The inflammatory/immune biomarker soluble urokinase receptor (suPAR) may offer a valuable new tool for identifying patients at increased risk of chronic kidney disease (CKD), according to a study in The New England Journal of Medicine.

“SuPAR promises to do for kidney disease what cholesterol has done for cardiovascular disease,” commented senior author Jochen Reiser, MD, PhD, who is Ralph C. Brown, MD, professor and chairman of medicine at Rush University Medical Center in Chicago.

Lead researchers Salim Hayek, MD, and Arshed Quyyumi, MD, both at Emory University, Atlanta, measured suPAR in 3683 individuals from the Emory Cardiovascular Biobank, a prospective registry of patients undergoing cardiac catheterization. Median age was 63 years; about two-thirds of those studied were men.

In this cohort of patients with cardiovascular disease, the median suPAR level was 3040 pg/mL. As a group, patients with higher suPAR levels had a lower estimated glomerular filtration rate and a higher rate of proteinuria.

SuPAR was then evaluated for association with change in eGFR over time and with incident CKD in 2292 participants. In adjusted models, higher baseline suPAR was associated with a faster decline in eGFR: median annual change -4.2 mL/min/1.73 m² for those in the highest quartile of suPAR versus -0.9 mL/min/1.73 m² for those in the lowest quartile. Five-year decline in eGFR was about 20 percent for subjects in the highest quartile of suPAR and 15 percent for those in the third quartile, compared to 7 percent in the two lower quartiles.

The suPAR-related decline in eGFR was greatest among subjects with a normal baseline value (greater than 90 mL/min/1.73 m²). The association was independent of race, diabetes, or proteinuria.

Of 1335 participants with a normal baseline eGFR (60 mL/min/1.73 m²), 24 percent developed CKD during follow-up.

NIH, VA Research Poised to Win in 2016 Budget

By Grant Olan

On November 2, 2015, President Barack Obama signed into law the Bipartisan Budget Act, a top ASN policy priority that opens the door for a funding increase for kidney research at the National Institutes of Health (NIH) and Department of Veterans Affairs (VA). The act raises the overall federal discretionary spending levels for 2016 and 2017. However, Congress still needs to pass a budget for 2016 that details exactly how much funding all the federal agencies—including NIH and the VA—can spend.

Congress avoided a government shutdown at the start of the 2016 fiscal year by passing a short-term appropriations bill that funds the government until December 11. Congress must pass another funding bill to avoid a government shutdown by December 11; they can either enact another short-term appropriations bill or an appropriations bill that funds the government through the end of the 2016 fiscal year.

“The Bipartisan Budget Act was a victory, but it is not complete until Congress passes a year-long 2016 budget that increases federal funding for NIH and VA research,” Frank “Chip” Brosius, MD, ASN Research Advocacy Committee Chair commented. “I urge lawmakers to work together to ensure

New, Early Marker of Kidney Disease Said to Predict Development of CKD

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ASN outlines its options for helping nephrologists maintain career excellence

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Sustained low-efficiency dialysis for critically ill patients with AKI

Policy Update
Physicians may opt for merit-based pay or alternative payment models as sustainable growth rate is replaced

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New, Early Marker

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up. Relative to the lowest quartile of suPAR, risk of CKD was about three times higher for subjects in the highest quartile and twice as high for those in the third quartile.

Forty percent of patients with suPAR levels above the median developed CKD, compared to 10 percent of those with lower levels. For subjects with very high suPAR levels—greater than 4020 pg/mL—estimated 10-year risk of CKD was about 80 percent.

In validation studies in a cohort of women from the Women’s Interagency HIV Study, the association between suPAR and kidney disease was still significant, but weaker. This likely reflected the younger age and better health of women in the validation group.

SuPAR, as well as its membrane-bound form, plays a direct role in regulating cell adhesion and migration via integrin binding, Reiser’s lab has previously presented evidence that suPAR is involved as a circulating blood factor in the pathogenesis of focal segmental glomerulosclerosis and diabetic kidney disease. These findings prompted the researchers to suspect that suPAR may play a broader role in the development of CKD.

Could suPAR testing to assess kidney disease risk really become as familiar as cholesterol testing for cardiovascular disease risk? While not yet FDA-approved for use in direct patient care, the suPAR blood tests are relatively inexpensive and are already being used in Europe for other purposes.

“One characteristic of suPAR is that it is unmodifiable to some degree by lifestyle—for example by stopping smoking,” said Reiser. “Also, if suPAR is high, we can particularly watch those patients and be more aggressive in terms of giving proper medications to control high blood pressure and diabetes, which contribute to CKD.”

Sanja Sever, PhD, co-first author of the study, commented: “SuPAR testing could also be useful for stratifying nephropathy risk in patients with diabetes—for example, in clinical trials testing nephropathy drugs.” Sever is associated with Harvard Medical School.

Hayek and Reiser agree as to the next steps toward routine testing of suPAR:

• Exploring whether a change in suPAR is associated with reclassification of risk
• Determining what lifestyle or therapeutic measures lead to a change in suPAR levels
• Designing a trial in which subjects are randomized according to their suPAR levels to usual care versus therapies shown to modify suPAR

Answers to these points will also provide insights as to whether suPAR might be a new therapeutic target in CKD. If so, “We may envision an injectable antibody that binds to suPAR and basically neutralizes it,” Reiser said.

NIH, VA Research

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these programs have the resources everyone broadly agrees are needed. The US scientific workforce, research enterprise, and patients depend on it."

Given the widespread bipartisan support NIH and VA research enjoys, as well as the recognition that NIH and VA research is underfunded, expectations are that lawmakers will boost funding for the programs. However, Democrats are threatening to oppose 2016 budget bills that include ideological policy riders—controversial provisions that would not pass as their own bills—such as limits on US Environmental Protection Agency regulations under the Clean Air and Water acts.

If Congress is able to pass a budget bill by December 11, a government shutdown would bring significant consequences for some researchers. During the last shutdown in 2013, which lasted 16 days, research programs that are funded through annual appropriations were affected. NIH, for instance, was unable to fund new grants and contracts during that time. ASN has been urging lawmakers to come to agreement, support medical research and other important public health programs, and avert a government shutdown.

ASN budget advocacy

ASN has been actively campaigning for NIH and VA budget increases, along with the Coalition for Health Funding, the coalition NDD United, and Friends of VA Medical Care and Health Research. The society met with 57 congressional offices during ASN Kidney Health Advocacy Day in April 2015 and organized Kidney Community Advocacy Day, which brought together 16 kidney patient and health professional organizations this past September for 112 congressional office meetings.

ASN has also organized and participated in congressional briefings. ASN sponsored a Coalition for Health Funding and Congressional Public Health Caucus Leadership briefing on November 18. Benjamin L. Margolis, MD, a nephrologist at the University of Michigan, spoke to a packed audience about the impact of federal austerity on kidney patient and health professional organizations this past September for 112 congressional office meetings.

“Due to the current funding environment, we are at risk of losing a whole generation of scientists and severely impairing our ability to respond to the country’s healthcare needs in the future,” Dr. Margolis said. Research yields critical new therapies patients desperately need and helps our economy. Investing more in medical research is smart for patients and smart for our country.

What’s next?

The budget battles do not end with passage of the 2016 budget. The Bipartisan Budget Act only provides budget relief in 2016 and 2017, but federal austerity measures capped federal discretionary spending through 2021. ASN will continue to work with stakeholders in the kidney and research communities to campaign for budget relief in years 2018 to 2021, as well as steady and sustained funding increases for NIH, NIDDK, and VA research.

Table 1

House and Senate Appropriations Committees 2016 budget proposals

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