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Universiteit Leiden



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Title: Pathogenic role of complement in renal ischemia/reperfusion injury

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STELLINGEN (PROPOSITIONS)

behorende bij het proefschrift getiteld

Pathogenic role of complement in renal ischemia/reperfusion injury

- 1. Hypoxic human renal tubular cells, in contrast to mouse renal tubular cells, primarily activate the classical pathway of complement demonstrating important species differences. (this thesis)
- 2. Presence of plasma proteins in urine (proteinuria) might lead to complement activation and generation of terminal complement complex C5b-9 independent of a renal contribution. (this thesis)
- 3. In clinical kidney transplantation there is an acute but very transient release of terminal complement complex C5b-9 from the allograft after reperfusion. (this thesis)
- 4. Complement activation following renal ischemia/reperfusion is preceded by deposition of MBL and tubular injury. (this thesis)
- 5. Therapeutic inhibition of MBL during renal ischemia/reperfusion protects against kidney dysfunction, tubular injury, leukocyte accumulation and expression of proinflammatory mediators. (this thesis)
- 6. MBL induces renal tubular injury following ischemia/reperfusion independent of complement activation. (this thesis)
- 7. MBL appears to be a double-edged sword in human disease, where the disease dictates whether the presence or absence of MBL influences the clinical outcome. (*J Immunol. 2012; 188:885, Expert Rev Anti Infect Ther. 2011; 9:1179*)
- 8. MBL binding to apoptotic cells does not necessarily lead to complement activation, but rather facilitates phagocytic uptake by macrophages. (Eur J Immunol. 2003; 33:2853, J Leukoc Biol. 2009; 86:737)
- 9. Although the complement-activating effects of MBL are well-known, the effector functions of MBL mediated via the collagenous region are still poorly understood. (Immunol Rev. 2009; 230:9)
- 10. MBL is cytotoxic to human colorectal carcinoma *in vivo* independent of complement activation. (PNAS 1999 ;96:371)
- 11. Failures, repeated failures are fingerposts on the road to achievement. (Charles F. Kettering; Charles F. Kettering, A Biography, 1957, p40)
- 12. The history of organ transplantation started when God created Eve from Adam's rib. (Holy Bible, Genesis 2:22-23)
- 13. Knowledge is a process of piling up facts; wisdom lies in their simplification. (Martin H. Fischer; Encore: A Continuing Anthology, March 1945, p309)
- 14. You never know how much you really believe anything until its truth or falsehood becomes a matter of life and death to you. (C.S. Lewis; A Grief Observed, 1961, p25)

Pieter van der Pol Leiden, 12 november 2013