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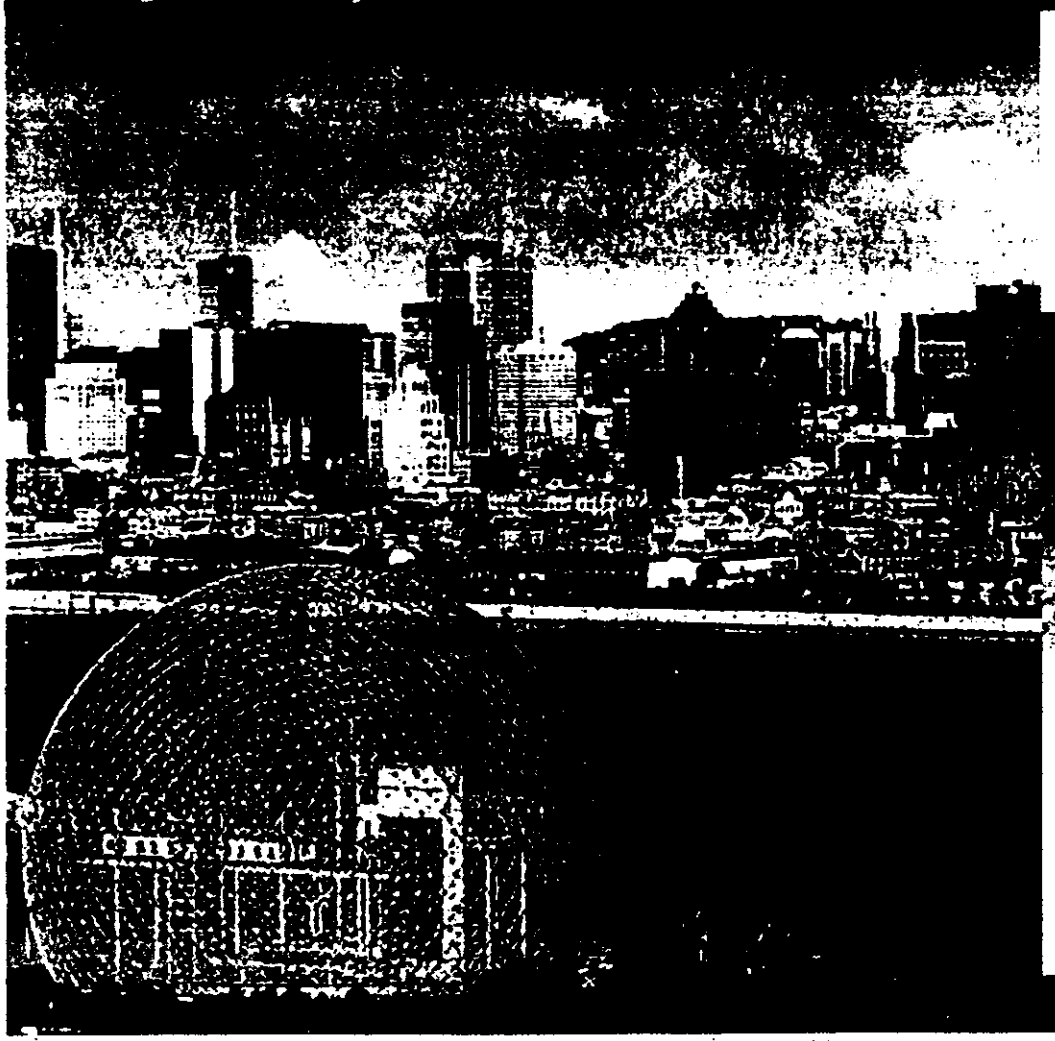

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T45.48

Cellular Immune Response Against a Native Strain of *L. infantum* in a Murine Model of Visceral Leishmaniasis.

