ANIMAL MODELS IN GASTROENTEROLOGY

Blandizzi Corrado

Division of Pharmacology and Chemotherapy, Department of Internal Medicine,
University of Pisa

The significance of animal research to understand the pathophysiological basis of human diseases and develop novel pharmacological treatments is a matter of continuous debate. The human gastrointestinal tract comprises a large variety of cellular systems which interact in a highly integrated manner to ensure an appropriate nutrient uptake, but also to oppose a defensive barrier against a number of pathogenic antigens and injurious agents. A further level of integration is represented by the nervous and hormone pathways deputed to drive proper brain-gut communications, the dysfunction of which is regarded as a major source of symptoms in functional digestive disorders. Based on these premises, animal models of gastrointestinal diseases must be regarded as valuable tools, which allow to investigate various pathological events, including peptic ulcer, intestinal inflammation and tumourigenesis, as well as to dissect different pathophysiological components, to characterize underlying molecular and genetic mechanisms, and to design novel strategies for pharmacological interventions. The functional complexity of gastrointestinal tract can not be reproduced in other simple experimental models, including reductionist tissue culture systems, even if the latter can be exploited to investigate selected and highly defined processes which may be relevant to digestive diseases. For instance, experimental models of chronic gastric ulcer, with particular regard for the acetic acid-induced ulcer, are known to closely resemble human peptic ulcers, since they respond well to various anti-ulcer drugs, such as proton pump inhibitors and several growth factors, their healing is negatively influenced by steroidal and non-steroidal anti-inflammatory drugs, and they are currently recognized as standard models for screening novel compounds as potential anti-ulcer drugs. When considering inflammatory bowel diseases, the development of a large variety of animal models in the past decade has fostered a rapid progression in our understanding of mucosal immunopathology as well as digestive motor alterations resulting from abnormal interactions between enteric immune system and nervous pathways. In particular, genetically engineered models of intestinal inflammation (transgenic and knockout mice) and adoptive transfer models, where bowel inflammation is evoked by selective transfer of specific cell types to immunocompromised host animals, have allowed an accurate analysis of the interplay between distinct cell systems in both health and disease, and have paved the way to the discovery of innovative biologic drugs targeted against key molecular determinants of gut inflammatory reactions.