Overlapping and distinct roles of C5a receptors C5aR and C5L2 in experimental kidney fibrosis

Ina V. Martin, Annika Bohner*, Peter Boor, Erdenechimeg Shagdarsuren§, Ute Raffetseder, Frank Lammert*, Jürgen Floege, Susanne Weber* and Tammo Ostendorf

Division of Nephrology and Immunology and §Institute of Molecular Cardiovascular Research (IMCAR), RWTH Aachen, Aachen, Germany, *Division of Gastroenterology, Saarland University Medical Center, Homburg, Germany. E-mail: imartin@ukaachen.de

Background and Aims

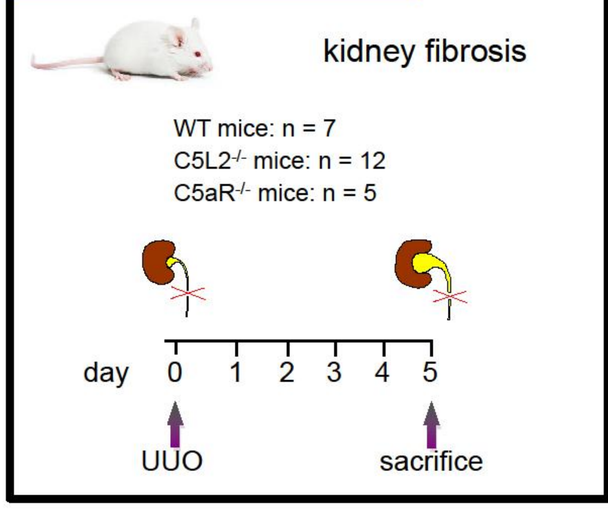
- C5aR induces pro-inflammatory signaling pathways upon C5a binding
- C5L2 is structurally homologous to C5aR but cannot activate G-proteins
- C5 deficiency and C5aR antagonism protect from kidney and liver fibrosis and reduce concomitant inflammation.

[Boor *et al.*, JASN, 2007; Hillebrandt *et al.*, Nat. Genet., 2005]

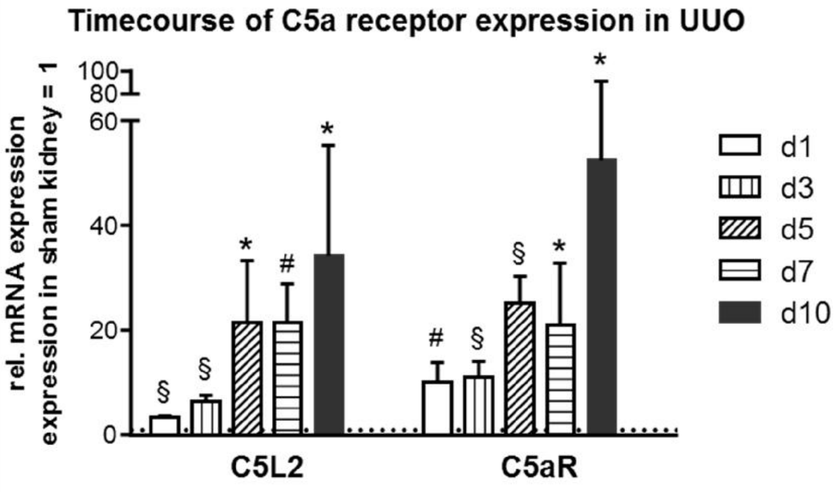
➡ What is the role of C5L2 in experimental kidney fibrosis?

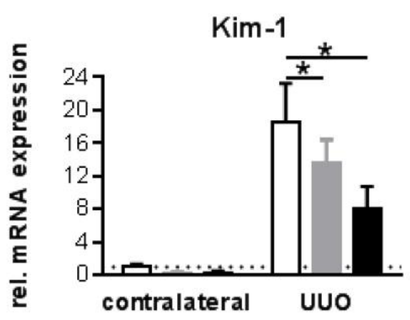
➡ Does C5aR deficiency also protect from kidney fibrosis?

