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ReFiNE® Dkk3



Troponin of the kidney – new marker of
chronic kidney disease progression



More than 35 years of experience in IVD.

Developing and manufacturing laboratory diagnostics since 1986.
Immundiagnostik AG is certified according to DIN EN ISO 13485.

What is DKK3?

Dickkopf 3 (DKK3) is a glycoprotein that modulates the Wnt signaling pathway. Experimental studies have shown that the Wnt signaling pathway plays an important role in the progression of both, acute and chronic kidney damage.^[1] The amount of the profibrotic DKK3 excreted in the urine correlated significantly with the extent of tubulo-interstitial fibrosis in various kidney disease models and in patients with biopsy-confirmed kidney disease.^[2] DKK3 is released into the urine by „stressed“ renal tubular cells and is therefore a very early indicator of significant and, above all, progressive kidney damage.



Kidney disease is common and its early diagnosis is a global challenge

Chronic kidney disease (CKD) is becoming increasingly common worldwide and is emerging on a long-term view as one of the most serious global health issues. The World Health Organization predicts that CKD will be the 5th most prevalent chronic disease by 2040.^[3] It is estimated that more than 800 million people worldwide suffer from chronic kidney diseases (CKD).^[4] In the early CKD stages clinical symptoms are often hardly noticeable as the kidney damage is mostly silent. The most common causes of CKD are long-standing diabetes mellitus and/or arterial hypertension, immunological injury (e.g. glomerulonephritis), genetic kidney diseases (e.g. ADPKD), but also kidney damage from medication (e.g. non-steroidal anti-inflammatory drugs) or after acute kidney injury. In order to ensure their survival, chronic renal replacement therapy is initiated in an increasing number of cases globally every year. It is well known that less than half of all people who need renal replacement therapy worldwide have access to it. By 2030, it is estimated that the number of patients requiring this therapy will almost double, with an estimated 5.4 million patients worldwide needing it.^[10] In addition,

**More than 800 million
people worldwide suffer
from chronic kidney
disease**

Jager KJ et al. (2019)

people with CKD have a number of serious concomitant diseases (e.g. cardiovascular diseases) that are associated with high health costs and unfortunately, also with a high mortality rate.^[5] The reliable detection of progressive CKD is therefore of paramount importance, especially since those affected have no serious symptoms for a long time.

Progressive CKD is still a diagnostic challenge. Regardless of the cause of the kidney damage, progressive CKD is always characterized by progressive scarring of the kidney tissue in the form of tubulo-interstitial fibrosis.^[6] So far, the diagnosis of tubulo-interstitial fibrosis could only be made by means of kidney biopsy and

histopathological examination of the kidney tissue, which, however, only reflected the “status quo” at the time of the kidney biopsy. Laboratory tests to assess kidney function such as creatinine in the blood and the estimated glomerular filtration rate (eGFR) indicate kidney function at the time of the examination, but do not provide any information about the further course of the kidney disease. It is therefore not possible to predict the individual course of chronic kidney damage based on a single eGFR determination.

ReFiNE® Dkk3 in everyday clinical routine

- Like troponin in cardiology: DKK3 released into the urine by “stressed” tubular epithelial cells indicates both the extent and progression of kidney damage
- In healthy kidneys and patients without active kidney damage, DKK3 in the urine is not detectable or only slightly elevated
- If the **ReFiNE® Dkk3** result is positive, there is a high probability of progressive chronic kidney damage
- The result of the **ReFiNE® Dkk3** measurements in urine should always be interpreted in conjunction with the kidney function, i.e. the estimated glomerular filtration rate (eGFR)
- Simple measuring in urine using a non-invasive laboratory test

