Mechanism-Guided Novel Therapies for Treating Inflammatory Diseases

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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, peptide therapeutics represent a class of agents that display many physicochemical advantages. Among them, the phosphopeptide P140 is very promising for treating patients with systemic lupus, and probably more largely patients with chronic inflammatory diseases. P140/Lupuzor is currently evaluated in phase III-clinical studies worldwide. This peptide targets key elements of chaperone-mediated autophagy, which are hyperactivated in lupus. The «correcting» effect of P140 on autophagy results in a weaker signaling of autoreactive T and B cells, leading to a significant improvement of physiopathological conditions. These findings open novel avenues of therapeutic intervention in pathological conditions in which reduction of autophagy activity is desired. Promising data have been obtained in animal models mimicking Sjögren’s syndrome and neurological autoimmune diseases. After the era of drugs classified as «disease-modifying» therapeutics, a new type of «mechanism-guided» therapies starts to emerge for treating inflammatory diseases.