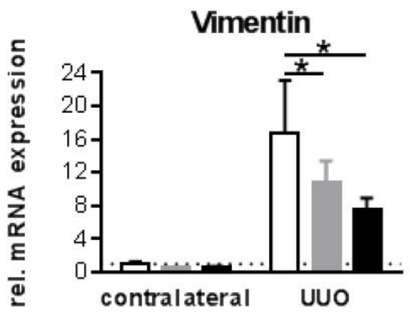
Methods



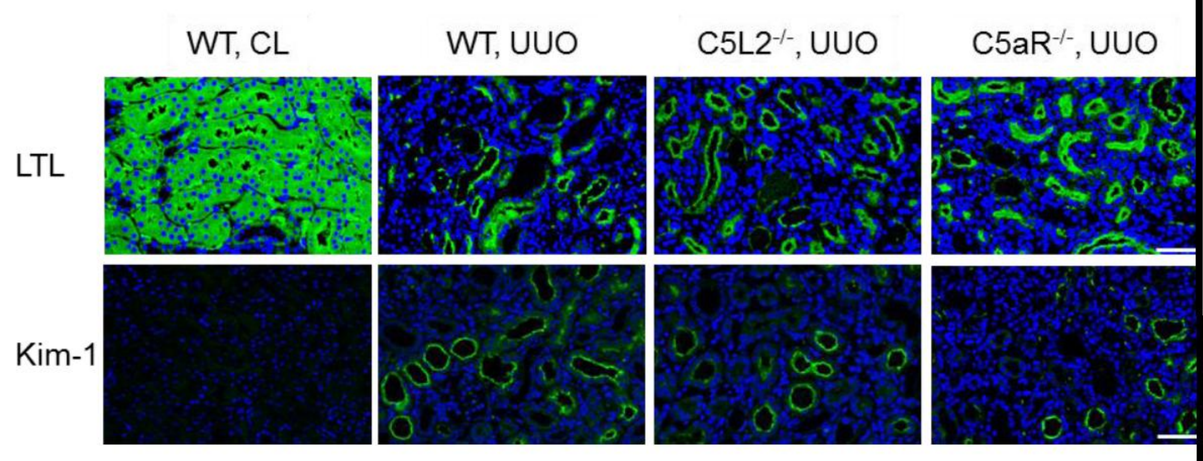
Results



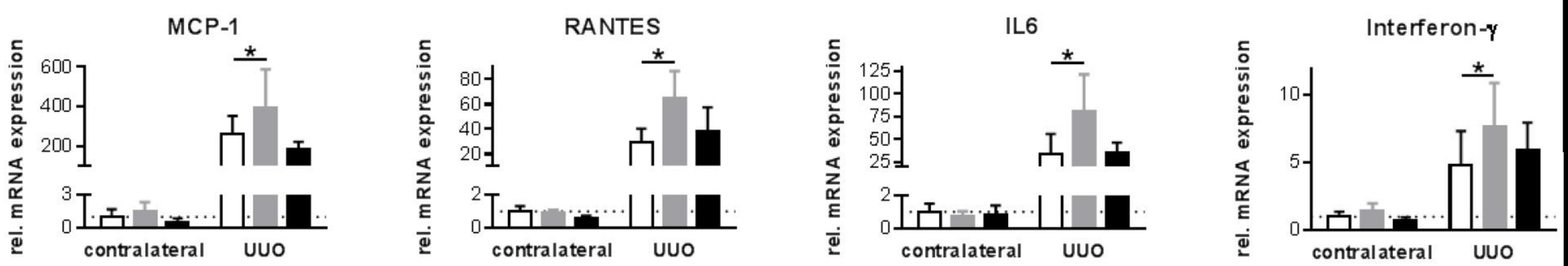




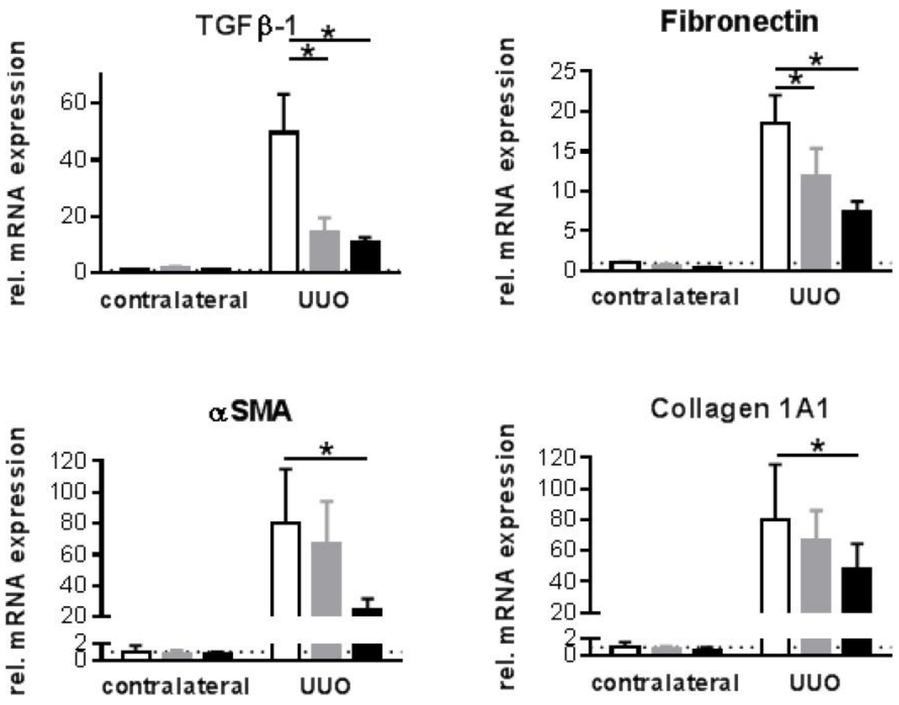
C5aR AND C5L2 BOTH MEDIATE TUBULAR INJURY