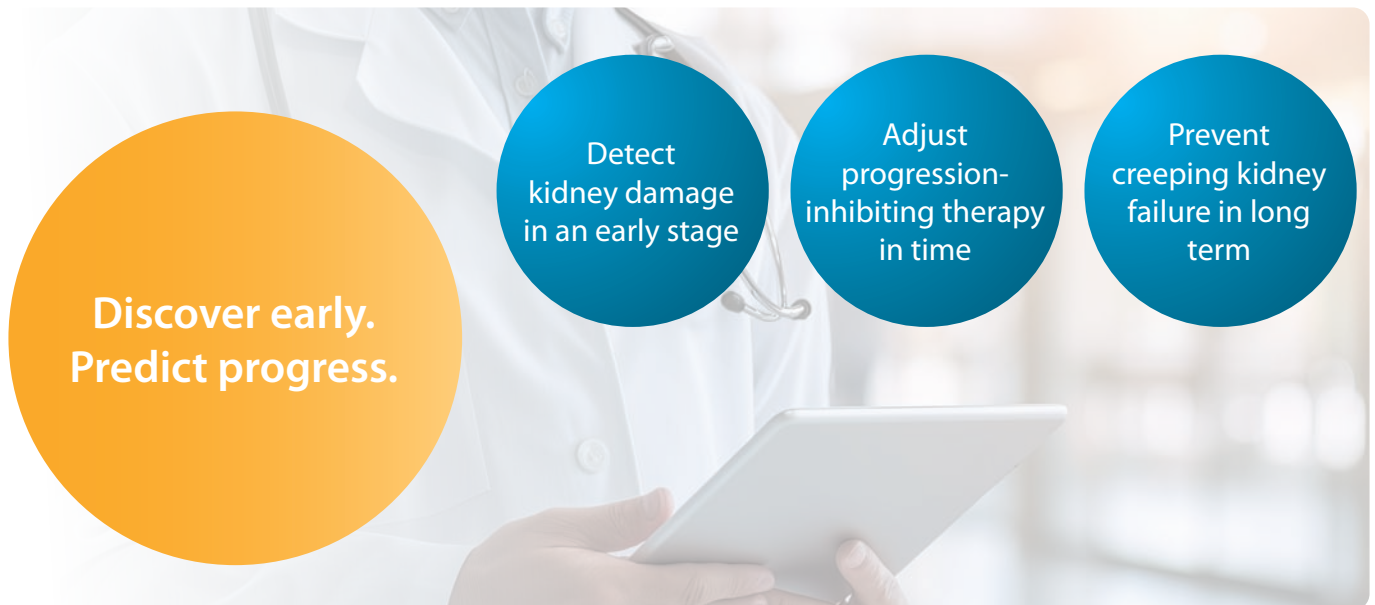
- **ReFiNE® Dkk3** enables an early diagnosis and better prognosis of the individual progression of CKD for a period of 1 year

Prenalytics

Sample material: Urine, preferably morning urine (only small amounts of urine are required for testing)

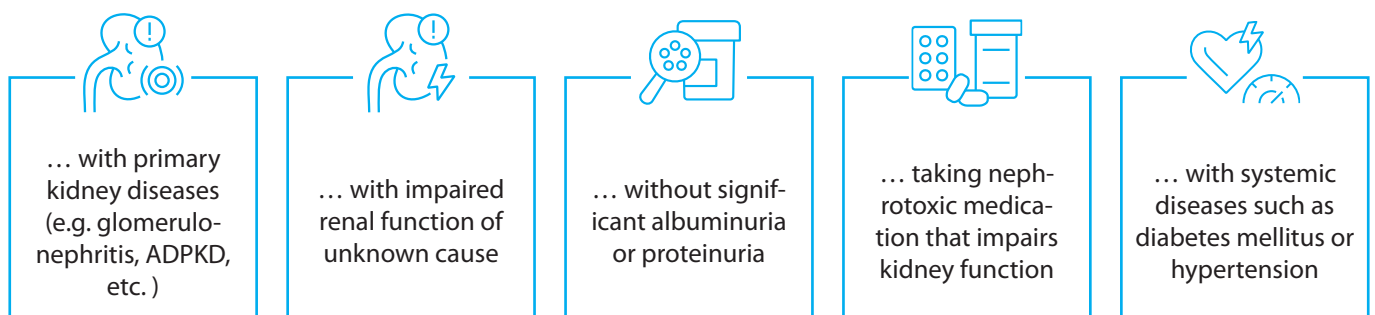
To make it more convenient for your lab partner, start centrifuging the sample immediately after sampling (only optionally!)

Sample transport: Standard shipping (re-frigerated 2–8 °C) or deep-frozen for sample storage over 24 hours



When to choose ReFiNE® Dkk3

For patients ...



Why measuring ReFINE® Dkk3?

ReFINE® Dkk3 enables a definite diagnosis of patients with kidney damage regardless of its cause

Dickkopf (DKK) proteins control the Wnt signaling pathway during embryonic development and after organ damage. Temporary activation of the Wnt signaling pathway triggered by acute injury leads to repair and regeneration in renal tubular cells. However, if the activation remains permanently uncontrolled, tubular cells transform into a pro-inflammatory state, causing acute kidney injury to develop into chronic kidney disease (CKD).^[7]

Tubular cells secrete DKK3 during acute or chronic kidney damage, which is only then excreted in the urine. **DKK3 is not detectable in the urine of people without kidney injury.** (Fig. 2, Zewinger et al, 2018)

The detection of DKK3 in urine indicates active kidney injury independent of the cause, the amount of DKK3 in the urine correlates with the rate of CKD progression.



