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综述

EGFR抑制剂耐药机制研究的新进展

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摘要 表皮生长因子受体(EGFR)通路在肿瘤发生、发展过程中起到非常重要的作用，它已成为肿瘤分子治疗领域最主要的研究和开发靶点之一。目前有单克隆抗体与小分子受体酪氨酸激酶抑制剂两类EGFR抑制剂在临床治疗中取得成功。然而，该类药物在临床前研究及临床治疗中已经出现耐药现象。由于EGFR调节多种细胞功能，该耐药现象可能与多个传导通路紊乱有关，包括配体自分泌/旁分泌的产生、受体突变、下游信号蛋白的组成性活化以及旁路信号途径的激活。本文就EGFR抑制剂耐药机制的最新研究进展进行综述。

关键词 表皮生长因子； 耐药； 单克隆抗体； 小分子酪氨酸激酶抑制剂

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Mechanisms of resistance to EGFR inhibitors

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Abstract

The epidermal growth factor receptor (EGFR) pathway plays a crucial role in tumor development and progression, and it has been one of the most studied and exploited targets for molecular cancer therapy. Two classes of anti-EGFR agents, monoclonal antibodies and small molecules targeting the receptor tyrosine kinase, have shown antitumor activity in clinical application. However, preclinical and clinical studies have demonstrated the occurrence of resistance to these drugs. Since EGFR is implicated in a wide array of intracellular functions, the phenomenon of resistance to these agents may result from the derangement of different molecular pathways, including autocrine/paracrine production of ligands, receptor mutations, constitutive activation of downstream signaling proteins, and activation of alternative pathways. The last studies on the mechanisms of resistance to EGFR inhibitors are reviewed.

Key words epidermal growth factor receptor drug resistance monoclonal antibodies small molecule tyrosine kinase inhibitors

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