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On the history of biological drugs: the true discovery of the IL-1 receptor antagonist

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Pasero, Marson and Gatto have recently published their article about the introduction of biological drugs in the field of rheumatology. (1) The discovery of the IL-1 receptor antagonist (IL-Ra) is attributed to a group of researchers in Denver led by William P. Arend. (2) Jean-Michel Dayer has critically reviewed the various phases that led to the discovery of the IL-1 and the tumor necrosis factor (TNF). (3) Through a personal communication he tells us how actually some time before, he and his team in Geneva had suspected the existence of a powerful IL-1 inhibitor. (4) Therefore, the focus of their research was directed to diseases characterized by the expansion of the monocytic component such as, for example, some acute leukoses. In this way, they were able to isolate a 17kDa growth factor from the urine of patients with monocytic leukemia that was capable of blocking the biological activity of IL-1 (5) but not that of TNF-alfa (6), thus presenting itself as a possible IL-1 receptor antagonist *in vivo*. Then in 1987, the real mechanism of the action of this molecule was identified and this was confirmed with the name *receptor antagonist*. (7) This is an important clarification of any uncertainties that may remain about the chronology of a discovery that was to open new horizons in the study of inflammatory rheumo-arthropathy, and also for therapy. It also shows us how tracing the historical steps of a subject that is, after all, still relatively new and in a stage of continuous evolution is difficult and, in some aspects, risky. Luckily, the leading characters in this recent history can help us by providing a direct source of information. For the same reason, the recent report of the discovery of TNF and of its superfamily (8) by another leading role player in this extraordinary scientific era, Bharat B. Aggarwal, can throw light on aspects of the subject of which a simple review of the literature can offer but a glimpse.

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