Monocyte-derived dendritic cells from highly atopic individuals are not impaired in their pro-inflammatory response to toll-like receptor ligands.

BACKGROUND: Toll-like receptor (TLR) agonists are widely used as adjuvants in specific immune therapy protocols for patients with atopic disposition. Monocyte-derived dendritic cells (mDCs) are thought to be important target cells for these compounds. OBJECTIVES: To compare surface markers, TLR expression, TLR functionality after ligand stimulation, and genetic polymorphisms in the TLR 2-, 3-, and 4-genes in mDCs from atopic vs. non-atopic patients. METHODS: mDCs from highly atopic individuals (total serum IgE>1000 IU/mL) and healthy control persons (total serum IgE<75 IU/mL) were screened for TLR 1-10 expression by real-time PCR. Receptor function was analysed by IL-12 and TNF-alpha production after incubation with the respective ligands peptidoglycan (PGN) (TLR 2), polyriboinosinic-polyriboctydylid acid (poly IC) (TLR 3), lipopolysaccharide (LPS) (TLR 4), flagellin (TLR 5), and CpG-DNA/non-CpG-DNA (TLR 9). Haplotype-tagging single-nucleotide polymorphisms of the TLR 2-, 3-, and 4- genes were analysed for genetic associations. RESULTS: mDC from atopic patients showed a very similar pattern of TLR expression as controls with strong expression of TLR 2, 4, 5, 6, and 8, moderate expression of TLR 1 and 3, and no or very low expression of TLR 7, 9, and 10. After stimulation with TLR ligands, mDCs from atopic patients acquired a mature
phenotype with a tendency towards a higher up-regulation of the co-stimulatory molecules CD80, CD83, and CD86 than control mDCs. IL-12 and TNF-alpha were produced at a similar level in both groups of DCs. Among the different TLR agonists, poly IC showed the strongest activation of DCs, followed by LPS, PGN, and flagellin. This was paralleled by a strong functional expression of protein kinase R and retinoid-inducible gene-I (RIG-I), two additional poly IC-sensing receptors in both groups. Genetic analysis of single-nucleotide polymorphisms in the TLR 2-, 3-, and 4-genes in both groups revealed no major allele or genotype differences. CONCLUSIONS: mDC from atopic patients are not restricted in their response to TLR-ligands. TLR agonists seem to be suitable to induce pro-inflammatory immune responses and maturation in mDCs from highly atopic individuals and represent reasonable adjuvants for specific immunotherapy reagents.

Zeitschriftentitel / Abkürzung: Clin Exp Allergy

Jahr: 2007

Band: 37

Heft / Issue: 3

Seiten: 381-90

Sprache: eng


Print-ISSN: 0954-7894

TUM Einrichtung: r Dermatologie und Allergologie

Occurences:

- Einrichtungen > Fakultäten > Fakultät für Medizin > Kliniken und Institute > Klinik und Poliklinik für Dermatologie und Allergologie > 2007

entries: