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Experimental and Molecular Therapeutics

Abstract #4584: Exploration of the mechanisms of PHY906 in reducing the intestinal toxicity caused by irinotecan

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Article

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Abstract

PHY906 is a standardized four-herb traditional Chinese formulation that has been used for over 1700 years in the treatment of gastrointestinal ailments and is currently in anticancer clinical trials in the US as an adjuvant to chemotherapy. Preliminary clinical results indicated PHY906 could decrease G.I. toxicity triggered by irinotecan for treating colon cancer. In a murine colon-38 allograft model, PHY906 (500 mg bid days 0-3) alone, does not significantly inhibit tumor growth. However, the combination of PHY906 and irinotecan (360mg/kg, day 1) had higher anti-tumor activity in comparison to irinotecan alone. Additionally, PHY906 decreased weight loss caused by irinotecan. The impact of PHY906 on the intestinal toxicity caused by irinotecan at day 2 and day 4 were studied. Adding PHY906 to irinotecan treatment, a) reduced irinotecan induced degenerative changes throughout different regions of the intestine on day 4 but not on day 2, b) reduced irinotecan induced DNA damage and apoptosis of intestinal cells on day 4, c) promoted the re-growth of crypt cells which could be partially attributed to the wnt3a-potential activity of the aglycone component(s) of PHY906 on day 4, d) inhibited TNF- α ; induced NF- κ B activity, e) decreased the infiltration of neutrophils in intestinal crypt areas and decreased pro-inflammatory cytokine levels. In summary, our studies suggest that PHY906 reduces intestinal damage caused by irinotecan through the



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inhibition of inflammation and enhancement of intestinal repair by promoting intestinal progenitor cell proliferation. **This work is supported by a supplement grant: CA-63477 from NCI, USA**

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Footnotes

- 100th AACR Annual Meeting-- Apr 18-22, 2009; Denver, CO
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