Title	Wild-type p53-dependent upregulation of c-myc mRNA is associated with indomethacin induced apoptosis in human gastric cancer cells
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WILD-TYPE p53-DEPENDENT UPREGULATION OF C-MYC mRNA IS ASSOCIATED WITH INDOMETHACIN-INDUCED APOPTOSIS IN HUMAN GASTRIC CANCER CELLS. G.H. Zhu, B.C.Y. Wong, C.K. Ching, *S.T. Yuen, *E.Y.T. Chan, K.C. Lai, S.K. Lam. Departments of Medicine & *Pathology, Queen Mary Hospital, the University of Hong Kong, Hong Kong.

Backgrounds: Apoptosis is believed to play a major role in gastric epithelial cell turnover, ulcerogenesis and tumorigenesis *in vivo*. We previously identified that nonsteroidal antiinflammatory drugs (NSAIDs) could inhibit cell proliferation and induce apoptosis in gastric cancer cell lines. In this study, we further explored the role of protooncogene and tumor suppressor genes in the mechanism underlying NSAID-induced apoptosis. *Methods*: Two different gastric cancer cell lines, MKN28 (mutant-type p53, well differentiated) and AGS (wild-type p53, poorly differentiated) were compared in apoptosis induction, cell cycle and apoptosis-related genes after being treated with various concentration of indomethacin for 24 hr. Cell apoptosis was characterized by acridine orange staining, DNA fragmentation and flow cytometry, and cell cycle by flow cytometry. The mRNA and protein of p53, $p21^{waf1/cip1}$ and c-myc were detected by Northern and Western blot. *Results*: Indomethacin could induce apoptosis of both cancer cell lines in a dose- and time-dependent manner without any alteration of cell cycle. Much more profound apoptosis effects were observed in AGS cells than in MKN28 cells. After 400μM indomethacin treatment, more than 50% cells underwent apoptosis in AGS compared to only less than 20% cell in MKN28. The level of p53, $p21^{waf1/cip1}$ and c-myc mRNA was kept constant in MKN28 cells during 24 hr exposure to indomethacin (400μM), but a progressive increase in c-myc expression was noted in AGS cells as early as 2 hr with a peak at 8 hr while p53 and $p21^{waf1/cip1}$ remained unchanged. In contrast to the unchanged p53 mRNA in MKN28, its protein level was profoundly elevated 4 hr after treatment, and kept sustained elevation until 24 hr. *Conclusions*: 1. Indomethacin-induced apoptosis in gastric cancer cells is not preceded by cell cycle arrest; 2. Poorly differentiated cancer cell line is more sensitive to the death inducer than well differentiated one; 3. Constitutive expression of wild-type p53 and/or its dependent overexpression of c-myc may contribute to the mechanism of indomethacin-induced apoptosis.

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Specific association of trisomy 22 with acute myeloid leukemia with monocytic features and inversion 16. Y.L. Kwong, K.F. Wong[+] , Division of Haematology and Oncology, Queen Mary Hospital, and [+]Department of Pathology, Queen Elizabeth Hospital, Hong Kong.

Background. Trisomy 22 is a rare karyotypic aberration in acute myeloid leukemia (AML). Previous data indicated that it might be associated with a specific type of AML showing monocytosis and eosinophilia. A relationship with inversion 16 [inv(16)(p13q22)] was also found. ***Aims.*** This study aims at defining the clinicopathologic, karyotypic and molecular features of AML with trisomy 22. ***Materials and Methods.*** A consecutive series of 170 cases of AML were reviewed. Morphological and cytochemical classification of the AML was performed according to standard FAB criteria. Karyotyping was performed on overnight fluorodeoxyuridine synchronised culture of marrow cells. Amplification for the fusion transcript *CBFB/MYH11* characteristic of inv(16) was performed by reverse transcription polymerase chain reaction (RT-PCR) with two pairs of nested *CBFB* and *MYH11* primers. ***Results.*** Three cases of AML with trisomy 22 were identified and their clinicopathological data are shown.

Case	Sex/Age	Hb	WBC	Plat	AML subtype	Karyotypic features	RT-PCR for *CBFB/MYH11*
1	M / 29	7.5	166.5	25.0	M4	47,XY,+22[10] / 46,XY[11]	positive
2	M / 39	9.1	11.2	39.0	M5a	48,XY,+9,+22[9] / 46,XY, del(7)(q22) [4] / 46,XY [1]	positive
3	M / 16	12.1	59.0	51.0	M4	47,XY,+22 [17] / 46,XY [2]	positive

Conclusion. Trisomy 22 is a rare karyotypic aberration. Two consistent associations were observed : AML with monocytic features, and inv(16). These findings indicate that trisomy 22 may be a secondary karyotypic aberration, and that its presence should prompt molecular investigations for inv(16) if the latter is not shown on karyotypic analysis.