Preface

In 2004, Pietro Ghezzi asked me to write a short introductory chapter for a book on TNF he was putting together for this very same series. The focus of what I wrote then was on TNF as an inflammatory agent. In fact, our finding, in the 1980s, that cachexia associated with inflammatory and infectious diseases was due to TNF opened the way to the development of anti-TNF drugs that are now standard treatment for chronic inflammatory disease.

Now, I am asked again to write about the continuation of this saga. In 1998, with Mike Brines and Carla Hand, I started investigating why patients who receive EPO feel well soon after the first treatment. That led to the discovery, published in 2000, that systemically administered EPO is neuroprotective in animal models of ischemic and traumatic brain injury. That paper opened the field of the neuroprotective action of EPO. The protective action of EPO was soon demonstrated in other tissues, hence the use of the term "tissue-protective cytokine" (1). As in the case of TNF, we had to fight the commonplace that EPO has only erythropoietic actions, that its receptor is present only in erythroid progenitor cells, and that EPO is produced only by the kidney (2).

As in the case of TNF, originally identified for its antitumor activities, we had to work against the common belief that EPO is solely an erythropoietic cytokine acting solely on erythroid progenitors. Several investigators also documented the expression of EPO in the central nervous system and other tissues, against the common belief that only the kidney and the foetal liver produce EPO.

From the perspective of pharmacological use, the erythropoietic action of EPO, by increasing the haematocrit and activating platelets, has some undesired side effects as a tissue-protectant, and this led to the development of novel non-erythropoietic EPO-derived tissue-protective molecules some of which are described here.

I believe that tissue-protection will be a new field of interest of cytokine biology, both in discovering novel actions of known cytokines and in developing new drugs. In this context, this book is a valuable collection of methodological papers that describe in detail the key models that have been used to characterize the tissue-protective actions of EPO and derivatives and will, hopefully, be of use in the discovery of new tissue-protective molecules.

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