Securin 參與氧化鍺造成人類大腸癌細胞之細胞毒性

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摘要

氧化鍺為一種無機鍺化合物，在中國倉鼠卵巢細胞中會降低 Cdk1 的活性並造成細胞停滯在 G2 時期，同時也會增加輻射敏感性。Securin 目前被認為是一個前致癌基因，可調控細胞增生以及腫瘤的形成。在本研究中，我們利用 securin 正常與缺失的人類大腸癌細胞，探討氧化鍺處理細胞後，securin 在氧化鍺所造成的細胞週期停滯及細胞死亡所扮演的角色。當細胞處理 1-10 mM 的氧化鍺，24 小時後，隨著處理濃度增加，在 securin 正常與缺失人類大腸癌細胞，皆可顯著增加細胞毒性。但 securin 缺失之人類大腸癌細胞對於氧化鍺的毒性較具有抗性。氧化鍺會抑制 securin 蛋白的表達及增加細胞週期 G2/M 停滯。p53 是一個腫瘤抑制蛋白，扮演平衡細胞存活及細胞凋亡的功能。氧化鍺會誘發活化的 p53(磷酸化-serine-15)及內生性 p53(DO-1) 蛋白的表達。本篇研究為首次提出氧化鍺可抑制 securin 蛋白的表達以增加細胞毒性，並觀察到 p53 的活化與 securin 蛋白的存在與否並無相關。

關鍵字：氧化鍺、securin、細胞死亡、p53

Involvement of securin on GeO2-induced cytotoxicity in human colorectal cancer cells

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Abstract

GeO2 (germanium oxide), an inorganic germanium compound, it can decrease the Cdk1 activity and arrest the cells at G2 phase on Chinese hamster ovary cells (CHO); nevertheless, it also enhances the radiosensitivity on CHO cells. Securin, a proposed proto-oncogene, regulates cell proliferation and tumorigenesis. However, role of securin on the GeO2-induced cell cycle arrest and cell death remain unknown. In this study, the effects of GeO2 on the expression of securin in two types of colorectal carcinoma cells were investigated. GeO2 (1-10 mM, 24h) increased the cytotoxicity in both colorectal carcinoma cells. The level of securin protein was decreased and the G2/M fractions were increased by GeO2. The depletion of securin proteins decreased the cytotoxicity after GeO2 treatment. p53, a tumor suppressor protein, balances the cell survival and apoptosis. GeO2 raised the levels of phosphor-p53 (serine-15) and p53 (DO-1) proteins in both the securin-wild type and the -null cells. Together, it is the first time to demonstrate that the inhibition of securin expression induced by GeO2 increases the cell death via a p53-independent pathway.

Key Words: germanium oxide; securin; cell death; p53