

# Celebrating science's next generation

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**Lila M. Gierasch, Editor-in-Chief, and George DeMartino, Associate Editor and Chair of the Herbert Tabor Young Investigator Award Committee**

Drum roll, please . . . It's time to announce the 2019 group of Herbert Tabor Young Investigator Awardees! Devoted readers of our editorials will know that we recently decided to refocus these awards on the first authors of some of the best work appearing in JBC (1), and we were thrilled to honor the first group of these rising stars in writing (2) and in person at last year's ASBMB annual meeting. This past fall, we again asked for your help (3) in identifying the most exciting and influential papers published in JBC in 2018 to make sure we were not overlooking any potential awardees. We are so grateful for the many of you who took the time to share your thoughts, both for the specific suggestions made and for the continued demonstration that the biological chemistry community values the contributions of and ideas brewing in this new generation of scientists.

Along those lines, we have two additional announcements to share with you. First, we know that not all "new" scientists are "young," and we want to be explicit that we also value those researchers who've come to science later in their lives. As such, future iterations of this award will be known as the "Herbert Tabor Early Career Investigator Award." Second, we know that the challenges faced by early career scientists cannot all be solved with a single award. As a result, we have spent time in the last two years talking with early career scientists about what JBC can do to most effectively support the next generation of scientists. We have been piloting an "early career reviewer" system, layered on top of our existing review process, and there are other ideas on the table. We have recently created a committee dedicated to turning ideas into actions and are eager for more input and engagement with early career investigators. If you are an early career scientist, please e-mail [jbc@asbmb.org](mailto:jbc@asbmb.org) to let us know what you see as the most critical challenges you face, with any suggestions for how JBC can support you, or to be considered as an early career reviewer or for other upcoming initiatives.

## Now, on to the 2019 awardees!

The papers from this talented group showcase the kind of deep mechanistic dives that biological chemists are most famous for. The first three provide critical new insights that merit rewriting of textbooks, as they solve a long-standing mystery in feedback regulation with an unexpected twist, expand current paradigms of iron chemistry in cells, and provide a mathematical explanation for an evolutionary relic. The second three demonstrate how ably biological chemists can interrogate human health and disease: These studies visualize antigen binding by an antibody in clinical development, reveal a new enzyme that promotes colon cancer, and uncover the biochemical basis for cataracts. We love that these papers represent the breadth of

the biological chemistry community, and we hope you find their results as fascinating as we do!

**Margaret Wangeline**, a postdoc in Randy Hampton's lab at the University of California San Diego, coined the term "mallostery," shorthand for "allosteric misfolding," in her investigation of feedback regulation within the sterol pathway (4). The paper shows that treatment with the isoprenoid GGPP initiates misfolding and thus clearance of the enzyme HMG-CoA reductase. The reviewers of the study noted "the specificity of this reaction is remarkable" and described the study as "cleverly designed," "beautifully written," and "a significant contribution to the field of proteostasis." In an Editors' Pick Highlight (5), Chua and Brown look forward to "more examples of this useful concept of mallostery [emerging] from the hazy zone between quality and metabolic control." On Twitter, [@lisamjarvis](https://twitter.com/lisamjarvis) also took interest in the new term, saying "Fun new word alert! (could also be used to describe a house of bad-behaving monks)."

**Fernando Cruvinel Damasceno**, a Ph.D. student in José Carlos Toledo, Jr.'s lab at the University of São Paulo, led a study examining the chemical role of intracellular iron (6). Although this metal has long been thought to catalyze production of hydroxyl radicals and thus serve as an oxidant, the group demonstrated that it can also serve the opposite role, dampening the effects of the strong oxidant peroxynitrite. These results thus broaden the conventional view of this biologically important metal, with implications for redox biology, infection and inflammation (when peroxynitrite's precursors are generated), and beyond. Given these surprising findings, the referees particularly appreciated the "compelling data," noting "one strength of the manuscript is the amount of controls and the analysis of alternative hypotheses."

