

Gene Transfer to Liver Cancer Cells of B7-1 Plus Interleukin 12 Changes Immunoefector Mechanisms and Suppresses Helper T Cell Type 1 Cytokine Production Induced by Interleukin 12 Alone

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Abstract of:

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To investigate the cooperative effect of B7-1 and IL-12 in the induction of antitumour activity, we have developed retroviral vectors encoding human B7-1, murine IL-12, or both B7-1 and IL-12 coordinately. Murine transformed liver cells (BNL) were engineered to stably express B7-1, IL-12, or both by infection with corresponding retroviruses. No tumour was observed in 20, 75, and 95% of mice receiving, respectively, B7-1, IL-12, and B7-1/IL-12 modified tumour cells after 250 days of inoculation. In contrast, injection of parental BNL or BNL/Neo cells resulted in lethal tumour progression in all mice. Protection against rechallenge with parental tumour cells was observed only in mice who had rejected BNL/IL-12, but not in animals that rejected BNL/B7-1 or BNL/B7-1-IL-12. Growth of parental tumour cells was significantly delayed by simultaneous injection in a distant site of irradiated tumor cells engineered to express IL-12

or both B7-1 and IL-12 but no B7-1 alone. BNL/B7 and BNL/B7-1-IL12 showed similar efficacy in these experiments. Antitumour immunity induced by B7, with or without IL-12, was found to depend mainly on CD4+T cells with a minor contribution of a non-T cell mechanism; whereas the effect of IL/12 was dependent on CD8+T cells and on non T cell effectors. Immunization of mice with IL-12 modified BNL cells induced secretion of a Th1 pattern of cytokines while immunization with cells expressing both IL-12 and B7-1 resulted in inhibition of IFN- γ production. Immunization with BNL/B7-1-IL-12 cells in the presence of anti-human B7-1 Mab resulted in restoration of IFN- γ production to the levels found in animals injected with BNL/IL-12 cells. To summarize, in our model coexpression of B7-1 and IL-12 in tumour cells does not result in improved antitumoral activity as compared with expression of IL-12 alone. This may be related to the fact that B7-1 changes the mechanisms of antitumour immunity and inhibits IFN- γ y productions induced by IL-12 *in vivo*.

Variables independently associated with self-reported obesity in Europe

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Objective: The rapid increase in obesity rates over recent years suggest that cultural and societal influences are affecting the adjustment in the energy balance equation in addition to other physiopathological or genetic determinants. Therefore, a pan-EU study was carried out to explore the influence of sociodemographic factors as well as some attitudes (smoking and exercise) on the prevalence of obesity in the adult population of all 15 member states of the EU.

Design: Overall, a sample of 15 239 individuals aged 15 years and upwards in the EU completed the questionnaire. Subject selection was quota-controlled to make the questionnaire sample nationally representative following a multistage stratified cluster sampling. Self-reported height and weight were used to calculate body mass index (BMI).

Results: From the EU average results, it can be seen that only about half of the EU population (48%) is within the normal weight range, while the obesity (BMI ≥ 30 kg m $^{-2}$) prevalence was about 10% in the EU and the overweight prevalence was 36.6% and 25.6% among men and women, respectively. UK

subjects had the highest prevalence of obesity (12%), while Italians, French and Swedes had the lowest levels of obesity (about 7%). Concerning age and social class interactions, logistic regression analysis showed that high social class and younger individuals in all groups had a lower odds ratio for obesity prevalence. People with a higher level of education are less likely to be obese, while the interaction between educational levels and obesity was different for men and women. A low participation in various leisure-time physical activities, the lack of interest (precontemplation) in being involved in exercise/ physical activity and the increasing number of hours sitting down at work appear to be predictors of obesity. Single individuals were less prone to become obese than couples or widowed/divorced people. Finally, smoking status was statistically linked to the prevalence of obesity, since non-smokers or ex-smokers for more than 1 year presented a higher tendency for a BMI >30 .

Conclusions: This survey confirms that a priority area for health intervention aimed at preventing the development of obesity should be to increase levels of physical activity, although the approach will depend on the population, especially with respect to educational and socioeconomic aspects.