. In Norway, we are involved in the 'Typisk Norsk' study, in which colorectal cancer patients, post-surgery, are encouraged to adopt a healthy diet, rich in fruits and vegetables. The ComNet project is currently collecting comet assay data from a large number of human studies, in order to carry out a pooled analysis, and to obtain definitive answers to questions such as whether men and women have similar levels of DNA damage, how damage and repair relate to age, the effect of smoking, and the influence of nutritional factors. Ideally, prospective cohort studies are needed, to see whether DNA damage and repair are predictive markers of risk of cancer or other diseases.

As a postscript, I will describe a simple method for retrieval of leukocytes from frozen blood that could greatly simplify the collection and storage of samples from human trials.