

Copper and sulfur isotope variations in liver cancer

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In cancer, copper concentrations increase in the blood and in tumor cells, leading to deleterious side effects. The mechanisms of this copper accumulation and the source of extra copper burden are still poorly understood. We show that in hepatocellular carcinoma (HCC) patients, blood copper is enriched in ⁶³Cu compared to control subjects and demonstrate that this isotopic signature is not compatible with a dietary origin. It rather reflects the massive reallocation in the body of copper immobilized within cysteine-rich proteins such as metallothioneins. We also show that the blood of HCC patients is enriched in ³²S compared to control subjects, an enrichment compatible with the notion that at least 6% of blood sulfur originates from tumor-derived sulphides. We will discuss how the hypoxic conditions of the tumor microenvironment can impair the metabolism of copper and sulfur, notably by changing their redox state and, as a consequence, their ability to bind specific molecules.