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MOLECULAR WEIGHTS OF INTRACELLULAR AND SECRETED LYSERGYL CONTAINING PEPTIDES FROM RABBIT LYMPHOCYTES AND MURINE MOPC-315 MYELOMA CELLS. Robert M. Watt*, Daniel L. Sissors* and Edward W. Voss, Jr.* Univ. of Illinois, Urbana, IL 61801 (Sponsored by Charles H. Hockman)

In order to study the mode of action of drugs on mammalian protein biosynthesis, lysergyl containing peptides have been obtained from rabbit immune lymphocytes and murine plasmacytoma cells incubated in vitro in the presence of d-lysergic acid diethylamide (LSD). The peptides harvested bear covalent intrinsic radio-labels of ^{14}C-LSD, ^{3}H-LSD, or ^{3}H-leucine. The molecular weights of both the intracellular and extracellular materials have been determined or estimated by gel filtration in denaturing solvents and SDS-polyacrylamide gel electrophoresis. A relatively large molecular weight component (> 55,000) and a low molecular weight component (< 5,000) are the principal components quantitatively in both materials. The lysergyl peptides have also been analyzed in immuno-precipitin assays as to their structural relationship to the immunoglobulin molecule or other cellular proteins. Results suggest that LSD interferes with the de novo biosynthesis of several cellular proteins in the lymphocyte and is not specific to the immunoglobulin molecule. (Supported by Illinois Mental Health Grant 533-03)

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REGULATION OF Ig NUCLEOTIDE SEQUENCE TRANSCRIPTION IN NORMAL LYMPHOCYTES AND PLASMACYTOMA CELLS. R. Bachvaroff, S. Scupp*, J.H. Ayvazian*, F.T. Rapaport. New York University Medical Center, 560 First Avenue, New York, New York 10016.

Previous studies indicate that incorporation of 5-bromodeoxyuridine (BrdU) into DNA during cell proliferation does not affect continuous transcription of mRNA for membrane IgM but may inhibit production of secreted IgM. In further studies, mouse spleen B lymphocytes were stimulated with E. coli lipopolysaccharide (LPS) in the presence of BrdU until 50-55% of the thymidine (Tdr) in one DNA strand was replaced by BrdU (calculated by buoyancy shift of DNA in CsCl gradients). Such cells synthesized and secreted total protein with specific activity equal to that of LPS-stimulated cells cultured in equimolar Tdr. While retaining a high density of surface IgM, the BrdU cells, however, failed to secrete μ or κ -chains. After enzymatic stripping of such cells, α-amanitine inhibited regeneration of surface IgM, suggesting that BrdU differentially inhibits transcriptional maximization of IgM nucleotide sequences. In an attempt to study similar effects in plasmacytoma cells, MOPC 315 and MOPC 70 were cultured in the presence of BrdU until 60-65% of the Tdr in one DNA strand was replaced by BrdU. Such cells continued to produce light chains, as well as α (MOPC 315) or γ (MOPC 70) in amounts equal to those observed in untreated cells. This result points to profound differences between the transcriptional regulation of Ig nucleotide sequences in normal lymphocytes and in plasmacytoma cells. (Supported by USPHS Grant AI-13213-01).

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Humoral and cellular response to H-2 antigens in protein deficient mice. Inés Malavé* (Spons. Inés de Hurtado) Instituto Venezolano de Investigaciones Científicas
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The response to H-2 antigens was assessed in C57BL/6 mice (B6), fed diets with 8% (D) or 27% (N) protein. After primary immunization with normal DBA/2 spleen cells the number of alloantibody secreting PFC per 10^7 spleen cells detected on L5178Y cells (also H-2^d) approximately doubled in D animals. Anti-H-2 hemagglutinins were moderately increased during the primary response and diminished during the secondary response in D animals while 2-mercaptoethanol resistant antibodies were strikingly diminished in D mice in both responses. Thus, protein restriction depressed IgG synthesis and the regulation of the IgM response but did not inhibit primary PFC formation. The DNA synthetic response of thymus and lymph node cells from D parental mice transfered i.v. into lethally irradiated adult B6D2 F_1 hybrids was significantly higher than that of N parental cells, while the difference between the proliferative response of D and N spleen cells was less marked. Added D or N thymocytes syngeneic with the recipient had similar suppressor activity on the proliferative response of parental cells in irradiated hosts. The increased proliferative response of D lymphoid cells could indicate therefore selection of competent cells during protein deficiency.