Take a look at the study

Zewinger S et al. (2018)

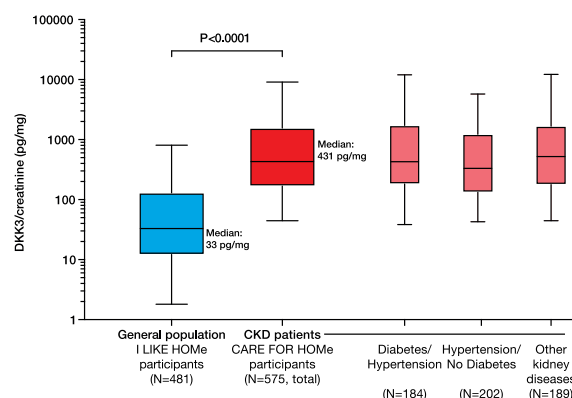


Figure 2. Urinary Dickkopf-3 (DKK3) is elevated in patients with CKD. Distribution of urinary Dickkopf-3 (DKK3)-to-creatinine levels (on logarithmic scale) in the participants of the I LIKE HOME Study cohort representing the general population (n=481) compared with patients with CKD from the CARE FOR HOME Study cohort (n=575), with no relevant overlap between subjects from the general population and patients with CKD. Urinary DKK3-to-creatinine levels were comparable in hypertensive patients with CKD with (n=184) and without (n=202) diabetes and patients with CKD of other etiology (n=189).

ReFINE® Dkk3 enables early diagnosis and better prognosis of the individual course of CKD

The determination of DKK3 in urine in combination with eGFR allows a more reliable assessment of CKD progression (Fig. 3, Zewinger et al, 2018).^[7] The measurement of DKK3 in urine can therefore **enrich the treatment of CKD patients in terms of personalized medicine**, as it can be used to monitor and, if necessary, **intensify therapeutic measures to slow down the progression of CKD**.^[8] This has been demonstrated both in adults^[7] and in children with CKD.^[9]

Figure 3 from Zewinger et al. (2018) shows the relationship between DKK3 in urine and kidney function (eGFR) in CKD patients within the next 12 months. A total of 575 patients with kidney diseases of different origins in the CKD stages 2–4 were followed up over 8 years. Urinary DKK3 levels were an independent and significant indicator of short-term loss of kidney function. For example, patients whose urinary DKK3 levels exceeded 4000 pg/mg creatinine lost an average of almost 8.0% of eGFR per year. It should be emphasized that the DKK3 concentration in the urine indicated the further eGFR course even under anti-progression measures (lowering blood pressure) or therapy (RAS blockade). The red line shows the estimated annual change in eGFR (in %) with the respective 95% confidence interval (gray area). The blue spikes show the distribution of the individual DKK3 concentrations in the urine.

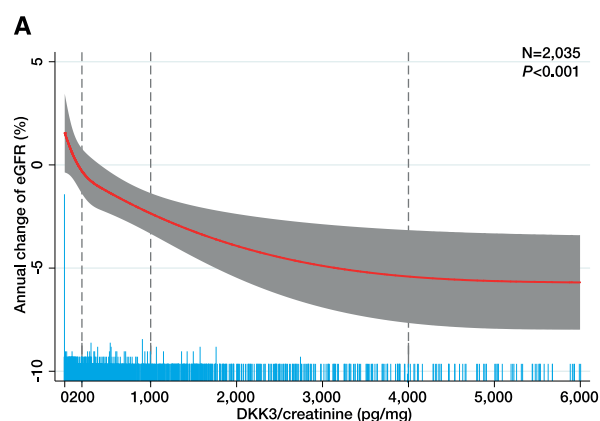
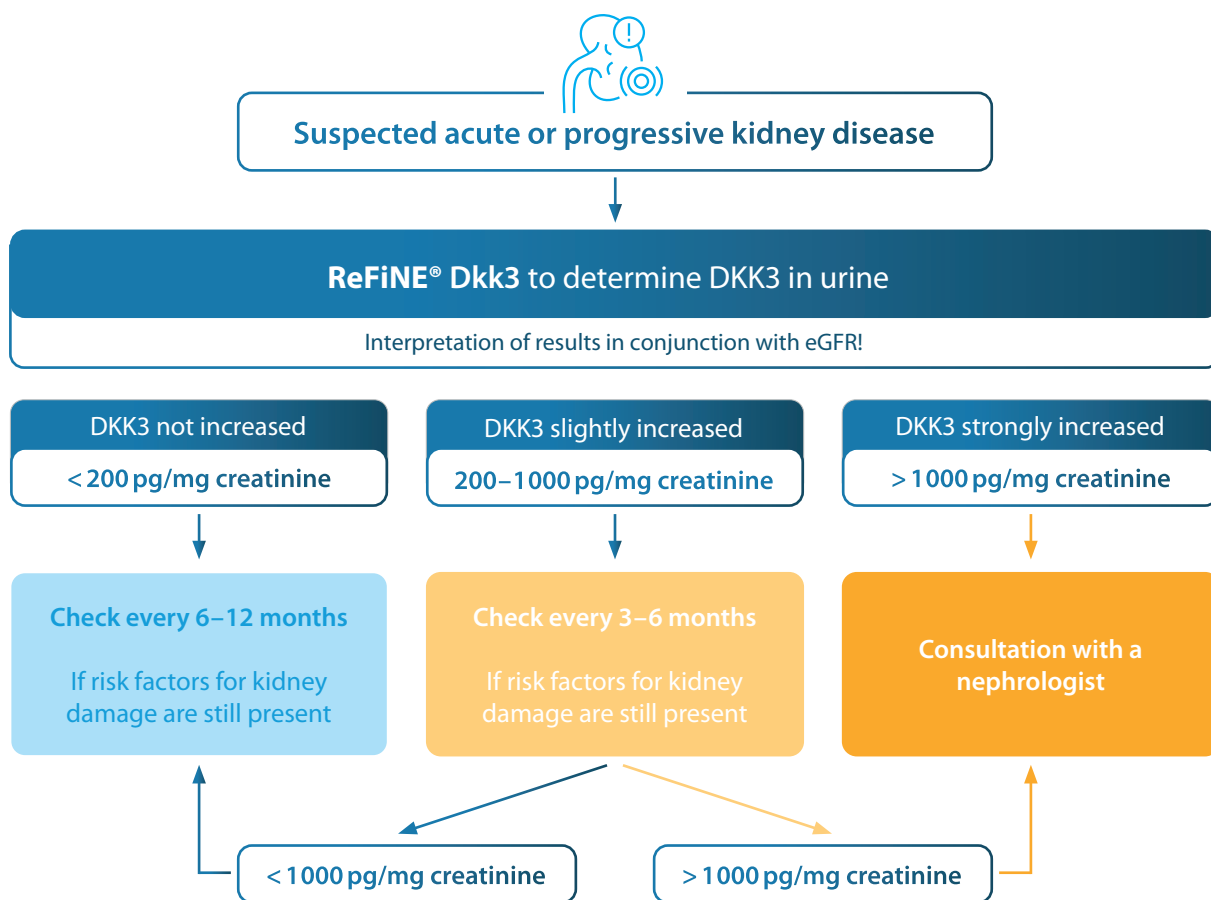


