Review

UHN Microarray Centre

IL-24 may play a role in the resistance of mammary carcinogenesis in Copenhagen rats

Review of: Xuan W, Li Y-J, Liu G, Ben-David Y, Archer MC. Interleukin-24 Induces Expression of β_4 Integrin but Suppresses Anchorage-Independent Growth of Rat Mammary Tumor Cells by a Mechanism That Is Independent of β_4. Mol Cancer Res 2009, 7(3)

The identification of genes that confer susceptibility or resistance to breast cancer could lead to alternative methods for the detection and treatment of breast cancer. Mutagenic N-nitroso compounds, such as methylnitrosourea (MNU), are associated with red meat consumption and may be implicated in human cancer (1). It is also known that some rat strains are more susceptible to mammary tumours than others as, for example, Wistar-Furth rats develop multiple mammary tumours following a single injection of MNU, whereas Copenhagen rats develop few, if any, tumours (2,3).

Previously, studies were conducted to identify genes associated with tumour resistance by infusing an oncogene (v-Ha-*ras*)-containing retrovirus into the mammary ducts of resistant F_1 rats from Copenhagen x Wistar-Furth cross (4). Although v-Ha-*ras* can overcome anchorage-dependent growth in some cells (5), this study unexpectedly found that a significant number of rat mammary cell lines continued to grow in an anchorage-dependent manner. The study also found that cells that grew in an anchorage-independent manner showed a positive correlation with the expression of cyclin D1 (4), a gene that has also been shown to stimulate anchorage-independent growth in human mammary epithelial cell lines (6).

This current study, which builds on the previous work by this group, investigated the differential expression of genes in the anchorage-dependent and anchorage-independent mammary carcinoma cell lines. Using the UHNMAC Agilent Service (44K Whole Rat Genome arrays), this study found that the expression of interleukin-24 (IL-24), a known tumour suppressor gene (7), and β_4 integrin was highly correlated with anchorage-dependent growth. IL-24 was also found to inhibit cell migration and invasion in vitro, and suppress the growth of breast cancer cells in vivo (3). IL-24-induced inhibition of cell proliferation was associated with transcriptional up-regulation of cell cycle inhibitor $p27^{Kip1}$ mediated by Stat3 activation.

Although this study found, for the first time, that β_4 integrin is a downstream target of IL-24; the data shows that β_4 integrin does not play a direct role in regulating the proliferative capacity of rat mammary tumour cells (3). This is in contrast to another study that found β_4 integrin actually enhances anchorage-independent growth in human breast carcinoma cells (8). Xuan suggests the possibility that overexpressed IL-24 may override the growth enhancing action of β_4 integrin. Interestingly, the expression of α_6 integrin was similar in anchorage-dependent and anchorage-independent cells, and was not induced by IL-24.

The results also found that expression of cyclin D1 is not affected by expression of IL-24 suggesting that the suppression of anchorage-independent growth by IL-24 is independent of cyclin D1. This study concludes that IL-24 suppresses the growth of rat mammary carcinoma cells and may play a role in the resistance of Copenhagen rats to mammary carcinogenesis.

References

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