核酸药物在炎症性疾病领域的研究进展Δ

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摘　要　当炎症持续激活或调控失衡时，可诱发慢性组织损伤和器官功能障碍，并广泛参与动脉粥样硬化、炎症性肠病等多种炎症性疾病的发生发展。核酸药物因具有高靶向性、长效性和可编程性，为炎症性疾病的治疗提供了新方向。本文综述了核酸药物的分类、作用机制及其在炎症性疾病中的应用进展，发现小干扰RNA（siRNA）可通过RNA干扰机制特异性切割靶mRNA，抑制目标蛋白表达；反义寡核苷酸（ASO）可通过诱导微RNA（miRNA）降解或调控剪接过程抑制靶蛋白表达；miRNA可通过调控多个炎症靶基因实现网络化干预。目前，siRNA药物Lumasiran、Nedosiran（用于Ⅰ型原发性高草酸尿症）和Inclisiran（用于动脉粥样硬化），ASO药物Donidalorsen（用于遗传性血管性水肿）、Volanesorsen和Olezarsen（用于家族性高乳糜微粒血症综合征）、Lademirsen（用于奥尔波特综合征），miRNA药物Obefazimod（用于炎症性肠病）、Remlarsen（用于病理性纤维化）在炎症性疾病领域已有重要突破，有望成为新一代抗炎治疗策略，为慢性炎症和纤维化疾病患者带来更加精准、高效的治疗选择。

关键词　核酸药物；炎症性疾病；小干扰RNA；反义寡核苷酸；微RNA

Research progress of nucleic acid drugs in the field of inflammatory diseases

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ABSTRACT　When inflammation is continuously activated or dysregulated, it can induce chronic tissue injury and organ dysfunction, and participate in the occurrence and development of various inflammatory diseases such as atherosclerosis and inflammatory bowel disease. Owing to high targeting, long-acting efficacy and programmability, nucleic acid drugs provide a new direction for the treatment of inflammatory diseases. This article reviews the classification, mechanism of action and application progress of nucleic acid drugs in inflammatory diseases. It is found that small interfering RNA (siRNA) can specifically cut target mRNA through RNA interference to achieve inhibiting the expression of the target protein; antisense oligonucleotide (ASO) can inhibit target protein expression by inducing microRNA (miRNA) degradation or regulating splicing processes; miRNA can achieve network intervention by regulating multiple inflammatory target genes. At present, important breakthroughs have been made in the field of inflammatory diseases with siRNA drugs including Lumasiran, Nedosiran (for primary hyperoxaluria 1) and Inclisiran (for atherosclerosis), ASO drugs including Donidalorsen (for hereditary angioedema), Volanesorsen and Olezarsen (for familial chylomicronemia syndrome) and Lademirsen (for Alport syndrome), as well as miRNA drugs including Obefazimod (for inflammatory bowel disease) and Remlarsen (for pathological fibrosis). These drugs are expected to become a new generation of anti-inflammatory therapeutic strategies and bring more precise and efficient treatment options for patients with chronic inflammation and fibrotic diseases.

KEYWORDS　nucleic acid drugs; inflammatory diseases; small interfering RNA; antisense oligonucleotide; microRNA

炎症是机体应对病原体侵袭、组织损伤及代谢紊乱的重要防御反应，在维持免疫稳态和组织修复过程中发挥关键作用[1]。然而，炎症反应持续激活或调控失衡时，可诱发慢性组织损伤和器官功能障碍，并广泛参与动脉粥样硬化（atherosclerosis，AS）、炎症性肠病（inflammatory bowel disease，IBD）、遗传性血管性水肿（hereditary angioedema，HAE）及病理性纤维化等多种炎症性疾病

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