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Editorial

Happy Birthday *ACS Bio & Med Chem Au*!

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January 2022 marks the one-year anniversary of *ACS Bio & Med Chem Au*, ACS's premier open access journal for medicinal, biochemical, and biomedical content. I want to thank Professor Shelley Minteer, the editor of the nine gold open access journals, Amelia Newman, our managing editor, the staff at ACS Publications, our Associate Editors Professors Afsaneh Lavasanifar and Stuart Conway, and, of course, all who have supported the journal by submitting and reviewing manuscripts. We ask our community of scientists to help make *ACS Bio & Med Chem Au* one of the very best journals in the field of biological and medicinal chemistry by submitting their very best work and by holding manuscripts to very high standards of rigor and impact during the review process. In another editorial to be written in the coming few months, Professors Afsaneh Lavasanifar, Stuart Conway, and I will review the type of content that is both acceptable and unacceptable for the journal and will provide standards to instruct reviewers on how best to review manuscripts.

Our first anniversary issue of the journal brings a mixture of perspectives, reviews, and research articles. Given the ongoing COVID-19 pandemic, we are pleased to present an article from the laboratories of Sanchita Hati and Sudeep Bhattacharyya from the University of Wisconsin, Eau Claire entitled "Pre-Existing Oxidative Stress Creates a Docking-Ready Conformation of the SARS-CoV-2 Receptor-Binding Domain". Using molecular dynamics simulations, the authors determined that the redox state of the receptor-binding domain of the SARS-CoV-2 spike protein and the peptidase domain of the human cell surface receptor angiotensin converting enzyme II affect the structural complementarity between the two binding partners via large conformational changes, with disulfide bonds inducing a ready-to-bind conformation. They propose that pre-existing oxidative stress, prevalent among those at high risk for infection and associated mortality, elevates the binding affinity of the spike protein for the human receptor (DOI: 10.1021/acsbiomedchemau.1c00040). We also thank the authors for providing the cover art for this issue of the journal.

A second research article, from the laboratory of Bo Liedberg at the Nanyang Technological University in Singapore, is entitled "Amphiphilic Membrane Environments Regulate Enzymatic Behaviors of Salmonella Outer Membrane Protease". In this work, the authors use the *Salmonella enterica* outer membrane protease E (PgtE) as a model to understand the specific protein−lipid interactions that drive the conformational plasticity and function of integral membrane proteins. PgtE is involved in tissue infiltration and the survival of the organism and plays an important role in bacterial resistance against innate and acquired immune defenses of infected mammals. PgtE requires the binding of lipopolysaccharide as a cofactor in its reaction. The authors find that PgtE exhibits hysteretic enzymatic behavior in its detergent-stabilized form and in the outer membrane-embedded native state in live bacteria, displaying a pronounced lag phase before achieving steady state. In addition to characterizing the protein's activity under several environmental conditions, the authors show that when the protein is reconstituted in a phospholipid bilayer composed of 1-palmitoyl-2-oleoyl-glycero-3-phosphocholine, PgtE no longer requires lipopolysaccharide as a cofactor (DOI: 10.1021/acsbiomedchemau.1c00027).

A third research article, from the laboratory of Krishna Mohan Poluri at the Indian Institute of Technology Roorkee, is entitled "Elucidating the Eradication Mechanism of Perillyl Alcohol against *Candida glabrata* Biofilms: Insights into the Synergistic Effect with Azole Drugs". The authors had as an overall goal to develop new and novel treatments against the genus Candida, which are clinically the most prominent human fungal pathogens. Essential oils, many of which are derived from terpenes, have been known for some time to exhibit wound-healing, antiproliferative, immune-modulatory, antiaging, and hypoglycemic activities. In this study, the effect of the terpene perillyl alcohol on *C. glabrata* was investigated. The authors found that perillyl alcohol inhibits the growth of the organism and eradicates its biofilms. This effect was mediated through multiple pathways, including, among others, by reducing carbohydrate and eDNA content in the extracellular matrix, by affecting mitochondrial activity and inducing cytochrome C release from mitochondria, and by inhibiting DNA replication and progression to S-phase in the cell cycle. Moreover, the natural product acted synergistically with azole-containing drugs such as miconazole (DOI: 10.1021/acsbiomedchemau.1c00034).

