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PREVENTIVE EFFECT OF MUSHROOM PHELLINUS LINTEUS ON THE INHIBITION OF GAP JUNCTIONAL INTERCELLULAR COMMUNICATION BY H₂O₂ IS INVOLVED IN THE UP-REGULATION OF ERK2 AND p38

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Gap junctional intercellular communication (GJIC) is a cellular event underlying the tumor promotion process and that treatment to prevent the down-regulation or to up-regulate GJIC is important in preventing tumor promotion. We evaluated the potential preventive effect of Mushroom Phellinus Linteus (PL) against the promoting action of hydrogen peroxide (H₂O₂) in WB-F344 rat liver epithelial cells. Cells were preincubated with PL (1-100 μg/ml) for 24h followed by a stimulating treatment with PL and H₂O₂ (500 μM) for 1h. Fluorescent dye (Lucifer Yellow) coupling between adjacent cells was evaluated by SL/DT (Scrape-Loading/Dye-Transfer). The distribution, quantity and phosphorylation pattern of connexin 43 were detected using immunofluorescence analysis and Western blotting. PL (5-100 μg/ml) significantly prevented down regulation and hyperphosphorylation of connexin 43 by H₂O₂. Immunofluorescence analysis for connexin 43 demonstrated numerous punctate fluorescent spots along the intercellular plasma membrane in controls, which were significantly decreased by H₂O₂. PL prevented the decrease of Connexin 43. Interestingly, we also found that PL increased quantity of some MAPK (ERK2, p38). In conclusion, we suggest that PL might act as an

anti-tumor promoter via its ability of prevent down-regulation of GJIC through activation of ERK2 and p38.