# Thoughts on Turning 29

Josephine P. Briggs
Editor-in-Chief, JASN
Washington, DC

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With this issue, the *Journal of the American Society of Nephrology* (JASN) turns 29 years old. The journal has a tradition of change every 5 or 6 years, a revamp, with a new Editor in Chief and a new team of Deputy and Associate Editors. This issue, the first in volume 29, introduces the next team. I am delighted to have been selected to be the next Editor in Chief of the journal. I step into a position held by a small group of extraordinary physician-scientists, and I approach this job a bit humbled by their accomplishments but also excited by the potential for continued change and thrilled at the strong team of Deputy and Associate Editors listed on the masthead who have agreed to serve with me.

These are, in many ways, wonderful times for science, including the science that matters for nephrology. There are amazing new tools to understand the basic biology of the kidney and to explore disease pathogenesis. Validation of biomarkers is becoming a true science. There is remarkable work going on to translate basic insights into practical application and to target therapeutic interventions more precisely. The methods to pull information out of real-world care are increasingly robust. Research is bringing rigorous data to policy decisions. Good times across the entire spectrum of nephrology research.

In some ways, however, these are also tough times for scientific publishing. Facing the information overload of the Internet age, we are all reading and gathering information differently and living with changing publication incentives. Journal editorial teams need to be wise—ready to adapt but also intent on conserving what is best.

Briefly, our vision for the journal starts with its current strength. JASN's central focus will remain the publication of the best primary research in nephrology. The core of the journal is and should continue to be original research reports of the highest quality. Our scope is the entire range of renal research from the most basic—structural biology, cell biology, kidney physiology—through the entire translational process and extending to the most applied, including observational studies, epidemiology, clinical trials, dissemination and implementation research, and policy analysis.

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**Correspondence:** Dr. Josephine P. Briggs. Email: josie.briggs@gmail.com



The first and in many ways, most critical job of the editorial team is to implement tough-minded, rigorous, fair, and reasonably speedy peer review. The current JASN team, so ably led by the previous Editor in Chief Karl Nath and the current co-Editors in Chief Alfred Cheung and Matt Griffin and watched over by the superb Managing Editor Bonnie O'Brien, have excellent processes in place. They have been doing everything to make the transition as easy as we could hope for. We are in their debt.

The journal has the luxury (and tough responsibility) of selecting for publication from a robust stream of excellent work and can publish only about 15% of the submitted original papers. Hence, peer review is a big job. Timeliness is one important metric of how well we are doing. The process will continue to start with a triage step, where the editorial team looks carefully at each submission and decides whether to send it out for external review. The current JASN team has been triaging approximately 55% of submitted papers, and we expect to hold the rate about the same. Triage seems harsh—it is harsh—but is in the interest of authors as well as editors, because the answer comes quickly. We will aim to have most triage decisions back to submitting authors in a week. The next steps will be in the hands of our excellent panel of Associate Editors who will find reviewers, nudge them for timely responses, try to reconcile conflicting advice, and come back to the entire editorial team for a final decision, with the goal of first decisions sent back to authors by 4 weeks. To help in the process, we have recruited an expanded team of statistical experts listed as our Statistical Editorial Board on the masthead. We expect to incorporate statistical review into the assessment of papers earlier and more often.

The editorial team will certainly encounter some tough issues. Standards are changing; debate is sometimes intense, and consensus is elusive. We hope to discuss some of the hardest topics in editorial commentaries, at times inviting input from you: our readers and authors. Here are a few examples of some of the difficult questions ahead.

(*1*) In the reproducibility debates, what about prespecified sample sizes and blinding in animal studies? Should our norms change? When should the standards vary (for example, for exploratory phase versus validation phase work)?
(*2*) In setting statistical standards, how much detail about data handling should be expected? When should we weigh in on the "frequentist versus Bayesian" debate? When is $P \leq 0.05$ not good enough?
(*3*) Data sharing: what are the right expectations in nephrology for sharing clinical research data, and what role should the American Society of Nephrology journals play?
(*4*) Data presentation: how can we push standards of data presentation that maximize utility for future analysis without sacrificing clarity?
(*5*) Pragmatic trials in nephrology: can we relax standards of intervention fidelity and still get good answers?

The editorial team also recognizes important responsibilities to our readership. A couple of new features aim to enhance interest and readability.