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RATIONALE: In Visceral Leishmaniasis (VL) the outcome of the infection depends of a delicate balance between the induction and the regulation of the inflammatory response in target organs. Early inflammatory cytokine responses mediate protective immunity against *Leishmania*, while the late appearance or lack of regulation appears to mediate pathology. Models of VL in mice, using international reference strains of *L. donovani* or *L. infantum/chagasi*, resemble the visceral disease in humans, showing a prompt increment in the parasite load in the liver, followed by spontaneous resolution associated with an effective cell-mediated immune response (CMI); while the spleen shows a relative low parasite burden during the course of infection. METHODS: An experimental model of VL was established in BALB/c mice, with a native strain of *Leishmania*, isolated from a dog reservoir and characterized as *L. infantum* (MCAN/VE/98/IBO-78). Spleen and liver samples were taken at different times post infection (pi). Detection of T cells, Dendritic Cells, Macrophages, IL-2R and cytokines was performed by immunohystochemistry. RESULTS: Major changes during the course of infection occur in the spleen and not in the liver. Moderate increase of parasite burden, splenomegaly, cellular activation and T cell proliferation was seen in the spleen, together with a Th1 cytokine response (IL-12, IFN-γ), that peaks at day 35 pi. The inflammatory cytokine TNF-α is also involved, showing increased levels at the onset and the resolution phase of the infection. Once the infection in the spleen is resolved, the down regulation of inflammatory cytokines occurs, associated with an increase in the number of cells producing regulatory cytokines (IL-4, IL-10, TGF-β). The kinetics of cytokines are also associated with structural changes in the spleen architecture, a feature not observed in the liver. CONCLUSIONS: In contrast with the response observed in models using reference strains of *Leishmania*, the native strain of *L. infantum* studied does not seem to activate CMI in the liver and remains in the organ at very low levels, or the infection is restrained by elements of natural immunity, while in the spleen a controlled, effective CMI is mounted against the parasite. Financed by grants FONACIT S1-2001000861MS, S1-98000041FT and Iniciativa Científica Milenio 4572-VE

T45.49

Seroepidemiology of Toxoplasmosis in Women Referred to Ardabil Laboratory of Health Center for Medical Examination before Marriage, Iran, 2002.

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Objectives: Infection with Toxoplasma gondii can cause sever illness when the organism is transmitted to fetus or when it is reactivated in immune-suppressed persons. The aim of this study was to determine the antibody prevalence of toxoplasmosis in women referred to laboratory of health center for medical examines before marriage.

Methods: This cross-sectional study was performed on 504 sera collected from women in Ardabil city, Iran, in 2002. The samples were studied by indirect immunofluorescent assay (IFA) for determination of IgG and IgM antibodies to toxoplasma.

Results: The seroprevalence of IgG antibody at a titer of ≥ 1:20 was 34.7%. There was the most of antibody titer frequency in 1:20 titer (11.7%) and the least of them in 1:3200 (0.4%) and 1:6400 (0.4%) titres. Only 20 persons (4%) showed IgM antibody against Toxoplasma gondii.

Conclusion: As 65.3% of these women in Ardabil city were seronegative, health education to omit its risk factors, especially during the pregnancy is necessary.

T45.50

Reciprocal CD40 Signals Via p38MAPK and ERK-1/2 Induce Counteracting Immune Responses and Are Differentially Modulated by *Leishmania*.

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Macrophages play host to *Leishmania*, a protozoan parasite that causes leishmaniasis in 0.5 million people annually. It is proposed that the macrophage expressed CD40 interacts with CD40 ligand on T cells to induce IFN-gamma, a Th1-type cytokine that restricts the amastigote growth. Here, we demonstrate that weak CD40 signals induce extracellular stress-related kinase (ERK)-1/2-dependent IL-10 induction whereas stronger signals induce p38-mitogen activate protein kinase (p38MAPK)-dependent IL-12 production. p38MAPK and ERK-1/2 are found to counter-regulate each other. We observed that the CD40-induced p38MAPK phosphorylation, iNOS2 expression and anti-leishmanial function were impaired in *Leishmania*-infected macrophages but were restored by anisomycin, a p38MAPK activator. Anisomycin's effects were reversed by SB203580, a p38MAPK inhibitor, emphasizing the role of p38MAPK in CD40-induced iNOS2-dependent leishmanicidal function. On the other hand, *Leishmania* augments the CD40 signaling via ERK-1/2, inducing IL-10 that inhibits CD40-induced p38MAPK activation, iNOS2 and IL-12 expression. Anisomycin administration, ERK-1/2 inhibition or IL-10 neutralization restores CD40-induced p38MAPK activation and parasite killing in macrophages and in BALB/c mouse, a susceptible host, and establishes a host-protective Th1-type memory response. These data unfold a novel immune evasion strategy, where a parasite differentially modulates the CD40 engaged reciprocally functioning signaling modules. Also implicated in these findings is a scientific rationale to define novel anti-parasite drug targets and to bypass the problem of drug resistance.

T45.51

Morphological and Functional Disturbances in Murine Hypothalamus-Pituitary-Adrenal (HPA) Axis during Experimental Acute Trypanosoma cruzi Infection.

