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9.2 Microsatellite instability and mismatch repair gene mutations are common in young colorectal cancer patients in Hong Kong

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Colorectal cancer (CRC) is one of the most common cancers throughout the world. We have previously shown that Hong Kong, like other rapidly developing Asian countries, showed a rapidly rising incidence of CRC over the last decade, and that rapid increase is entirely attributable to classical late onset (>50) patients. Surprisingly, there is a much higher incidence of young CRC (<45) in Hong Kong compared to other countries. This high incidence in the young population was steady over the last 20 years while the overall incidence of CRC rapidly increased. The pattern suggested a hereditary predisposition in our population. In this study, we investigated the incidence of microsatellite instability (MSI) in 116 local CRC of varying ages. All were Chinese patients with family histories not satisfying the Amsterdam's criteria. By analysing 10 microsatellite loci, the incidence of MSI varies with the age group of the patients with the highest (over 60%) for those under 30, and the lowest (below 15%) for those over 45. There were statistically significant difference in the incidence of MSI tumours between those <36 and >35 years old (p=0.00023), and between those <46 and >45 years old (p=0.028). For those with MSI tumours, germline mutation in either hMSH2 or hMLH1 were found in half of the young patients analysed. Our results indicated that MMR gene mutations are significant in contributing to the high incidence of young CRC in Hong Kong Chinese. As majority of them do not have a family history satisfying the Amsterdam's criteria, they are not classified as HNPCC and proper surveillance programme may not have been offered to them and their families. In this context, microsatellite analysis could help to identify these patients.

9.3 Cytokines expression by tumour associated macrophages in non-small cell lung carcinomas–an in situ study

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Macrophages are pleuripotent cells commonly found in malignant tumours. Amongst their diverse potentials, their capacity for tumoricidal, inflammatory, phagocytic, tissue remodelling and angiogenic activities may exert different and contrasting effects on tumour growth. In vitro experiments have mainly studied the cytostatic and tumoricidal functions of tumour associated macrophages (TAM) isolated from tumour homogenates, and the understanding of the role of TAM remains incomplete.

Purpose: To investigate the role of TAM in malignant tumours by studying the expression of the macrophage products IL-1ß, monocyte chemotactic peptide -1(MCP-1) and lsozyme (Lyz) in lung carcinomas.

Methods: TAM were identified by immunohistochemical study using the macrophage markers CD 68 and Ki-MiP antibody in 11 squamous cell and 12 adenocarcinomas of the lung. The expression of IL-1ß, MCP-1 and lysozyme were detected by RT-PCR and their cellular origin were studied by in situ hybridization using radiolabelled riboprobes.

Results: TAM were present in all tumours but their location and expression profile were heterogeneous. There was a marked accumulation of TAM along the tumour-stroma interface, where most TAM strongly expressed the macrophage marker lysozyme, and a small number expressed MCP-1. TAM were also abundant within the connective tissue separating or surrounding tumour islands, but morphologically they resembled resident macrophages and showed rare and weak expression of the molecules studied. A few TAM were found within tumour cell clusters where Lyz and MCP-1 were occasionally expressed. In all the cases studied, the expression of the inflammatory cytokine IL-1ß was infrequent and found at sites of necrosis and polymorph accumulation.

Conclusions: TAM accumulation in malignant tumours was heterogeneous and their expression profile was location-dependent, rendering an in-situ approach essential for the study of macrophage functions in tumours. The most active site of expression of macrophage products occurred mainly at the tumour stroma junction, indicating an active interaction with tumour cells at the tumour invasion front. The findings provide important information for the designing of macrophage-related modalities of cancer treatment, and have important implications on the development of new drug delivery systems using liposome technology.