Activation of Tumor Necrosis Factor- α and Lymphotoxin- α via Anti-CD40 in Human B Cells

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Key Words

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Activation of human resting B cells by anti-CD40 monoclonal antibody and IL-4 results in proliferation and IgE iso-type switching [1, 2]. Because tumor necrosis factor (TNF)- α and lymphotoxin (LT)- α are known autocrine growth factors for B cells [3, 4], we examined the capacity of anti-CD40 and/or interleukin (IL)-4 to induce TNF- α and LT- α mRNA and protein expression in tonsillar B cells and in the B cell line Daudi. mRNA was detected by Northern blot analysis, surface proteins were detected by flow cyto-metric analysis and secreted proteins were measured by EL-ISA.

Anti-CD40, but not IL-4 alone induced in both tonsil B and Daudi cells strong expression of LT- α mRNA and weak expression of TNF- α mRNA. This induction was augmented by IL-4 (fig. 1). Anti-CD40 and anti-CD40+IL-4 strongly induced the expression of surface LT- α , but caused a small increase in surface TNF- α (fig. 2). Anti-CD40 and anti-CD40+IL-4 induced the secretion of LT- α by Daudi cells (medium < 7pg, anti-CD40 125 pg and anti-CD40+IL-4 190 pg), but not by tonsillar B cells. There was no detectable induction of TNF- α secretion in Daudi or tonsil B cells.

TNF α

LT α

t-i t

t-i t

Fig. 1. a Induction of TNF- α and LT- α mRNA in B cells. Purified human tonsillar B cells were incubated for 24 h with medium, anti-CD40 (5 μ g/ml), IL-4 (100 IU/ml) or anti-CD40+IL-4. b Induction of TNF- α and LT- α mRNA expression in the human B cell line Daudi. Cells were stimulated for 24 h as indicated above.

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mTNF α

mLT α

Fig. 2. CD40-mediated expression of membrane TNF- α and membrane LT- α expression in B cells. Purified tonsil B cells were incubated for 24 h with medium, anti-CD40 (5 μ g/ml) or anti-CD40+IL-4 (5 μ g/ml+100 IU/ml, respectively). Surface expression of TNF- α and LT- α are indicated as solid lines. Negative isotype controls are indicated with dotted lines.

medium

anti-CD40

anti-CD40+IL-4

IL-4 induces strong expression of membrane LT- α in B cells and suggests an important role in B cell

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These results indicate that anti-CD40 induces strong expression of membrane LT- α in human B cells and suggest

that membrane LT- α may play an important role in B cell

activation via CD40.

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