インターロイキン8の病態生理作用の確立と阻害物質の開発

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Establishment of pathophysiological role of interleukin 8 and development of its inhibitors

Research Project

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Allocation Type

Single-year Grants

Research Field

Immunology

Research Institution

Kanazawa University

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Interleukin 8 / Pathophysiology / Disease / Antibody / Treatment / Gene / NFkB / Anti-inflammatory drug

Research Abstract

A novel leukocyte chemotactic and activating factor, interleukin 8 (IL 8) was identified, biochemically purified, and molecularly cloned by us in 1987 at National Cancer Institute. Since then, we have established the essential involvement of IL 8 in various disease models in rabbits, including lung

reperfusion injury, acute skin inflammation, and joint arthritis using a monoclonal antibody against IL 8. These works established for the first time an endogenously produced chemotactic factor has an essential role in causing inflammation. During the last two years studies, we further established that IL 8 is involved in serum sickness type glomerulonephritis and PPD-induced delayd type hypersensitivity. We also generated antibodies against murine as well as human IL 8 receptors and studied the expression on various types and maturation stages of leukocytes. We also examined the regulation of the expression of IL 8 receptors on T lymphocytes and found that IL 8 receptors are highly upregulated by treating with interferon gamma and TNF alpha. On the other hand, we previously revealed that NFkB in synergy with AP-1 or NF-IL 6 confers the responsiveness to various inflammatory stimuli to activate IL 8 gene. Here, wehave found that NFkB is an end target of the established anti-inflammatory and immunosuppressants, glucocorticoids and FK506. These observations indicate that novel anti-inflammatory drugs can be developed targeting the pathway (s) leadinf the activation of NFkB.To facilitate the approach, we developed LPS-dependent cell-free activation system of NFkB and identified a protein kinase which binds and specifically phosphorylates a negative regulator of NFkB, IkBa.

Research Products (111 results)

All | Other

All | Publications (111 results)

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