Five additional contributions in the first issue of Volume 2 of *ACS Bio & Med Chem Au* are part of a virtual issue focused on Radical *S*-adenosylmethionine (SAM) enzymes in honor of a pivotal bioinformatics paper published 20 years ago that established that these enzymes constitute a superfamily.[1] A separate editorial that describes this superfamily in more detail is forthcoming. In short, this superfamily is arguably the most functionally diverse and one of largest, growing from about 600 constituents in the initial bioinformatics study to about

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700 000 unique sequences currently in the UniProt database.[2] Most of radical SAM (RS) sequence space contains unannotated function, and the goal of many in the field is to elucidate these unknown functions. The contribution from the laboratories of John Gerlt and Douglas Mitchell at the University of Illinois Urbana—Champaign, entitled "Radical-SAM.org: A Resource to Interpret Sequence-Function Space and Discover New Radical SAM Enzyme Chemistry" (DOI: 10.1021/acsbiomedchemau.1c00048), describes an excellent web resource for advancing the study of the RS superfamily. This resource is an offshoot of the well-known Enzyme Function Initiative resource (DOI: 10.1021/acs.biochem.9b00735).

Many RS enzymes cluster into one of about 25 different groups based on sequence similarity. One of the largest of these groups is composed of enzymes that also bind cobalamin, most of which, but not all, function as methyltransferases. This group of RS enzymes has been among the most difficult to study. The perspective from Craig Townsend's laboratory at Johns Hopkins University, entitled "Evolution of Methods for the Study of Cobalamin-Dependent Radical SAM Enzymes", takes us from the beginning, when it was difficult to isolate these enzymes in a soluble and useful state, to the present, wherein we have now begun to study these enzymes mechanistically in vitro as well as structurally (DOI: 10.1021/acsbiomedchemau.1c00032). Another of the largest groups of RS enzymes are those labeled as having SPASM or TWITCH domains. Many of these proteins act on ribosomally produced peptides that are then modified post-translationally, and these matured peptides exhibit myriad functions such as antibacterials, quorum sensing agents, and enzyme cofactors. The review from the laboratory of John Latham at the University of Denver, entitled "How a Subfamily of Radical *S*-Adenosylmethionine Enzymes Became a Mainstay of Ribosomally Synthesized and Post-translationally Modified Peptide Discovery", describes some of the initial studies on RS enzymes having SPASM domains and how they led to the development of an entire subfield of RS enzymology (DOI: 10.1021/acsbiomedchemau.1c00045).

RS enzymes carry out some of the most challenging biological chemistry known. Indeed, they are involved in the maturation of some of the most complex metallocofactors in nature, including heme, the iron−molybdenum cofactor of nitrogenase, the site where dinitrogen is reduced to ammonia, and the H-cluster of the [FeFe]-hydrogenase, where hydrogen gas is reversibly converted to protons and electrons. The review from the laboratory of Yvain Nicolet at Université Grenoble Alpes, entitled "Radical SAM Enzymes and Metallocofactor Assembly: A Structural Point of View", focuses on these two systems and the maturation factors that produce the complex metallocofactors found in nitrogenase and hydrogenase (DOI: 10.1021/acsbiomedchemau.1c00044). Lastly, the perspective from David Britt's laboratory at University of California, Davis, entitled "Proposed Mechanism for the Biosynthesis of the [FeFe] Hydrogenase H-Cluster: Central Roles for the Radical SAM Enzymes HydG and HydE", describes detailed mechanistic, spectroscopic, and structural studies to elucidate the function of several proteins involved in generating the H cluster of the [FeFe]-hydrogenase (DOI: 10.1021/acsbiomedchemau.1c00035).

Finally, I want to recognize our wonderful editorial advisory board and thank them in advance for their support in setting and upholding the standards for the journal. We have a highly diverse and highly accomplished group of 28 editorial advisory board members from all over the world (Table 1) and all continents except for Antarctica (still trying to find some people down there!). Their expertise spans the broad disciplines in biological research that are represented by the journal, including chemical biology, metalloenzymology, plant science, medicinal chemistry, natural product biosynthesis, enzymology, bio-organic chemistry, bioinorganic chemistry, computation and theory, antibiotic development and antibiotic resistance, and X-ray crystallography, among others. Afsaneh, Stuart, and I are looking forward to a very special 2022 as we surpass all of the milestones that we have set for the journal. We look forward to working with all of you in the near future.

Table 1. Members of the Inaugural Editorial Advisory Board of *ACS Bio & Med Chem Au*

name	institution	country
Lucia Banci	University of Florence	Italy
Anna Barnard	Imperial College London	United Kingdom
Maria-Laura Bolognesi	University of Bologna	Italy
Ivone Carvalho	Universidade de São Paulo	Brazil
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Notes

Views expressed in this editorial are those of the author and not necessarily the views of the ACS.

REFERENCES

(1) Sofia, H. J.; Chen, G.; Hetzler, B. G.; Reyes-Spindola, J. F.; Miller, N. E. Radical SAM, a novel protein superfamily linking unresolved steps in familiar biosynthetic pathways with radical mechanisms: functional characterization using new analysis and information visualization methods. *Nucleic Acids Res.* **2001**, *29* (5), 1097−106.

(2) The UniProt Consortium. UniProt: the universal protein knowledgebase in 2021. *Nucleic Acids Res.* **2021**, *49*, D480−D489.