Towards a mechanism-based approach to treat autoimmune and inflammatory diseases specifically with small peptides

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Nowadays, pharmacologic treatments of inflammatory and autoimmune diseases are largely palliative rather than curative. They result in non-specific immunosuppression, which can be associated with disruption of natural and induced immunity with significant, sometimes dramatic, adverse effects. Among the novel strategies that are under development, tools that target specific molecular pathways and cells, and more precisely modulate the immune system to restore normal tolerance mechanisms, are central. In these approaches, peptides represent a class of therapeutic drugs that display many physicochemical advantages in terms of stability, toxicity, absence of immunogenicity and unwanted side effects. Among peptide therapeutics of interest, the phosphopeptide P140 is very promising for treating patients with systemic lupus, and probably more largely patients with chronic inflammatory diseases. This peptide displays very favorable properties in terms of ADME (absorption, distribution, metabolism, and excretion). P140/Lupuzor is currently evaluated in phase III-clinical studies worldwide. This peptide targets key elements of endo-lysosomal autophagy, which is hyperactivated in lupus. Promising data have also been obtained in animal models mimicking Crohn's disease, neurological autoimmune diseases, Sjögren's syndrome and asthma. After the era of drugs classified as "disease-modifying" therapeutics, a new type of "mechanism-guided" therapies is beginning to emerge for treating inflammatory diseases.

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