## **Utilizing Human Isotope Profiles for Early Detection of Chronic Diseases**

**ANTON EISENHAUER**<sup>1</sup>, FRANÇOIS L.H. TISSOT<sup>2</sup>, GIOVANNI ALOISI<sup>3</sup> AND ANTHONY DOSSETO<sup>4</sup>

<sup>1</sup>GEOMAR Helmholtz Centre for Ocean Research Kiel

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Chronic diseases (CDs) such as cancer, coronary artery disease, neurodegenerative disorders like Alzheimer's, kidney failure, and metabolic diseases of the musculoskeletal system represent the leading health challenges within the European Union, incurring annual treatment costs exceeding 10% of the European Union Gross Domestic Product of 2021. Despite extensive research into traditional molecular and peptide-based biomarkers, including gene-based markers, the development of sensitive and specific indicators for CDs remains inadequate for the advancement of predictive, preventive, and personalized medicine. Consequently, numerous health organizations are prioritizing the exploration of novel approaches to biomarker discovery. One promising avenue, emerging from the field of isotope geochemistry, involves analyzing trace metals—such as calcium (Ca), copper (Cu), zinc (Zn), iron (Fe), and selenium (Se)—and their naturally occurring isotopes (44Ca/42Ca. <sup>65</sup>Cu/<sup>63</sup>Cu, <sup>66</sup>Zn/<sup>64</sup>Zn, <sup>56</sup>Fe/<sup>54</sup>Fe, <sup>80</sup>Se/<sup>76</sup>Se etc.) within the human body. These elements, recognized in medical contexts as essential or non-essential micronutrients, exhibit isotopic variations that may serve as potential biomarkers. Preliminary studies suggest that isotope-based biomarkers offer distinct advantages due to their specific associations with particular CDs and their ability to circumvent the complexities of organic chemistry that often obscure traditional biomarkers. Notably, the application of calcium isotopes has shown promise as an early indicator for metabolic bone diseases, including osteoporosis, renal failure, and the early detection of bone metastases in prostate cancer. For instance, research indicates that variations in natural calcium isotope ratios in blood and urine can effectively diagnose osteoporosis in postmenopausal women, offering a diagnostic accuracy comparable to that of dual-energy X-ray absorptiometry (DXA) scans. However, before the widespread adoption of the Human Isotope Profile (HIP) approach, it is imperative to facilitate the transfer of technical expertise and methodological concepts from Earth sciences to medical research. This necessitates cross-disciplinary collaboration and technology transfer between physicians and isotope geochemists to overcome existing disciplinary barriers and advance the development of reliable isotopic biomarkers for early CD diagnosis.

<sup>&</sup>lt;sup>2</sup>California Institute of Technology

<sup>&</sup>lt;sup>3</sup>Institut de Physique du Globe de Paris

<sup>&</sup>lt;sup>4</sup>Wollongong Isotope Geochronology Laboratory. School of Science. University of Wollongong