Trace Elements, Ageing and Sex: Impact on Genome Stability

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Ageing is a complex biochemical process causing a multitude of physiological and pathophysiological changes in the human body, such as ageing-associated alterations in essential trace element (TE) levels. Nevertheless, studies focusing on the interplay of nutritional TE intake, their homeostases, interactions, as well as their impact on health status in the context of ageing are scarce. Thus, the interdisciplinary research unit TraceAge investigates these research questions focusing on the essential TEs iron, copper, manganese, selenium, iodine, and zinc.

Among others, ageing-associated alterations in TE level impacts on genome stability, by interfering with DNA damage response (DDR) and DNA repair mechanisms. Its maintenance is vital to ensure a reliable cellular functionality and hence prevent diseases. To investigate the impact of alterations in the TE status on different genomic stability related endpoints in murine liver, feeding studies in animals of different age and sex were conducted. In this context, changes in mRNA and protein expression levels of different DDR and DNA repair genes and proteins were evaluated via quantitative real-time PCR and Western Blot analysis. Additionally, the total amount of DNA strand breaks was determined by alkaline Comet Assay and 8-oxo-7,8-dihydro-2'-deoxyguanosine levels were assessed applying an ELISA kit. Base excision repair (BER) represents the major cellular repair mechanism for oxidative DNA lesions, removing a broad and frequently occurring damage spectrum, thereby contributing greatly to the maintenance of genomic stability. BER incision activity was evaluated by a non-radioactive incision activity assay based on using DNA damage-containing oligonucleotides. Furthermore, poly(ADP-ribosyl)ation status, which is an essential reversible post-translational modification of proteins with poly(ADP-ribose) as early event in DNA damage response, was quantified *via* stable isotope dilution liquid chromatography tandem mass spectrometry. Besides the investigation of genomic stability endpoints, TE levels in murine liver and serum were analysed via inductively coupled plasma tandem mass spectrometry.

By bringing together the mentioned endpoints, we aim to get further insights into the complex interplay between the TE status, ageing, sex, and genomic stability in murine liver.