The iron-erythropoiesis cross-talk in health and disease

Antonella Nai

San Raffaele Scientific Institute, Italy

Iron and erythropoiesis are reciprocally regulated. Erythropoiesis requires about 25mg of iron daily for the production of more than 200 billion red blood cells. Iron is not only essential for heme/hemoglobin synthesis, but also for the control of the production of erythropoietin (EPO), the cytokine that drives erythropoiesis. On a reciprocal side, erythropoiesis controls iron homeostasis regulating the transcription of hepcidin (*HAMP*), the master regulator of iron metabolism. To signal iron needs to the liver, erythroid cells release in the circulation erythroferrone (ERFE), an EPO target gene, that inhibits *HAMP* sequestering its activating ligands. A recently identified link between iron homeostasis and erythropoiesis is Transferrin Receptor 2, that reciprocally regulates EPO signaling and hepcidin expression based on available iron.

The understanding of the mutual crosstalk between iron homeostasis and erythropoiesis significantly improved in the last years, leading to pinpointing novel players and to the elucidation of the pathophysiology of disorders deriving from its deregulation. One example is represented by iron loading anemias, characterized by excessive ERFE production and hepcidin suppression. The other and opposite is the iron deficiency/iron restricted erythropoiesis that occurs in genetic IRIDA and acquired inflammatory disorders, due to excessive hepcidin production.

This lecture will give an overview on the mechanisms governing this complex system, with a focus on innovative therapeutic approaches.