gy of idiopathic disturbance of spermatogenesis in man. The analyses of the target autoantigens are now in progress.

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P2-45.

The effects of adjuvants on autoimmune responses against testicular and epididymal antigens in mice

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Both the testis and the epididymis are immunologically privileged organs in which haploid germ cells expressing various autoimmunogenic antigens are protected. Therefore, a subcutaneous injection with testicular homogenate (TH) can easily induce systemic immune responses against the autoantigens of haploid germ cells. Experimental autoimmune orchitis (EAO) is a model of immunologic male infertility and pathologically characterized by lymphocytic inflammation in the testis accompanied by the spermatogenic disturbance. Classically, the murine EAO with epididymitis and vasitis is induced by immunization with TH+Complete Freund's Adjuvant (CFA)+Bordetella Pertussigens (BP), and it has been considered that the treatment with these two adjuvants is helpful to enhance the immune responses as adjuvants, resulting in breakdown of the testicular immune privilege. However, there remains a possibility that CFA and BP themselves affects autoimmune responses against the testicular and epididymal antigens without TH. In the present study, we examined this possibility using Western Blotting and immunohistochemical staining. Western Blotting analyses showed that various kinds of serum autoantibodies were detected in mice injected with CFA and BP alone. Immunohistochemically, these serum autoantibodies were reactive with not only spermatids and spermatozoa but also Sertoli cells and epididymal duct epithelium. Therefore, these results indicate that the treatment with adjuvants alone can evoke autoimmune reactions against various autoantigens in the testis and the epididymis irrespective of no use of TH.

P3-46.

培養細胞脂肪肝モデルの作成と胆汁酸の脂肪肝に対する効果

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【背景】 脂肪肝は、肥満、糖尿病、脂質異常症等の生活習慣病と密接に関連し、肝炎や肝線維化などの肝障害の原因となる。現在、実験動物脂肪肝モデルに対し、より簡便・迅速に作成、解析しえる培養細胞モデルは少ない。核内受容体 LXR が活性化され SREBP1c の転写活性が高まると、その標的遺伝子発現が増加し、脂肪酸合成が高まる。一方、核内受容体 FXR が活性化されると、SHP を介して、LXR-SREBP1c 経路を阻害し、脂肪酸合成抑制へ働く。LXR は Oxysterol を、FXR は胆汁酸を、それぞれ生理的なリガンドとして脂質代謝を調節している。今研究では、培養細胞脂肪肝モデルを作成し、胆汁酸が脂肪蓄積と分解に及ぼす効果を検討した。

【方法】 ヒト及びマウス非癌化正常肝細胞株 Fa2N-4 細胞、AML12 細胞に、内因性・合成 LXR リガンド; Oxysterols, To901317 を添加して作成した。このモデルに対し、脂肪肝形成前後に、内因性・合成 FXR リガンド; 胆汁酸 (CDCA、UDCA)、INT747, GW4064 を添加し、脂肪酸合成抑制・分解効果を検討した。細胞内脂肪蓄積を Oil-Red 染色と中性脂肪定量にて、脂肪酸合成系 / 分解系関連遺伝子発現を PCR 法にて評価した。

【結果】 LXR リガンドにより SREBP1c 標的遺伝子 (ACC、FAS、SCD-1) の発現増加を伴い、培養肝細胞で脂肪肝が認められた。各 FXR リガンドの添加は、SHP 遺伝子発現を有意に増加させ、肝脂肪