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SUPPRESSOR CELL FUNCTION IN THYROID AUTOIMMUNE DISEASE IS AFFECTED BY PLASMID ENCODED PROTEINS OF ENTEROPATHOGENIC YERSINIA

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INTRODUCTION

Autoimmune thyroid disease(AITD) and Yersinia enterocolitica(Y.e.) show striking crossreactivities of humoral and cellular immunity (1,2,3). Since Y.e. also has binding sites for thyrotrophinTSH).the role Y.e. might play for the pathogenisis of AITD became a matter of interest. Recently it became evident that a pre-requisite of virulence in enteropathogenic Y.e.-infections is the presence of a 42-46 MDa plasmid which is rapidly lost after subcultivation(4). This plasmid mediates virulence functions such as serum- and phago cytosis resisitance or cell adherence(5). The plasmid also encodes for at least 6 proteins against which humans and animals produce antibodies after Y.e.-infections. In calcium deficient culture medium these immunogenic release-proteins(RPs) are secreted in high quantities(6).

We recently reported that patients with AITD have high frequencies of RP-antibodies of IgM,IgA and IgG class as well as antibodies to a 25 kDa RP.This 25 kDa RP shows antigenic homologies with the TSH-receptor(7). Moreover,in Graves`disease(GD) antibodies to the 25 kDa RP and antibodies of IgA class emerge early at the onset of the disease but later than the TSH-receptor antibodies are detected in patients`blood(8). Within 12 months thereafter these antibodies vanish(9).

Since bacteria carrying the plasmid affect some properties of macrophages,i.e. cell adherence and pagocytosis resistance(5),we now investigate the functional effect the RPs and Y.e.-plasma membranes(YOP) might have on the immnune surveillance in patients with AITD. In the present study we looked at the effect of RPs and of Y.e.-plasma membranes on lymphocyte stimulation with an unrelated antigen,tetanus toxoid antigen(TTA).

MATERIAL AND METHODS

Patients profile

Patients with Graves`hyperthyroidism and normal individuals who previously had been sensitized to TTA were assessed for RP antibodies. All GD patients(n=5) were RP antibody positive and had TSH-receptor antibodies. If their last TTA vaccination was more than 2 years ago,the individuals were re-sensitized with their consent.

Lymphocyte fractions

Heparinized peripheral blood was submitted to Ficall density centrifugation. The lymphocyte fraction (PBL) was suspended with sheep red blood cells(SRBC). The spontaneously formed rosettes(SRBC-R) were separated from non.T-cells on Ficoll and finally the SRBC were lysed with water. One part of PBLs was plated for 2 hours in plastic dishes with complete RPMI 1640 medium with 20% fetal calf serum(FCS). The adherent cells and the non-adherent lymphocytes were collected,counted and stored for the reconstitution experiments. The yield of adherent macrophages(φM) varied from 2-4% of the initial PBLs.

Antigens

TTA was kindly provided by BEHRING SA,Marburg,FRG. The standard concentration used was 2Lf/ml TTA. Y.e.-RPs were separated from the calcium deficient medium by ultrafiltration(AMICON,PM 10).RPs were resuspended by sonification and passed through a 0.45μ sterile filter. The Y.e.-seroptypes used were O:3 and O:9 strains. In lymphocyte cultures RPs were used at 100ng/ml final concentration.

For the preparation of bacterial outer membranes(YOP), membranes were disrupted by sonic lysis(10). The membranes were washed,extensively sonicated and passed through a 0.45μ filter. The protein which passed the filter was used at 10ng/ml final concentration.

When indicated, indomethacin(IM) was applied at 1-10ng/ml.

Lymphocyte cultures

Cells were cultured in 96 well plates,5 well per sample. The complete culture medium contained 10% FCS. Lymphocytes were used at 1.5×10^6 cells/ml. When indicated,2% adherent φM were added.

Lymphocytes were cultured for 6 days with TTA with or without adding: φM,RPs,YOPs,IM.For the last 24 hours 0.5μCi/ml ^{3}H-thymidine (^{3}H-TdR).Thereafter,cells were collected with an automated cellharvester applying the sequence water,TCA 10%,ethanol.Samples were counted in a scintillation counter and calculated as stimulation index(SI) ± standard deviation(SD). Stimulation or inhibition of the TTA response were expressed as % of the stimulation with TTA alone (TTA=100%).

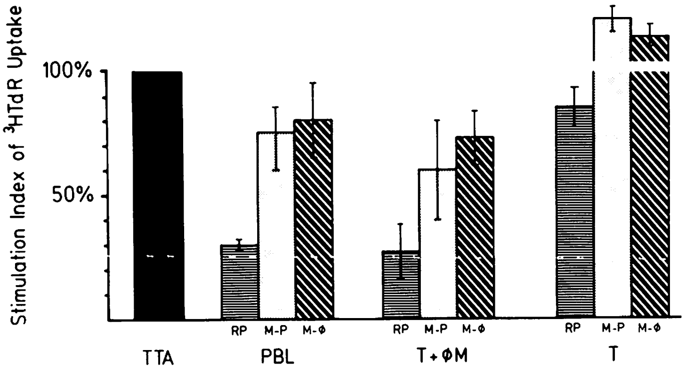

Figure 1: Effect of Y.e.-plasmid encoded antigens on the TTA response of normal peripheral blood lymphocytes.
RP Release Proteins, M-P YOP from Y.e.with/ Mφ without plasmid, φM macrophages, T=T-lymphocytes, T=tetanus toxoid antigen.

