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Peroxiredoxin 2 is upregulated in colorectal cancer and contributes to colorectal cancer cells' survival by protecting cells from oxidative stress

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Abstract Peroxiredoxin 2 (Prdx2) is a member of the peroxiredoxin family, which is responsible for neutralizing reactive oxygen species. Prdx2 has been found to be elevated in several human cancer cells and tissues, including colorectal cancer (CRC), and it influences diverse cellular processes involving cells' survival, proliferation, and apoptosis, which suggests a possible role for Prdx2 in the maintenance of cancer cell. However, the mechanism by which Prdx2 modulates CRC cells' survival is unknown. The current study aimed to determine the effect of elevated Prdx2 on CRC cells and to further understand the underlying mechanisms. The results of this study showed that Prdx2 was upregulated in CRC tissues compared with the matched noncancer colorectal mucosa tissues and that Prdx2 expression was positively associated with tumor metastasis and the TNM stage. In the LoVo CRC cell line, Prdx2 was upregulated at both the RNA and protein levels compared with the normal FHC colorectal mucosa cell line. In addition, the LoVo CRC cell line was significantly more resistant to hydrogen peroxide (H_2O_2)-induced apoptosis because of a failure to activate pro-apoptotic pathways in contrast to Prdx2 knockdown cells. Suppression of Prdx2 using a lentiviral vector-mediated Prdx2-specific shRNA in the LoVo cell line restored H_2O_2 sensitivity. Our results suggested that Prdx2 has an essential role in regulating oxidation-induced apoptosis in CRC cells. Prdx2 may have potential as a therapeutic target in CRC.

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Introduction

Colorectal cancer (CRC) is an important global health problem. CRC is the third and second most commonly diagnosed cancer worldwide in males and females, respectively, with over 1.2 million new cancer cases and 608,700 deaths estimated to have occurred in 2008 [1]. Despite the remarkable progress in CRC diagnosis and treatment, the recurrence rates are still high. Therefore, the discovery of molecules essential to the carcinogenesis and malignant behavior of CRC cells as well as new therapeutic strategies to treat CRC is important for improving the prognosis and therapy of CRC patients.

The mammalian peroxiredoxins (Prdxs) are in a superfamily of thiol-dependent antioxidant proteins that has six members (Prdx1–6), and their main function is to reduce reactive oxygen species (ROS), such as hydrogen peroxide (H_2O_2) [2]. High ROS levels can damage DNA and induce tumorigenesis [3, 4]. Alternatively, the induction of ROS formation by chemotherapy and ionizing radiation, such as cisplatin, can be used therapeutically to cause DNA damage-induced cell death [5]. Cisplatin causes DNA damage and triggers the generation of ROS, which subsequently leads to cell death [6, 7]. Wang et al. showed that dioscin induces cancer cell apoptosis through elevated oxidative stress induced by the downregulation of Prdxs [8]. In recent years, elevated expression levels of individual Prdx isoforms have been detected in several human carcinomas [9–11]. Prdxs participate in the cellular antioxidant defense system and may affect tumor development or progression.

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