C5a is a target to prevent peritoneal tissue damage in acute peritoneal injury in rats

Mizuno T, Mizuno M, Imai M, Suzuki Y, Kushida M, Yamada K, Noda Y, Maruyama S, Okada H, Okada N, Matsuo S, Ito Y.

Meijo University Faculty of Pharmacy
Nagoya University Graduate School of Medicine
Nagoya City University Graduate School of Medicine

Abstract:

The complement system contributes to maintenance of homeostasis in peritoneum, just as in other tissues. In peritoneal dialysis (PD) therapy, physical stresses such as exposure to peritoneal dialysate, catheter trauma and peritonitis induce peritoneal injuries which can prevent continued long-term PD therapy. Therefore, protection of the peritoneum is an important target to enable long-term PD therapy in patients with end-stage renal disease. We previously showed that neutralizations of membrane complement regulators (CRegs), Crry and CD59, in rat caused acute peritoneal injuries to develop. C5a is a key effector molecule of the complement system, released during acute inflammation. Control of C5a has been proposed as a strategy to suppress inflammatory reactions and, because peritoneal injuries are accompanied with inflammation, we hypothesized that C5a targeted therapy might be an effective way to suppress peritoneal injuries.

In the present study, we have used the established acute peritonitis model induced by neutralization of CRegs to investigate effects on acute peritoneal injuries of inhibiting C5a with intravenous (iv.) or intraperitoneal (ip.) administration of an anti-C5a complementary peptide (AcPepA). Both iv. and ip administration of AcPepA significantly suppressed accumulation of inflammatory cells and reduced tissue damage, accompanied with decreased C3b deposition. Comparison with a C5aR antagonistic peptide (C5aRA), AcPepA showed similar suppressive effects for the peritoneal injuries. Our results suggest that C5a is a target to prevent peritoneal injuries in PD patients on prolonged therapy or with infectious complications.

This certificate is presented to

Aegean Conferences

Tomohiro Mizuno

XXIV ICW 2012 CRETE • GREECE

in recognition of an excellent research contribution (poster presentation)
that was selected for an

Aegean Conferences Trainee Award

(US$ 1000)

at the

XXIV International Complement Workshop

10-15 October 2012 in Chania, Greece

Professor John D. Lambris
Executive Director of Aegean Conferences, Inc