Children with Down syndrome show quantitative, phenotypical and functional differences of effector T-cells compared to immunocompetent controls

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Introduction and hypothesis

Trisomy 21 is not only associated with an increased susceptibility to respiratory infections suggesting a deficiency of the adaptive immune system but is also associated with a higher incidence of autoimmune disorders.

This study focuses on the investigation of the antigen-specific humoral and cellular immune response as well as the phenotypical cell features and quantitative analysis of lymphocyte subpopulations in children with Down syndrome (DS) compared to age-matched immunocompetent controls (C).

Subjects and methods

• Subjects (Table 1)
  - 40 children with Down syndrome (age: 7.38 ± 1.11 years)
  - 51 controls (age: 8.80 ± 0.97 years)

• Methods
  1. Antigen-specific stimulation of T-cells (Fig. 1)
     Functional and phenotypical characterization

Whole blood samples were stimulated for 6h with specific antigens of cytomegalovirus (CMV), varicella zoster virus (VZV), mycobacteria (PPD) and polyonal stimulated with Staphylococcus aureus Enterotoxin B (SEB). After 2h of incubation, brefeldin A was added to inhibit secretion of induced cytokines.

2. Cell-surface staining of lymphocyte subpopulations
   - Quantitative analysis

3. Quantification of humoral immune response using ELISA (CMV and VZV IgG)

Results

• Children with DS showed a higher proportion of NK-cells within the lymphocytes whereas the B-cell percentage was decreased and the percentage of T-cells did not differ in both groups (Fig. 2).

• Within the T-cell population, children with DS revealed less CD4+ and more CD4+CD8+ double positive T-cells (Fig. 3).

• Within the CD4+ T-cells, a higher proportion of regulatory T-cells, TH17-cells, and a higher TH1/TH2 ratio was detectable in children with DS (Fig. 4 A, B).

• Children with DS showed a higher expression of the anergy markers PD-1 and CTLA-4 on CD4+ T-cells (Fig. 4 C).

• Both groups showed an age-appropriate extent of endemic infection with CMV, VZV and mycobacteria and no pronounced differences in antigen-specific immune response were detectable (Table 2, Fig. 5).

• Frequency of polyclonally activated effector T-cells in children with DS were significantly higher than in controls (Fig. 5).

Conclusion

• Besides a general proportional shift of leukocyte and lymphocyte subpopulations, effector T-cells seem to be functionally impaired which may contribute to a higher susceptibility towards infections.

• The simultaneously higher fraction of reactive effector T-cells may represent a compensatory effect of functional anergy and/or be a consequence of a more pronounced history of infections.

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