

PAC triggers apoptosis in colon cancer cells by repressing cyclin D1 via STAT3/JAK2 pathway inhibition

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Globally, cancer of the colon is the third leading cause of cancer in males and the fourth leading cause of cancer in females. Unfortunately, only few patients experience complete pathologic responses to chemotherapy, mainly because of their resistance to treatment. Hence, it is imperative to look for novel agents high efficiency and less side effects. We have shown here that PAC, a novel curcumin analogue, has potent anti-colon cancer properties both in vitro and in vivo. Indeed, PAC triggered apoptosis in colon cancer cells through the mitochondrial pathway and down-regulated cyclin D1 as well as other important oncogenes, such as survivin and C-Myc. Interestingly, knocking down of cyclin D1 with specific siRNA enhanced the pro-apoptotic effect of PAC, suggesting that this effect is mediated through the inhibition of cyclin D1. Additionally, PAC delayed the cell cycle at G2/M phase in colon cancer cells and up-regulated the tumor suppressor proteins p16 and p21. These effects seem to be mediated through the inhibition of the STAT3/JAK2 pathway, since PAC inhibited these 2 important protein kinases. Importantly, these effects were also observed in vivo in tumor xenografts. These results indicate that PAC could constitute a powerful, yet not toxic, new chemotherapeutic agent against colorectal tumors.

Biography

Abdelilah Aboussekhra obtained his PhD in molecular genetics from the University of Paris XI (Orsay) in 1992. The topic of his doctoral research was DNA repair mechanism in *S.cerevisiae*. His first Post-Doctoral position was with Dr. Rick Wood in the Imperial Cancer Research Found (Clare Hall, London), then he joined the institute of cell Biology (ETH, Zurich) where he worked with Dr. Fritz Thoma on the role of chromatin in modulating nucleotide excision repair. He joined King Faisal Specialist Hospital and Research center (Riyadh, Saudi Arabia) as Scientist and he established his own laboratory (DNA repair and Apoptosis). His present position is Senior Scientist and Head of the Cancer Biology and Experimental Therapeutics Laboratory in the Molecular Oncology Department. Currently, his main interest is directed towards breast cancer and the role of stromal fibroblasts in the development and spread of these tumors.

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