Fundamental discoveries on the role of innate immunity and inflammation in cancer

In the middle of 19th century, Rudolph Virchow proposed the existence of a causal link between inflammation and cancer. The hypothesis did not gain much traction for more than a century. The basic observations were there: the growth and the development of the tumor stroma bear striking similarities to the process of wound healing, as synthetized by Harold F Dvorak in the catchy definition that “tumors are wounds that do not heal”.

The dominating paradigm for the understanding of tumorigenesis remained, however, the genetic one: cancers are due to cell-autonomous alterations capable of conferring a selective advantage to the cancer cell. The appreciation of the ecological components of cancer and of the role of the cancer microenvironment remained scarce.

What was needed was a determined effort to enroot the idea into solid biological and molecular bases. Mantovani was a pioneer in this enterprise.

Throughout the ‘80s and the ‘90s, his laboratory produced seminal discoveries on the role of tumor-associated macrophages and inflammatory cytokines in cancer initiation and progression. The turning point in the history of the concept of inflammation and cancer was an extremely influential review, written in 2001 together with Fran Balkwill. In this, Mantovani, elaborating on his discoveries and those of other labs, laid the foundation for a renewed paradigm of studies on the relationships between innate immunity and cancer. This sparked a flurry of activities throughout the world, which included additional seminal contributions from Mantovani’s group. This culminated with the acceptance of the idea of inflammation as a determining factor in tumor development: a concept with enormous implications, first and foremost from the therapeutic viewpoint.

Witness to this paradigm shift is the fact that the first review on the “Hallmarks of cancer”, by Hanahan and Weinberg in 2000, did not include inflammation. Its revised version of 2011 included tumor-promoting inflammation as one of the 10 hallmarks of tumorigenesis.

This hallmark of cancer is a tribute to the work of Mantovani and to that of all the others that allowed this fundamental paradigm shift.