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A tale of metal ions in cancer: from metalloplasia to metal-based therapy and diagnosis

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Several d-block metal ions (Fe, Cu, Zn, Mn, Co and Mo) are essential elements for humans, where they cover fundamental bio-chemical functions such as oxygen transport and redox catalysis.[1] As a consequence, a deficiency of essential metal ions can cause pathologies such as anaemia (Fe) and Menkes disease (Cu). On the contrary, the levels of certain metal ions such as Cu are elevated in cancer tissues and in the blood of cancer patients.[2] This is in line with the role of metal ions in biochemical processes involved in cell growth and replication (*metalloplasia*), which are at the basis of tumour progression.[3] Hence, anticancer approaches targeting metal ions are being developed. As metal ions promote cancer, one strategy consists in reducing metal ions overload through *chelation therapy*, that is the administration of suitable ligands that bind the excess metal ions. A second metal-based strategy exploits the capacity of certain ligands or metal-complexes to induce cell death. The first example of such metallodrugs was the widely used *cisplatin*, whose cytotoxic activity was serendipitously discovered in 1965 by the biophysicist B. Rosenberg while studying the effects of electric fields on bacterial cells.[4] In this context, we have recently investigated the reactivity of anticancer Cu complexes under physiological conditions using both experimental and computational methods, providing remarkable insights into the possible mechanism of action of such Cu-based drugs.[5-7] Besides cancer therapy, metal ions also represent important tools for cancer diagnosis. Indeed, lanthanide(III) ions such as gadolinium(III) and lutetium(III)-177 are found in contrast agents for magnetic resonance imaging (MRI) and radiotracers for positron emission tomography (PET), respectively.[8]

References

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