(*1*) We are strengthening the Perspectives section. We have recruited Tom Hostetter as Perspectives Editor and plan to include in each issue one or more insightful short essays on topics important to our discipline.
(*2*) We are adding the requirement that each original article include a short Significance Statement designed to help the reader quickly see the major point of the study. This feature will help busy readers identify papers of special interest to them at a glance.
(*3*) We will be encouraging to authors to provide a simple schematic drawing illustrating the major hypothesis of the work.
(*4*) We are adding a Letters to the Editors section to invite comments on papers that we publish, hoping that these letters will stimulate continued dialogue about the work.

Finally, beginning with the July issue of the journal, we will be making changes in the "look and feel" of the journal, both the print and online versions, hoping to make the printed journal more accessible and the online journal more clickable.

Twenty-nine is a great age for people and for journals. Once perhaps, it was associated with being "over the hill." Not anymore. In our times, it suggests a readiness to take on any challenge. We invite you to join us in a toast to JASN's 29th birthday and to follow with us through the changes ahead.

## DISCLOSURES

None.

# Glomerular Disease Pathology in the Era of Proteomics: From Pattern to Pathogenesis

Mark Haas
Department of Pathology and Laboratory Medicine, Cedars-Sinai Medical Center, Los Angeles, California

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Among glomerular diseases, even the very uncommon ones, fibrillary GN (FGN) has always been among the most poorly understood. From an early description as "Congo red-negative amyloidosis-like glomerulopathy,"[1] its ultrastructural appearance has both captivated and confused renal pathologists. In the 1990s, it was hotly debated whether FGN was a variant of immunotactoid glomerulopathy (or *vice versa*) or a separate entity,[2,3] despite clear differences between the two lesions with regard to the size, shape, and pattern of the fibrils by electron microscopy (EM) and in their association with hematologic malignancies, the latter being far more commonly associated with immunotactoid glomerulopathy.[4] Although immuno-EM studies have suggested that the fibrils in FGN contain immune complexes rather than matrix components,[5] its pathogenesis, including the antigen(s) within the immune complexes, has remained unclear, and perhaps as a result, attempts at treatment of FGN have been largely unsuccessful.[4]

Use of the sequential methods of laser capture microdissection followed by liquid chromatography and mass spectroscopy (ref. 6 reviews the methodologies) has enabled investigators to investigate the proteins within glomeruli isolated from formalin-fixed, paraffin-embedded tissue sections of renal biopsies. This method of proteomic analysis has allowed for the discovery of new forms of renal amyloidosis[7] as well as the identification of individual components of the alternative pathway of complement in glomeruli from biopsies showing a membranoproliferative pattern of GN,[8] contributing to the reclassification of membranoproliferative GN from a morphologic pattern–based diagnosis to a pathogenesis-based diagnosis, the latter including C3 GN.

In this issue of the *Journal of the American Society of Nephrology* (JASN), groups from the Mayo Clinic and the University of Washington, working independently and each using glomeruli isolated from formalin-fixed, paraffin-embedded tissue by laser capture microdissection and a proteomic approach involving analysis by liquid chromatography and tandem mass spectroscopy (LC-MS/MS), each found DnaJ heat shock protein family member B9 (DNAJB9) to be abundantly present in glomeruli from biopsies with FGN but not present in normal glomeruli and glomeruli from biopsies showing other glomerular diseases, including different types of amyloidosis, immunotactoid glomerulopathy, diabetic nephropathy, idiopathic (smoking-related) nodular glomerulosclerosis, and light-chain deposition disease.[9,10] Each group also subsequently showed by immunofluorescence and immunohistochemistry that antibodies to DNAJB9 specifically labeled glomeruli from biopsies with FGN but not these other lesions and that staining for DNAJB9 colocalized with that for IgG in FGN glomeruli. The 100% sensitivity and specificity of DNAJB9 immunostaining for FGN indicate that such staining can be used diagnostically in lieu of EM in identifying patients with cases of FGN, a useful finding in cases where glomeruli for EM study are not available and in centers around the world that do not have access to EM or do not routinely perform EM in renal biopsy analysis. It is also possible that serum and/or urine levels of DNAJB9 or immune complexes containing this protein could serve as a useful biomarker for assessing disease activity and treatment efficacy in FGN.

The findings of the two groups[9,10] strongly suggest that the glomerular deposits in FGN contain, at minimum, DNAJB9 and

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**Correspondence:** Dr. Mark Haas, Department of Pathology and Laboratory Medicine, Cedars-Sinai Medical Center, 8700 Beverly Boulevard, Los Angeles, CA 90048. Email: mark.haas@cshs.org