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La **Dra. Julia Blanco**, Jefe de Sección del Servicio de Anatomía Patológica del HCSC, es una de las autoras del trabajo titulado:

"THE INFLAMMATORY CYTOKINES TWEAK AND TNF_ REDUCE RENAL KLOTHO EXPRESSION THROUGH NF_B"

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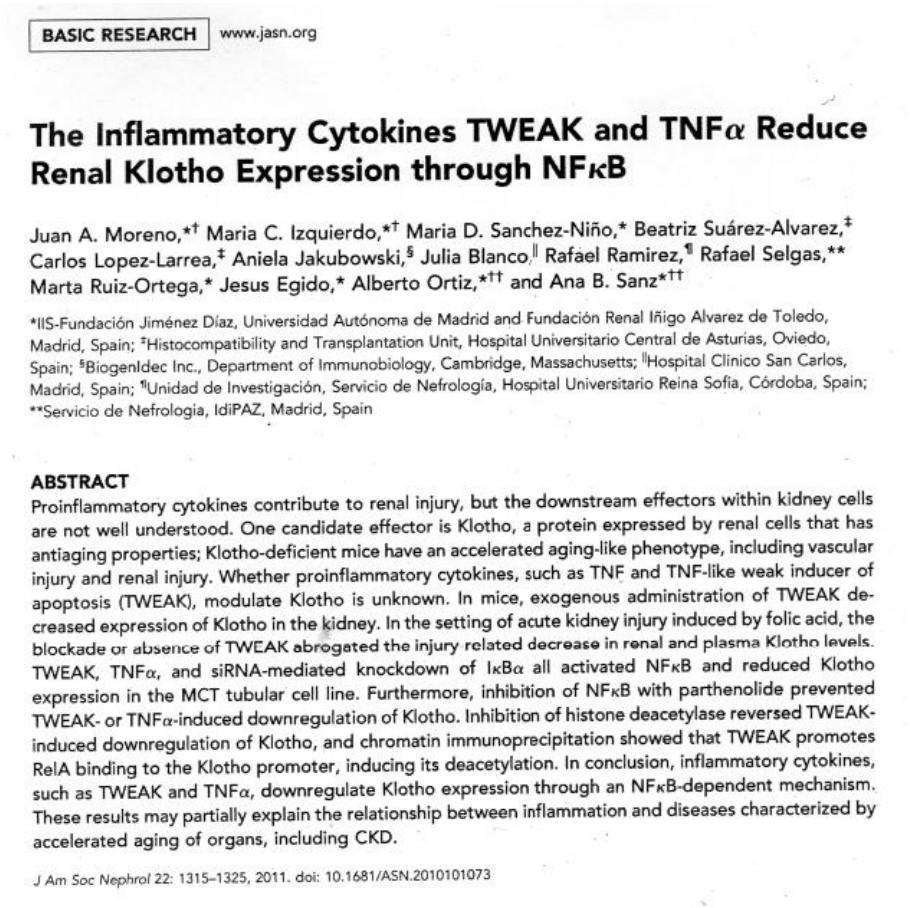
Dicho trabajo fue publicado en el 2011 en la revista Journal of the American Society of Nephrology (J Am Soc Nephrol 22: 1315–1325, 2011. doi: 10.1681/ASN.2010101073) que tiene un **factor de impacto de 9,663** y ocupa el primer puesto en el ranking de revistas en la categoría de Urología y Nefrología.



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The Inflammatory Cytokines TWEAK and TNFα Reduce Renal Klotho Expression through NFκB

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ABSTRACT

Proinflammatory cytokines contribute to renal injury, but the downstream effectors within kidney cells are not well understood. One candidate effector is Klotho, a protein expressed by renal cells that has antiaging properties; Klotho-deficient mice have an accelerated aging-like phenotype, including vascular injury and renal injury. Whether proinflammatory cytokines, such as TNF and TNF-like weak inducer of apoptosis (TWEAK), modulate Klotho is unknown. In mice, exogenous administration of TWEAK decreased expression of Klotho in the kidney. In the setting of acute kidney injury induced by folic acid, the blockade or absence of TWEAK abrogated the injury related decrease in renal and plasma Klotho levels. TWEAK, TNFα, and siRNA-mediated knockdown of IκBα all activated NFκB and reduced Klotho expression in the MCT tubular cell line. Furthermore, inhibition of NFκB with parthenolide prevented TWEAK- or TNFα-induced downregulation of Klotho. Inhibition of histone deacetylase reversed TWEAK-induced downregulation of Klotho, and chromatin immunoprecipitation showed that TWEAK promotes RelA binding to the Klotho promoter, inducing its deacetylation. In conclusion, inflammatory cytokines, such as TWEAK and TNFα, downregulate Klotho expression through an NFκB-dependent mechanism. These results may partially explain the relationship between inflammation and diseases characterized by accelerated aging of organs, including CKD.

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