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**DKK3: A novel diagnostic tool for improving the management of CKD patients and thus to mitigate the future burden of CKD**

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The prevalence of chronic kidney disease (CKD) is relatively high, at approximately 10% of the population, but only relatively few patients have end-stage renal disease and require renal replacement therapy. It is not possible at present to stratify patients reliably according to whether or not their kidney disease is progressing (rapidly). A new biomarker, urinary DKK3, identifies CKD patients at risk of kidney disease progression, regardless of the cause of kidney injury. ‘Therefore, it may be a novel diagnostic tool for improving the management of CKD patients and thus to mitigate the future burden of CKD’.

Although the prevalence of chronic kidney disease (CKD) is relatively high, at approximately 10% of the population, many patients live ‘well’ for a long time with stage-1 to stage-3 restriction of kidney function, with some patients even showing no sign of progression. Markers which stratify high-risk patients, i.e. those whose kidney disease is progressing and who are at high risk of needing renal replacement therapy within a few months or years, would be desirable in order to provide targeted therapy. The current assessment of risk based on deteriorating GFR and albuminuria/proteinuria is somewhat simplistic, in that some patients, e.g. patients with interstitial kidney diseases such as ADTKD (autosomal dominant tubulointerstitial kidney disease), do not experience severe albuminuria/proteinuria at all - even on reaching end-stage renal failure [1-3].

The pathomorphological correlate of progressive kidney damage is tubulointerstitial fibrosis, the mechanisms of which are the subject of intensive research at present. Damaged cells of renal tubules produce various cytokines which control regenerative processes, on the one hand, but which can also lead to the development of tubulointerstitial fibrosis. Regenerative processes may occur in the early stages of activation, via the well-known Wnt signaling pathway (signaling pathway for cell differentiation and proliferation/regeneration), but continuous Wnt activation is detrimental and induces tubulointerstitial fibrosis [4, 5]. Modulators of the signaling chain include Dickkopf-related (DKK) proteins, which interact
with the canonical Wnt signaling pathway. Urinary DKK3 can thus be used as a biomarker for tubular stress and progressing tubulointerstitial fibrosis – and therefore potentially as a marker for distinguishing progressing CKD patients from stable patients.

At the ERA-EDTA-congress in Copenhagen, Professor Fliser, Homburg/Saar, Germany, presented the results of a prospective cohort study [7] of patients with various CKD etiologies (N=575) and annual follow-up (2.035 patient years), a prospective clinical trial of patients with biopsy-proven IgA nephropathy (STOP-IgAN trial, N=96) and a cross-sectional general population study (N=481). Median urinary DKK3/creatinine concentration was significantly higher in patients with CKD as compared to the general population (33 [126] vs. 431 [1,388] pg/mg; p<0.0001). Besides, urinary DKK3 concentrations were significantly associated with CKD progression in patients with CKD. Urinary DKK3 >1,000 pg/mg creatinine and >4,000 pg/mg creatinine were associated with a mean annual eGFR decline of 2.4% (95% CI: -4.6 to -0.2%; p=0.007) and 7.6% (95% CI: -10.9 to -4.2%; p<0.001) independent of eGFR and albuminuria.

“These findings show that urinary DKK3 identifies CKD patients at risk for kidney disease progression, regardless of the cause of kidney injury. Therefore, urinary DKK3 might represent a novel diagnostic tool to improve the management of CKD patients and thereby to prevent the major burden of CKD,” explains Fliser, co-author of the study.

A newly developed Dkk3-ELISA test provides relatively simple identification: 1 ml of spot urine (frozen at -20°C, or cooled at 4°C if measurement is performed within 24 hrs) are required to determine Dickkopf-related protein 3 (DKK3).


About ERA-EDTA
With more than 7,500 members, the ERA-EDTA ("European Renal Association – European Dialysis and Transplant Association") is one of the biggest nephrology associations worldwide and one of the most important and prestigious European Medical Associations. It supports basic and clinical research in the fields of clinical nephrology, dialysis, renal transplantation and related subjects. It also supports a number of studies as well as
研究组，并已建立一个特别的“奖学金计划”（Fellowship Programme）为年轻研究人员，以及研究项目。为了参与年轻的肾脏科医生在所有活动，ERA-EDTA 创立了“年轻肾脏科医生平台”（YNP），一个非常活跃的委员会，其董事会包括40岁或更年轻的成员。此外，它已经建立了各种工作小组来促进肾脏科医生与其他医学学科（例如心脏病学，免疫学）的合作。此外，ERA-EDTA 成立了“欧洲肾脏最佳实践”（ERBP）咨询委员会，以制定和发布指南和立场声明。

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