EGCG对A431细胞NF-κB表达的表观遗传修饰效应及对光动力的影响

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Title: **Cancer preventive/therapeutic effects via NF-κB activation epigenetic modulation and coincident ALA-PDT co-effects in human A431 squamous cancer cells induced by EGCG**

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关键词: 表没食子儿茶素没食子酸酯; 表观遗传-NF-κB信号途径; 细胞凋亡; 5-氨基酮戊酸介导光动力疗法; 人表皮癌A431细胞系

Keywords: EGCG; epigenetic-NF-κB signaling modulation; apoptosis; co-effect on ALA-PDT; human A431 squamous cancer cell line

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摘要: 目的：研究表没食子儿茶素没食子酸酯（EGCG）对人表皮细胞癌A431细胞内核转录因子（NF-κB）表达的表观遗传修饰效应，探讨联合5-氨基酮戊酸介导光动力疗法（ALA-PDT）的增敏作用。方法：低氧诱导培养A431细胞，用MTT比色法检测不同浓度EGCG对A431细胞增殖的影响，MS(methylation specific)-PCR检测p16INK4α基因甲基化变化，免疫印迹检测NF-κBp65，DNMT1，HDAC1，CyclinD1，HIF-1α，VEGF，p16INK4α表达，并用免疫细胞化学染色观察A431细胞E-钙黏蛋白（E-cadherin）；用流式细胞仪检测EGCG联合ALA-PDT诱导的A431细胞凋亡。结果：EGCG具有抑制A431细胞增殖并诱导凋亡的作用，抑制效应呈浓度依赖性；p16INK4α基因甲基化水平减低显著；免疫印迹显示NF-κBp65，DNMT1，HDAC1，CyclinD1，HIF-1α，VEGF表达下调，p16INK4α表达上调；E-cadherin表达上调显著，呈浓度依赖性。EGCG联合ALA-PDT治疗组促凋亡作用显著。结论：EGCG对A431细胞具有抑制增殖、血管生成、侵袭的作用，通过影响NF-κB表观遗传修饰诱导细胞凋亡。EGCG联合ALA-PDT的促凋亡作用，增强了A431细胞对ALA-PDT的敏感性。

Abstract: Objective：The preventive/therapeutic effect via NF-κB activation epigenetic modulation induced by EGCG and co-effect on ALA-PDT by combined with EGCG in human A431 squamous cancer cells were investigated.Methods：In A431 cancer cells induced by EGCG，the p16INK4α gene was detected by MS (methylation specific)-PCR.The modulated epigenetic effects in A431 cancer cells induced by EGCG，including antiproliferation effect detected by MTT assay.Expressions of NF-κBp65，DNMT1，HDAC1，CyclinD1，HIF-1α，VEGF，p16INK4α were detected by immunoblotting，and anti-metastatic effect displayed by cadherin-immunocytochemistry and the apoptosis induced by EGCG detected by Annexin V-FITC.The therapeutic co-effect of ALA-PDT combined with EGCG on A431 cancer cells apoptosis was detected by Annexin V-FITC.Results：The epigenetic pattern of A431 cancer cells could be modulated via demethylation of p16INK4α gene by EGCG.The down-regulated NF-κBp65，DNMT1， HDAC1，CyclinD1，HIF-1α，VEGF and upregulated p16INK4α induced by EGCG were showed in immunoblotting.The anti-metastatic effect of enhanced cadherin-immunocytochemistry induced by EGCG also showed dose/time dependant.The apoptosis of A431 cancer cells could be induced by EGCG or ALA-PDT，further enhanced apoptosis of the cancer cells was induced by ALA-PDT combined with EGCG.Conclusion：EGCG with anti-oxidative activity can not only inhibit proliferative，

vasculogenesis and metastatic effects via epigenetic-NF-κB signaling pathway to induce apoptosis of A431 cancer cells, but also can further promote the apoptosis induced by ALA-PDT combined with EGCG via pro-oxidant activity as cancer preventive/therapeutic agent.

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