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We investigated herein the HPA axis in mice undergoing acute infection by Trypanosoma cruzi, the causative agent of Chagas disease. Immunohistological analysis of pituitary and adrenal glands of infected animals revealed diverse morphological and structural alterations such as vascular stasis, upregulation of extracellular matrix proteins (laminin and fibronectin), T cells and macrophage infiltration. Functionally, we detected by RIA a decreased in corticotropin-releasing hormone (CRH) and an increased in corticosterone contents in hypothalamus and serum, respectively. In addition, we did not detect any significant alteration in adrenocorticotropic hormone (ACTH) concentration in serum of infected animals. When we analyzed the effects of T. cruzi infection in adenopituitary AtT-20 cell line, the infected cultures presented lower levels of ACTH and proopiomelanocortin (POMC) production when compared to the non-infected ones. In infected AtT-20 cells we observed a strong phosphorylation of STAT-3. In contrast, we detected augmented synthesis of interleukin-2, interleukin-6, suppressor of cytokine signaling (SOCS-3) and inhibitor of activated STAT-3 (PIAS-3) in these cells. In conclusion, our data demonstrated that the HPA axis during the T. cruzi infection presents diverse morphological and functional alterations, also suggesting some direct and indirect influences of the parasite in the endocrine homeostasis.

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Keywords: Trypanosoma cruzi, HPA axis and transcription factors (IR)

T45.52

The Effect of the *Monocyte Locomotion Inhibitory Factor (MLIF)* Produced by *Entamoeba histolytica* upon Th1/Th2 Cytokines Expression by T CD4+ Lymphocytes.

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Introduction: The inflammatory reaction produced by *Entamoeba histolytica* is unusual in that it is intense in the acute phase yet, as the lesion progresses, only a very weak late inflammatory reaction can be found. This scarce inflammation may be associated with amebic products interfering with the late recruitment of monocytes to the inflammatory site. MLIF is a pentapeptide produced by *E. histolytica* in axenic culture, that displays anti-inflammatory effects both *in vivo* and *in vitro*. This factor may (a) interfere with leukocyte migration regulated by cytokines secreted by Th1/Th2 lymphocytes.

Objective: To study the effect of MLIF on activation and production of Th1/Th2 cytokines in human T CD4+ lymphocytes.

Methods: Human mononuclear cells were separated by Ficoll-Hypaque gradient and T CD4+ lymphocytes purified by negative selection. 5 X 10⁵ such lymphocytes were incubated for 24 h in the presence of PMA (50 ng/ml) or MLIF (50 mg/ml). The optimal amounts of MLIF and PMA were determined by a dose-response curve. Cells were analyzed by flow-citometry for cell activation using anti-CD69. Th1/Th2 regulation was studied by intracellular cytokines co-located with chemokine receptors (IL-2FITC- CCR5PE, IFN-gPE- CCR5FITC).

Results: Cells activated with PMA expressed CD69 in 13% and in 11% when activated by MLIF. Resting (RPMI) cells revealed 2%. While five % of resting cells expressed IL-2 and only 0.04% IFN-g, 40% of cells incubated with MLIF produced IL-2 and 12% IFN-g, and 48% and 24% of cells activated with PMA respectively. Two % of cells co-expressed IFNg-CCR5 in the presence of MLIF (vs 1% control), 0.04% co-expressed IL2-CCR5 (vs 2% control) and 18% co-expresses IL4-CCR4 (vs 3.2% control). Cells activated with PMA co-expressed 37% of INF-g-CCR5, 48% for IL-4-CCR4, while IL2-CCR5 remained undetected.

Conclusions: MLIF - as PMA - activated T CD4+ lymphocytes when incubated for 24 h, and induced Th1/Th2 cytokine expression in comparable fashion. (CONACYT GRANT 38104-M)

T45.53

Evaluation of Hydatid Cyst Components' Effect in Prevention of Hymenolepis Nana Infection in Rat.

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Introduction

Parasites are one of the important infectious agents in human and domestic animals. With regard to cross immunity between some species of parasites, this study was performed to determine the cross immunity effect between different components of hydatid cyst (fluid, membrane, protoscolex) and Hymenolepis nana in Rat.

Methods

In this survey 30 free parasite Rats with the same age and sex were selected. Rats were divided into two groups and each were divided into three subgroups. In the first three, hydatid fluid, protoscolex and membrane were injected respectively, and in the other three, the same components with adjuant were used. Each case group was compared with a control one. Immunization was performed by multiple injection. Three weeks after immunization, H nana eggs were administerd orally to the Rats. After observation of H nana eggs in stool of control groups, blood and stool samples were taken from all Rats of cases and controls and different biochemical, parasitological and immunological tests were performed on the samples.

Result

Stool test showed that non immunized Rats were infected by H nana but immunized Rats were not. Protein measurment especially Gammaglobulin demonstrated that the membrane of hydatid cyst represent strongest antigenic effect and hydatid fluid showed the weakest one. Biochemical and statistical analysis showed that the adjuvant increases the antigenicity of hydatid cyst components.

Conclusion

Components of hydatid cyst are immunogenic and prevents H nana infection in Rat and its, effectiveness will be increases by adjuvant. In human more investigation is needed.