FK 506 for Vascular Permeability Factor Production in Minimal Change Nephrotic Syndrome

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Fig. 1. Dose-response curve of FK 506 on VPF production of T lymphocytes in MCNS. T lymphocytes were cultured in the absence (Δ) or presence ($\circ$) of FK 506. * $p < 0.01$. stored at -80°C until use. The VPF assay on guinea pig's skin was performed according to Ovary's method [6]. The blue area surrounding each injection site was measured on the photograph by an image analysis division, Cardio 200, Kontron Instrument Co., Osaka, Japan. For statistical analysis, the non-parametric Wilcoxon's rank sum test was used. The results of VPF assay are given in figure 1. The control T lymphocyte culture supernatants revealed a marked reaction with the blueing area being 88.3 ± 6.8 (mean $\pm$ 1 SE) mm^2 . VPF activity of culture supernatants with 10^{-12} and 10^{-11} M of FK 506 was the same level as that of controls, revealing mean blueing areas of 96.1 and 80.4 mm^2 , respectively. The blueing area of supernatants with

Dear Sir,

Vascular permeability factor (VPF) derived from T lymphocytes may be the leading cause of massive proteinuria in minimal change nephrotic syndrome (MCNS) [1-3]. duced remission, to which inhibition of VPF production probably contributes. Cyclosporin (Cs) is also beneficial in MCNS and other nephrosis. Its effect on MCNS in vitro has been reported [4]. FK 506 is a novel immuno-suppressant [5]. It has recently been demonstrated to have potent immunosuppressive activity at concentrations several hundredfold lower than Cs. The in vitro effect of FK 506 on VPF production in MCNS has been studied.

Seven patients with MCNS between the age of 4 and 11 years, 3 girls and 4 boys, were included in this experiment. They were all in the active stage with massive proteinuria and abnormal blood chemical values. Lymphocytes were harvested from heparinized blood samples of patients and isolated by density gradient centrifugation in Ficoll-Conray. T lymphocytes were purified by passage over a nylon wool column and were adjusted to a final concentration of 1×10^6 cells/ml in RPMI 1640 containing 10% fetal calf serum. FK 506, provided by Fujisawa Pharmaceutical Co., Ltd., Osaka, Japan, was dissolved in methanol and diluted to the appropriate concentration with RPMI 1640. Various dose dilutions of FK 506 (10^{-12} – 10^{-7} M) were added to T lymphocyte

cultures. Control cultures received methanol in RPMI 1640. The final concentration of methanol in culture was adjusted to less than 0.1%. T lymphocyte cultures were incubated for 24 h in 5% CO₂ humidified atmosphere at 37 °C. After culture, the supernatants were harvested by centrifugation and

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10⁻¹⁰ M of FK 506 was 30.3 ± 6.5 mm². A significant inhibition was noted at a concentration of 10⁻⁹ M of FK 506 (p < 0.01). These results suggest that FK 506 inhibits VPF production in MCNS at a lower concentration than Cs [4].

Remission of steroid-resistant nephrotic syndrome from focal sclerosing glomerulonephritis has already been reported with FK 506 [7]. The mechanism of immunosuppression mediated by FK 506 and Cs appears to be remarkably similar. The safety of FK 506 has been confirmed [8]. Nephrotoxicity of FK 506 is less than that of Cs [9]. In the absence of overt system-specific toxic effect with FK 506, it should be the means for application to nephrotic syndrome, including MCNS.

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Announcements

Seminar on Autosomal Dominant Polycystic Kidney Disease

Vimercate, June 18, 1994

We are pleased to announce the Seminar on autosomal dominant polycystic kidney disease (ADPKD) that will be held on June 18, 1994, in Vimercate, Milan, Italy.

It is our aim to discuss contemporary issues relating to molecular genetics, cyst formation and enlargement, epidemiology, clinical features in adults and children, dialytic and transplantation aspects, hypertension, cystic liver disease, cerebral aneurysm, ethical aspects and genetic counselling in ADPKD.

The deadline for receipt of abstracts for poster discussion is May 16, 1994. No abstract form is needed: one typewritten page will be accepted. We are confident that the Seminar will be a rewarding experience for all attendees.

We look forward to welcoming you to Vimercate in June 1994.

Adalberto Sessa

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For further information, please write to:

Dr. M. Feriani

Secretariat of the

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Department of Nephrology

St. Bortolo Hospital

I-36100 Vicenza (Italy)

As in the previous edition a closed number of participants is scheduled. Further details will be given in the second announcement.

Course President: G. La Greca Vice President: C. Ronco General Secretary: M. Feriani

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