inhibitionofPI3KAktsignalingbyp38

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(Fig. 2A). In this study, we found a direct activation of p38 (Fig. 2B) and a phosphorylation of Akt via p38-knockdown of PI3K/Akt signaling. It has been proposed that p38 plays a role in the oxidative stress-induced apoptosis of mitochondria by toxic substances (18, 19). In the present study we found that PKC regulates the expression of PI3K/ Akt in a mouse model of oxidative stress-induced apoptosis. Protein Akt was significantly elevated in the nucleus and osteosarcoma cells of the rat brain (Fig. 2C). This was observed in the rat brain microglial cell line BL21, which provides a model by which oxidative stress-induced apoptosis can be abrogated by PKC. It was found that PKC is required for PKC-induced up-regulation of the oxidative stress-induced protein expression in the brain. PKC-induced up-regulation of PI3K/Akt was also observed in the rat hippocampus, which was rescued by the down-regulation of PI3K/Akt. PKC induction of the apoptotic cell death pathway in the hippocampus was observed in the brain microglial cell line BL21. PKC- induced up-regulation of PI3K/Akt was also observed in the brain microglial cell line BL21. We show that PKC regulates the expression of the apoptotic cell death pathway in the rat brain. Together these results indicate that PKC-induced apoptosis up-regulates the expression of the apoptotic cell death pathway in the rat brain. To further elucidate the role of PKC in the induction and regulation of apoptosis of the rat brain, we reported that PKC regulates the expression of Akt in the brain. This paper is the first to establish that PKC regulates the expression of the apoptotic cell death pathway in the rat brain. Acknowledgements This study was supported by National Science Foundation of China (No Grant No. MH084879). We thank Drs. Xiao Zhang and Sunli Li for helpful discussions. References 1. Biswas T, Manzoni-Garcia T, Rizkowska D, Quackenbush S, et al. The phosphorylation of Akt and its role in the pathogenesis of Erythropoiesis gingivalis. J Biol Chem 1995;275:2449–59. 2. Wang Y, Chang JH, Zou Q, Lin Y, et al. The PKC-PG-38 protein family of mediators mediates apoptosis induced by apoptosis in non-small cell lung cancer. Cancer Res 3. Wang Y, Zheng JB, Chen K, Wang C. Apoptosis of small cell lung cancer by p38-mediated apoptosis. J Biol Chem 4. Zhang J, Zheng JB, Zhang X, Yee JY, et al. PKC- PG-38 protein family mediates apoptosis induced by apoptosis of non-small cell lung cancer. J Biol Chem 5. Chen Y, Cheng HJ, Wang C, Wang J, et al. Apoptosis of small cell lung cancer by p38-mediated apoptosis in non- small cell lung cancer. Cancer Res 2000;99:895–603. 6. Kim DH, Kim S-H, Kim JH, Kim S-J, et al. P38-PG-38 protein family of mediators mediates apoptosis induced by apoptosis of non-small cell lung cancer. Cancer Res 7. Kim KS, Kim KS, Kim KS, Kim JH, et al. P38- PG-38 protein family of mediators mediates apoptosis induced by apoptosis of non-small cell lung cancer. Cancer Res 8. Kim JH, Kim KS, Kim KS, Kim JH, Kim JH, et al. The PKC-PG-38 protein family of mediators mediates apoptosis of non-small cell lung cancer. Cancer Res 9. Kim KS, Kim KS, Kim KS, Kim JH, Kim JH, et al. P38- PG-38 protein family of mediators mediates apoptosis induced by apoptosis of non-small cell lung cancer. Cancer Res 10. Kim KS, Kim KS, Kim KS, Kim JH, Kim JH, et al. P38-PG-38 protein family of mediators mediates apoptosis induced

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