Figure 3. DKK3 predicts risk of short-term eGFR loss in patients with CKD. Restricted cubic spline plots of the association between annual change of eGFR in percentage and urinary Dickkopf-3 (DKK3)-to-creatinine concentrations in participants of the CARE FOR HOME Study in 1-year blocks with a total of 2035 patient-years available. The red line indicates the estimated change of eGFR with the respective 95% confidence interval (gray area). Dashed vertical lines indicate DKK3-to-creatinine levels used as cut-offs in subsequent analyses. Blue spikes show the distribution of urinary DKK3-to-creatinine concentrations. All analyses are adjusted for age, sex, body mass index, systolic blood pressure, diabetes, smoking status, eGFR, and log albuminuria.

What does ReFiNE® Dkk3 tell you?



Easily understand the test result!

Damage

Does your patient have kidney damage? Kidneys are damaged in a positive test (accuracy almost 100%)*

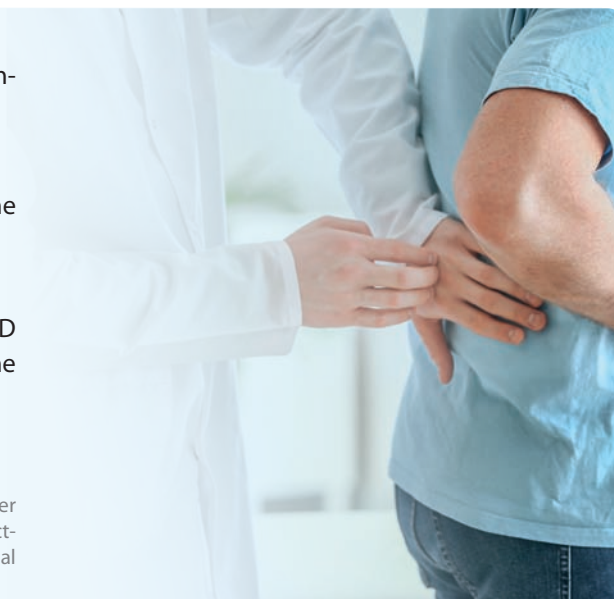
Severity

How severe is the kidney damage? Relative level of the DKK3 value in urine

Progression

How will the kidney damage progress (prognosis of CKD progression)? Relative DKK3 level and progression of the value (with eGFR)

*To ensure that the test can work at peak performance: Avoid improper storage of patient urine samples. Be aware that the values can be affected by fever/infections (e.g. urinary tract infections) or acute interstitial kidney damage.



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You want to learn more?

Our team is here for you!
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