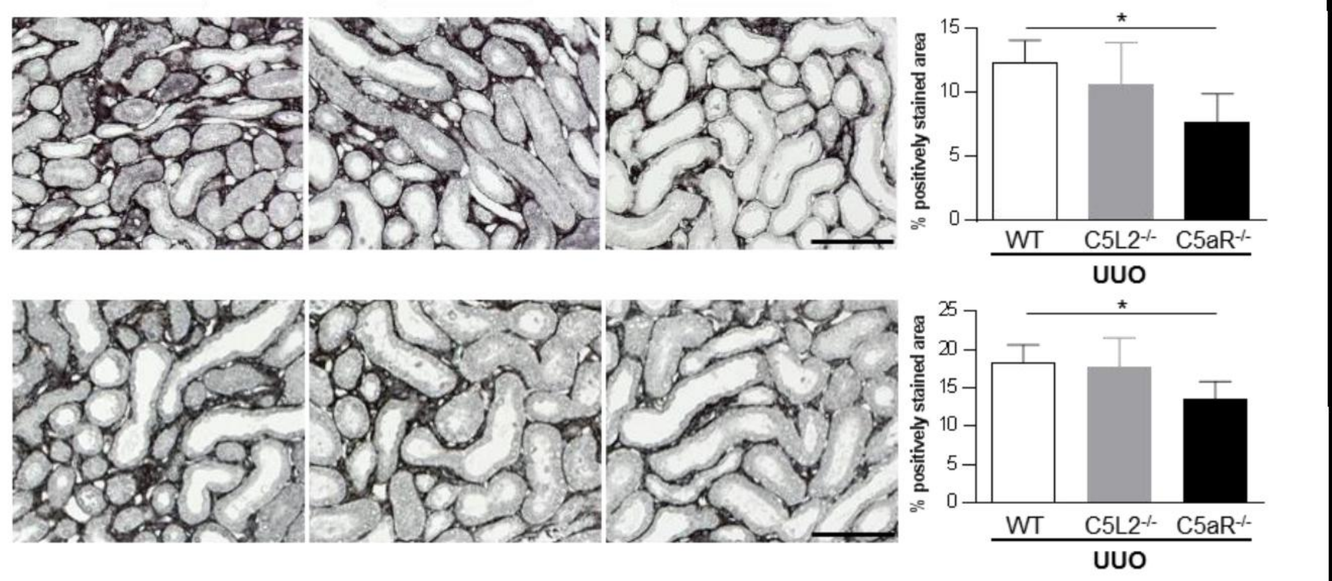


ENHANCED EXPRESSION OF PRO-INFLAMMATORY MEDIATORS IN C5L2$^{-/-}$-MICE

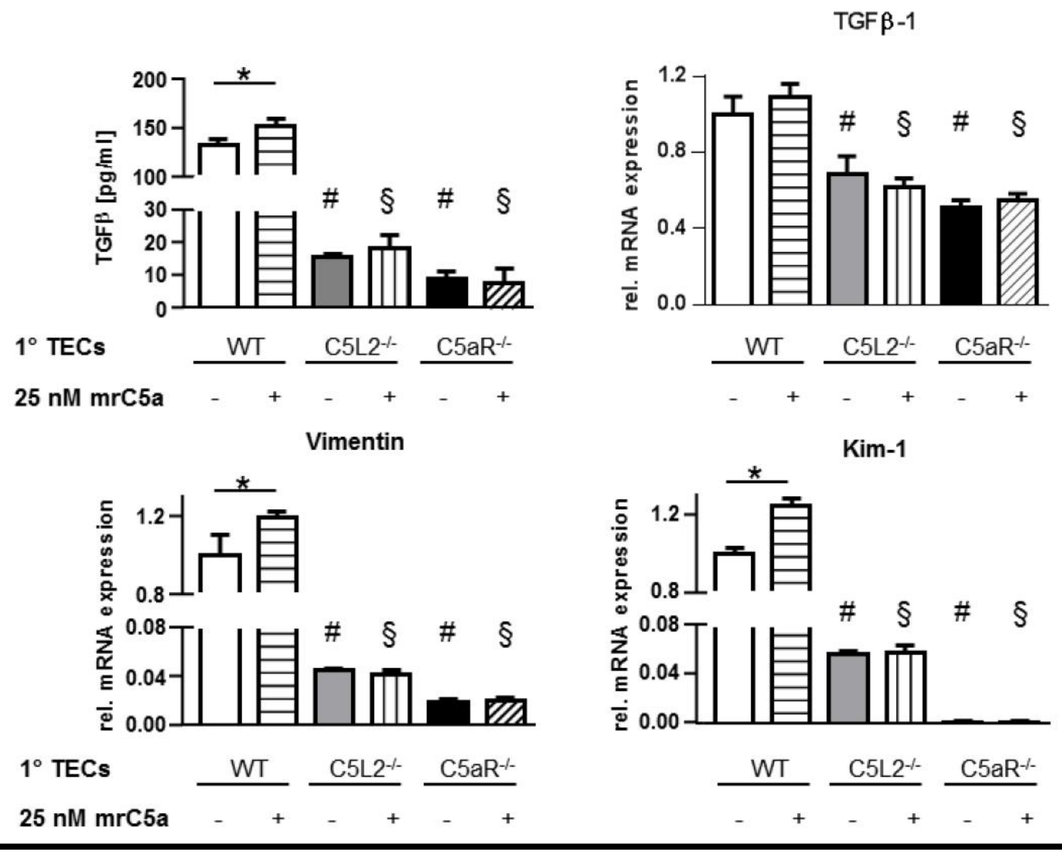


SIGNIFICANT REDUCTION OF EXTRACELLULAR MATRIX DEPOSITION ONLY IN C5aR$^{-/-}$-MICE





IN 1° mTECS, C5a MEDIATED TUBULAR CELL STRESS REQUIRES BOTH RECEPTORS, C5aR AND C5L2



Summary and Conclusions

in experimental renal fibrosis

- both C5aR and C5L2 mediate tubular cell injury *in vivo* and *in vitro*
- C5L2 has an anti-inflammatory role
- only C5aR shows pronounced pro-fibrotic effects

➡ C5aR and C5L2 possess overlapping and distinct functions

➡ C5L2 does not simply act as decoy receptor

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Ina Martin

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