REPLY: How to employ systems biology to describe complex pathway interactions and ultimately cellular responses will no doubt occupy biologists for many decades to come. Knepper and colleagues (2) have an important point when they say that our Editorial Focus (3) regarding their recent article in AJP-Cell (1) overlooked the statistical approach, Bayesian statistics, they used to narrow down (from 512 kinases) the possible protein kinases that might be responsible for the phosphorylation of aquaporin-2. The application of tools of this description will undoubtedly be essential in drawing together data (some of which are imperfect) from system-based approaches in an effort to describe essential biological processes. Knepper et al. are therefore correct to point out that in our Editorial we did not focus on this aspect of their paper but nevertheless it is a central part of their study. Our Editorial does, however, highlight the fact that statistical approaches used to mine systems-based data sets are tools from which hypotheses can be developed. These hypotheses can then be tested in specific (and often reductionist) experiments. It is this latter part of Knepper et al.’s study that we emphasized in our Editorial Focus, since the verification of the system-based approaches will be important in establishing if the statistical approaches employed in data analysis are robust. It is therefore the marriage of systems-based approaches with traditional reductionist experimentation that will, in our opinion, be necessary. At the present time neither systems biology approaches, and associated statistically analysis, nor, focused “reductionist” experimentation are sufficiently robust or sophisticated to describe complex biological systems independently of one another.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS
A.B.T. drafted manuscript; A.B.T. and R.P. edited and revised manuscript; A.B.T. and R.P. approved final version of manuscript.

REFERENCES