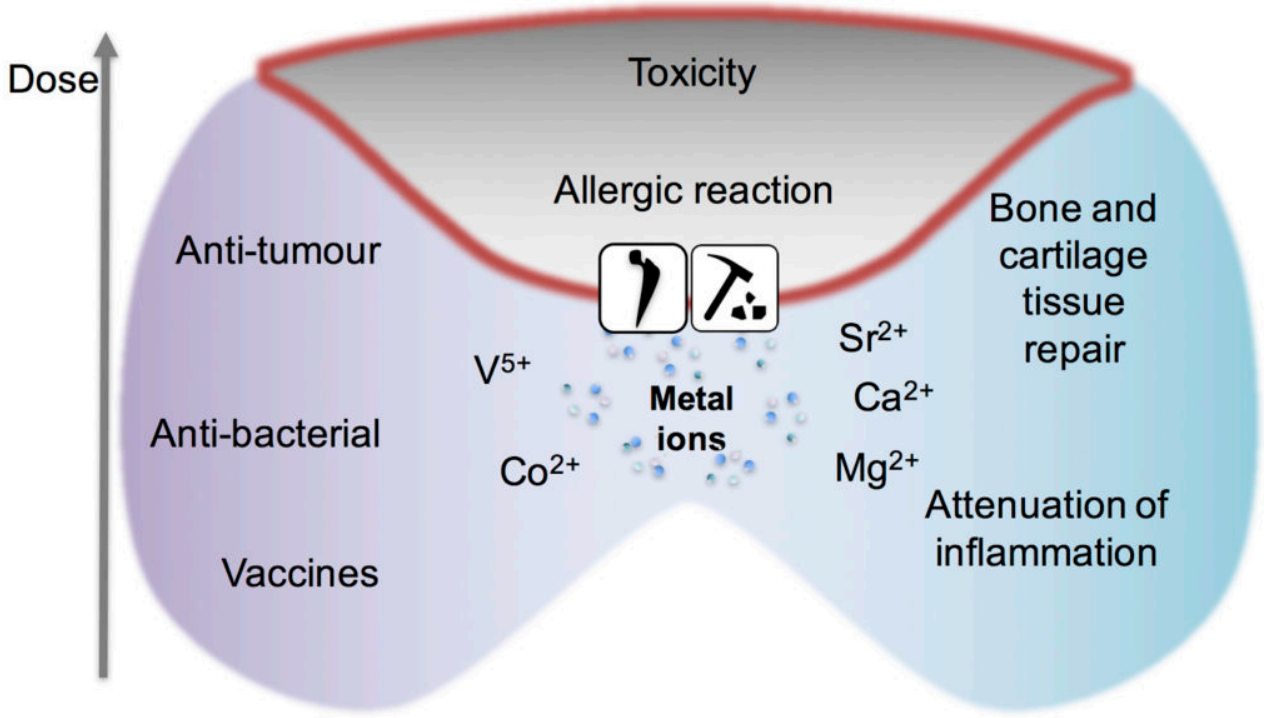
Metal ions are a promising tool for Regenerative Medicine?

Ions play a vital role in living systems because cells use ions to accelerate chemical reactions, to synthetize biologic molecules or as messengers. The transport of oxygen through the blood is possible due to the iron ion (Fe), that exists in the core of the hemoglobin molecule. In fact, ions are in our hearts and minds, since the contraction of the heart muscle and neural communication are orchestrated by ions such as calcium, magnesium, potassium and sodium.

The majority of us are only exposed to small doses metal ions mostly originating from our diet, but individuals involved in mining activities, or with metal implants, can be exposed to toxic doses of ions. Metal implants have been widely and successfully used in medical areas such as Orthopedics, Dentistry and Cardiology for about one hundred years. In these contexts, the most used metal alloys are CoCrMo (cobalt–chromium–molybdenum) and Ti_6Al_4V (titanium–aluminum–vanadium), which were tailored to be resistant to corrosion and wear and to minimize activation of the human immune system. However, in the last decade, some models of implants applied in Orthopedics raised concerns related to their toxicity, as high and uncontrolled amounts of ions were being released by these medical devices. Clinical studies showed that these high levels of metal ions in human body may lead to adverse effects, such as pain and allergic reactions, which prompted patients to seek revision surgeries.



Effects of metal ions on living systems depending on the dose: from toxic levels to therapeutics.

On the other hand, these studies also uncovered that in certain conditions metal ions may promote tissue regeneration, and help fight infections and cancer. So, new therapeutic approaches may be designed using low doses of metal ions, which are stable, inexpensive are can be integrated in innovative medical devices. Our review paper is focused on the application of metal ions to repair and regenerate bone tissue, which highly depends on a balance with the immune system.

The response of human immune system to metal ions can be stimulated in order to fight diseases such as cancer and infection. As an example, the local toxicity induced by certain metal ions, such as vanadium, may be useful to delay tumor growth or impair bacteria proliferation. Moreover, vaccination may profit from the type of immune response elicited by cobalt to improve production of antibodies. On the other hand, ions such as magnesium, calcium, strontium and cobalt may promote bone tissue repair. In presence of certain doses of metal ions, mesenchymal stem cells produce factors that induce bone and cartilage healing. These elements are also easily incorporated in matrices that, upon implantation, release them in a controlled fashion and support the growth of cells. Remarkably, this new interest in metal ions is accompanied by promising results achieved by biodegradable implants (e.g. magnesium alloys), namely when used as orthopedic screws and vascular stents. This review highlighted the potential for the use of metal ions, alone or in combination with drugs and biological molecules, in the development of novel solutions for unmet clinical needs. By promoting tissue regeneration, metal ions may improve implant-tissue interfaces, and thereby implant survival, but they also may be used to fight tumors and bacteria due to their affinity to key targets.

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