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ABILITY OF PROTEIN MALNOURISHED GUINEA PIGS TO PRODUCE MIF TO LOW DOSES OF ANTIGEN. Tim R. Kramer* (SPON: J. Finstad) Sloan Kettering Institute for Cancer Research, New York, N.Y. 10021

Chronic protein malnourished guinea pigs (GP) produce MIF to lower doses of immunizing bovine gamma globulin (BGG) than do normal nourished animals. In comparison to 27% casein protein fed animals (27%), young GP fed a 6% casein protein diet (6%) for 7 consecutive weeks displayed retarded growth rates. Following 4 weeks of designated dietary regimen, representative 6% and 27% fed animals were immunized according to 1 of 5 antigen dose protocols. These consisted of 4 groups receiving 0, 1, 10 or 100 µg BGG/Kg body weight, and 1 group receiving 100 µg BGG/animal. BGG was incorporated in adjuvant (H37Rv + IFA). The amounts of injected H37Rv were 100 µg/Kg for the 0, 1, 10 and 100 µg BGG/Kg groups and 100 µg/animal for the 100 µg BGG/animal group. Following immunization they were maintained on their specific dietary regimen for 3 additional weeks at which time their ability to produce MIF was evaluated against peritoneal exudate cells (PEC) from normal nourished GP. The 0 µg (ie. H37Rv only) BGG injected GP maintained on 6% and 27% dietary regimens failed to produce BGG induced MIF activity. Following immunization with 1 and 10 µg BGG/Kg, the 6% fed animals produced MIF with higher percent PEC inhibition activity than did the 27% fed animals. When the immunizing antigen doses were increased to 100 µg BGG/Kg and 100 µg BGG/animal these differences in MIF activity were not noted between the 6% and 27% fed animals. (Supported in part by USPHS, NCI, #CA 08748, CA 17404; NIAID #AI 11843.)

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INFLUENCE OF MALNUTRITION ON SECRETORY IMMUNITY IN CHILDREN. David N. McMurray*, Humberto Rey*V., Lawrence J. Casazza* and Ronald R. Watson: (Spon: L.K. Knoebel). Int. Ctr. Med. Res., Cali, Colombia; Univ. del Valle, Cali, Colombia; World Bank, Washington D.C.; and Indiana Univ. Sch. of Med., Indianapolis, IN 46202.

As part of a 2 year longitudinal study after birth, children 1.5 - 2 years of age were identified as well-nourished (26), Grade I (32), and Grade II and III (13) malnourished based on the Gomez classification of weight for age. Serum IgA was significantly higher in malnourished (Grade I, II and III = 70 mg/dL) compared to normal children (51 mg/dL). Serum IgM was also elevated in Grade II and III (124 mg/dL) compared to Grade I (99 mg/dL) and normal children (103 mg/dL). Serum levels of IgG and IgD were not affected. In contrast, levels of secretory IgA in tears were significantly depressed in Grade II and III (36 mg/dL) relative to the Grade I (61 mg/dL) and normal children (64 mg/dL). This marked decrease in IgA activity in the tears of severely malnourished children appears to be due to reduced synthesis of IgA and/or secretory component since IgG was actually elevated in Grade II and III children (8.9 mg/dL versus 5.1 mg/dL for normal). Levels of IgA and IgG were somewhat elevated above the mean in tears of children with symptoms of upper respiratory infection (cough, conjunctivitis, runny nose, fever). (Supported by USPHS, NIH Research Grant AI-10050 and HD-09098, Int. Ctr. Med. Res., and National Livestock & Meat Board).

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IMMUNOLOGICAL EFFECTS OF EARLY METHIONINE-CHOLINE DEPRIVATION. E.A.J. Williams*, B.M. Gebhardt and P. M. Newberne. M.I.T., Cambridge, MA 02139

Rats whose dams were fed a diet marginally deficient in methionine (0.3%) and choline (0.1%) during pregnancy (Group I) or during pregnancy and lactation (Group II) appear clinically normal at maturity. However, the mortality rate of these rats when infected with S. typhimurium is significantly higher (73% vs 20%) than that of rats littered to dams fed a complete diet during pregnancy and lactation (Group III). In the present study, 4 month old Wistar-Lewis rats from Groups I, II and III received .50 ml of a 20% SRBC suspension (.25 ml i.v. and .25 ml i.p.) on day 0. On day 5, spleens were removed and the number of IgM plaque forming cells (PFC) were determined by a modified Jerne-Nordin technique. Rats from Group III had 103 ± 24 (S.E.) PFC/10^5 lymphocytes, while rats from Group I had only 25 ± 8 PFC/10^5 lymphocytes ($p < .005$) and rats from Group II had 40 ± 16 PFC/10^5 lymphocytes ($p < .05$). 100% of the adjusted hemolysin titers of Group III were $\geq$ 1:20,560 while only 25% of both Group I and Group II had titers $\geq$ 1:20,560 ($p < .05$ and .10 respectively). 100% of the adjusted hemagglutination titers of Group III were $\geq$ 1:640 while 12.5% of the titers in both Group I and Group II were $\geq$ 1:640 ($p < .05$ and .05 respectively). (Supported by NIH Grant #2 R01 HD06917)