**Sandeep Eswarappa**, then a postdoctoral fellow in Paul Fox's lab at the Cleveland Clinic, credits Stryer's biochemistry textbook and a snowy Ohio afternoon for helping him recognize "an intriguing metabolic link between the citric acid cycle and EPRS," *i.e.* the bifunctional glutamyl-prolyl tRNA synthetase (7). He and his colleagues developed a mathematical model to examine the metabolic consequences of this gene fusion, shedding light on the evolutionary benefits to retaining the bifunctional sequence. The referees found the work "thoughtful" and "innovative," and noted that "in addition to providing insights about this specific question, the paper provides a template for the use of mathematical modeling to study other connections between amino acid pools and ARS activity and expression." In an Editors' Pick Highlight (8), Lluís Ribas de Pouplana describes the new results as providing "a tantalizing look into the possible evolutionary dance between heredity and cellular metabolism."

**Caroline Soliman**, a Ph.D. student in Paul Ramsland's lab at the Royal Melbourne Institute of Technology University, led a study to characterize the antibody F598, under development for treatment of infections, with its polysaccharide ligand (9). Understanding the basis for high affinity, selective carbohydrate binding remains a challenge in the field in general. However, Soliman's study provides particularly valuable insights, since—as noted by one of the referees—"little has been known of how this common polymer on bacterial pathogens can be targeted by antibodies." Another referee appreciated that "the manuscript reveals important novel information regarding the recognition mechanism of the antibody with its antigen and may shed light for therapeutic engineering." The referees weren't the only ones excited about the work; this paper has the highest Altmetric score of any JBC article.

**Kirstine Lavrsen**, then a graduate student in Hans Wandall's group at the Copenhagen Center for Glycomics, focused her interest in post-translational modifications on deciphering the role of glycosylation in colon cancer. She and her colleagues determined that one particular glycosyltransferase, GalNAc-T6, is highly up-regulated in cancer cells, and further showed that its expression alters glycosylation patterns and disrupts normal differentiation to promote cancer (10). The referees appreciated the clear "clinical significance" of the study as well as the challenges underlying the work, as the "GalNAcT family [is] a group of glycosyltransferases with identical activity but many genes. Previously it has been difficult to distinguish what function and cell type specificity each family member has." In an Editors' Pick Highlight (11), Liping Zhang and Kelly Ten Hagen additionally praised the "wealth of data" this work provides to the community "about the cellular, transcriptional, and glycoproteomic changes resulting from expression of a single GalNAcT."

**Eugene Serebryany**, a postdoctoral fellow in Eugene Shakhnovich's lab, credits isotopically resolved MS experiments for providing the first clue to a "hot potato" competition occurring in the eye lens. He and his colleagues went on to establish that one of the crystallins, previously thought to be biochemically inert, is an oxidoreductase that passes disulfide bonds to other crystallin molecules. This activity supports a new proposal for how these long-lived eye proteins avoid aggregation and why they eventually succumb, giving rise to cataracts (12). The referees describe this new hypothesis of "a long-term redox buffer that acts in the eye lens when the levels of GSH are . . . depleted" as having "far-reaching implications," and suspect the study might be "one of those instances in which direct *in vitro* biophysical experiments clarify a biological mechanism." In an Editors' Pick Highlight (13), Quinlan and Hogg help readers understand the complexity of the system in their own analogy of crystallin packing in the eye, suggesting "it is akin to the annual emperor penguin huddle in Antarctica, but on a completely different length and temperature scale!"

If you are interested in learning more about penguin packing, evolutionary dances, and hazy zones in biology, please join us at

the ASBMB Annual Meeting, taking place in Orlando, April 6–9, where the winners will receive their awards and present invited short talks in a special session on Tuesday, April 9, 2:30–3:45. To learn more about these scientists, please read the March issue of ASBMB Today, which includes more information about their career paths and how these papers took shape (14). If you want to find more exciting content from the 2018 issues of JBC, please check out our virtual issue, "The Year in JBC: 2018" (15), which highlights one great paper from each of our Table of Contents categories; the six papers from our awardees were excluded from this collection, since there were already too many good candidates to feature.

Congratulations to all of the awardees, and see you in Orlando!

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