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Iron is an essential element for almost all organisms, a cofactor playing a crucial role in a number of vital functions, including oxygen transport, DNA synthesis, and respiration. However, its ability to exchange electrons renders excess iron potentially toxic, since it is capable of catalyzing the formation of highly poisonous free radicals. As a consequence, iron homeostasis is tightly controlled by sophisticated mechanisms that have been partially elucidated. Because of its biological importance, numerous disorders have been recently linked to the deregulation of iron homeostasis, which include not only the typical disorders of iron overload and deficiency but also cancer and neurodegenerative diseases. This leads iron metabolism to become an interesting therapeutic target for novel pharmacological treatments against these diseases. Several therapies are currently under development for hematological disorders, while other are being considered for different pathologies. The therapeutic targeting under study includes the hepcidin/ferroportin axis for the regulation of systemic iron homeostasis, complex cytosolic machineries for the regulation of the intracellular iron status and its association with oxidative damage, and reagents exploiting proteins of iron metabolism such as ferritin and transferrin receptor. A promising potential target is a recently described form of programmed cell death named ferroptosis, in which the role of iron is essential but not completely clarified. This Special Issue has the aim to summarize the state-of-the-art, and the

latest findings published in the iron field, as well as to elucidate future directions.