RESULTS

Figure 1 shows how the RPs are suppressing the TTA response of normal PBLs(70%+4,n=5,$p < 0.05$). YOP-fractions,however,do not affect the TTA stimulation,regardlessly of whether they derive from bacteria with plasmid(M-P) or without(Mφ). A similar pattern is found with T-cells reconstituted with macrophages(øM). In the absence of macrophages the RPs do not influence the TTA response of T-lymphocytes. In contrast,PBLs from patients with GD are not affected by RPs which only produce an insignificant reduction of the TTA response(Figure 2). The YOPs,however, produce an excess stimulation.

Figure 3 demonstrates that the suppressive potency of RPs is macrophage dependent. Depletion of PBLs from macrophages or administration of indomethacin(IM) abolishes the suppression of the TTA response with normal PBLs.

CONCLUSIONS

Our experiments show for the first time that the plasmid of enteropathogenic Y.e. does interfere through its protein products with the immune surveillance in normal individuals. The suppressive effect of RPs on the TTA response is exerted on the adherent macrophages. The effect on the T-cell proliferation appears to be mediated by prostaglandins,since the cyclo-oxygenase blocker,IM, abolishes the suppression. Although phagocytosis resisitance and cell adherence of enteropathogenic Y.e. are attributed to the plasmid encoded YOP1 antigen,our membrane fractions did not suppress the TTA response. In constrast,both ,membranes from Y.e. with or without plasmid,stimulated lymphocytes from patients with GD,who were pre-sensitized by Y.e.(RP-antibody positive). This may indicate that the plasmid dependent(YOP1) suppressive effect is counteracted by the stimulatory properties of the membrane lipoproteins(10). The macrophages in GD appear not to react to the RPs,although phagocytosis resistance is plasmid encoded(5).

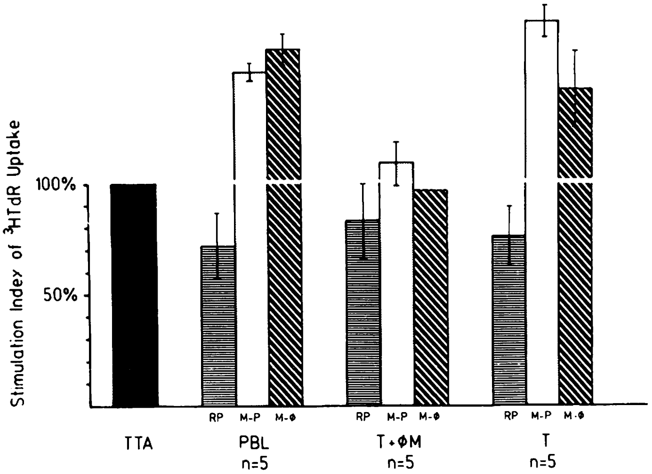

Figure 2: Effect of Y.e.-plasmid encoded antigens on the TTA response of PBLs from patients with GD.
RP= Release Proteins,M-P-YOP from Y.e. with /M-0 without plasmid
øM=macrophages;
T= T-lymphocytes
TTA= tetanus toxoid antigen

This could mean that macrophages are rendered inactive by RPs.Hence, bacteria can not be eliminated through phagocytosis and a latent or chronic infection might result. This scenario would be reflected by the persisting high prevalence of Y.e.-antibodies in GD-patients(8). In genetically committed individuals antigenic mimcry of RPs with thyroid antigens(7) would lead to the break of self-tolerance and the developement of AITD. These are,of course,hypothetical considerations,since in our system the Y.e.-RPs are secreted under non-physoilogical conditions,i.e. calcium deficiency. Further investigations will show what significance RPs might have in vivo.

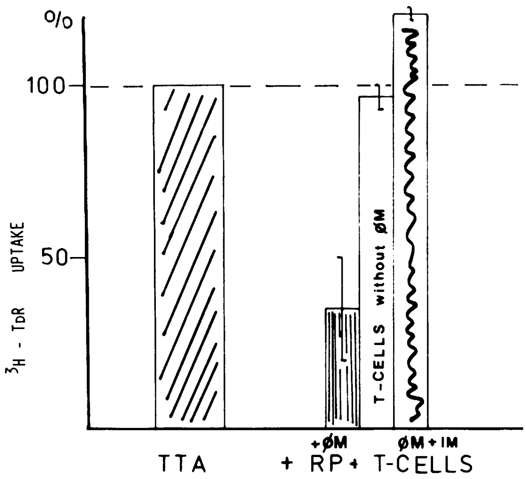

Figure 3: Effect of indomethacin on the RP mediated suppression of the TTA response with normal PBLs.
RP= Release Proteins
TTA= tetanus toxoid antigen;oM= macrophages
IM= indomethacin

REFERENCES

1. Bech K, Larsen JH, Hansen GM, Nerup J (1974) Lancet II:551

2. Lidmann K, Erikson U, Morberg A, Fragreus A (1976) Clin Exp Immunol 23:429

3. Bech K,Clemmensen O, Larsen JH, Bendixen G (1977) Lancet II:1060

4. Zink DL, Feeley JG, Wells JG, Vanderzant C, Vickery JC, Roof W, O`Donnovan GA (1980) Nature 283:224

5. Heesemann J, Algermissen B, Laufs R (1984) Infect Immun 46:105

6. Heesemann J, Gross U, Schmidt M, Laufs R (1986) Infect Immun 54:561

7. Wenzel BE, Heesemann J (1987) Hormone & Metab Res 17(s):77

8. Wenzel BE, Heesemann J, Wenzel KW, Scriba PC (1988) Lancet I:56

9. Wenzel BE, Heesemann J, Wenzel KW, Scriba PC (1988) J Endocrinol Inv 11/2:139

10. Pekkola-Heino K, Viljanen MK, Stahlberg TH, Granfors K, Toivanen A (1987) Acta path microbiol scand Sect C 95:27

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