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Interview: Prof. Tanja Kunej, a Pioneer of Multiomics, on 21st Century Systems Science Prospects and Challenges

Tanja Kunej

OMICS IS PLEASED TO FEATURE THIS MONTH an exciting interview with Prof. Tanja Kunej, a pioneer of systems science and multiomics scholarship. Prof. Kunej is also a sought after expert referee, and author in the field, particularly in developing new visionary taxonomies for emerging omics fields and their integration with systems science scholarship.

Prof. Kunej shared with the *OMICS* readership experiences and insights on 21st century systems science, where the field is advancing prospects and challenges ahead.

Prof. Vural Özdemir (Editor-in-Chief, *OMICS*)**:** Prof. Kunej, many thanks for your time and this interview for *OMICS*. You are a member of our editorial board and frequent contributor to the journal. Please tell us what sparked your interest to pursue a career in biology specifically, and systems science more generally?

Prof. Tanja Kunej: First, I would like to thank you for the opportunity to share my thoughts through the interview for the *OMICS: A Journal of Integrative Biology*, a journal with pioneering role in the translation of big data to health care.

I am grateful to all my inspiring professors and mentors. Looking back, these early experiences instilled in me a sense of curiosity for nature and the world at large, and an interest for continuous learning, particularly at the systems level, as well as teaching. Once I had entered the world of molecular biology, it became fascinating and impossible to leave. Genomics research is a great challenge and frontier of systems science because to see the big picture and make sense of the entire sphere of genomics information at the biological, clinical, and ecological scales, constant dynamic reading and rethinking of the multiomics literature are needed.

Prof. Özdemir: How would you describe your key research interests?

Prof. Kunej: Over the years, my research interests have evolved from single gene studies to whole genome, and then to the multiomics dimension about a decade ago. Since then I have sought to gain deeper insight into the biology of a single cell, whole organism and ecosystems from genome to metabolites surveying the advances in systems science. My goal is to generate a multiomics view of genome–phenome relationships; this is necessary to grasp the big picture in biology, environment, and society, and to have an overview of all omics levels from DNA, RNA, miRNomics, interactomics, glycomics, and many other omics types and their complex interplay. Regardless of which genetic element, molecular mechanism, trait, or disease is being considered, everything can and must be studied and contextualized in a multiomics view.

Prof. Özdemir: Could you share your opinion with the readers on the top 10 prospects for multiomics research over the next decade?

Prof. Kunej: The *first prospect*, in my opinion is that the multiomics approach will enable the development of more precise biomarkers for diseases and phenotypic traits. The future most likely lies in the development of multiomics network-based disease and trait modules. Future biomarkers will most likely consist of a combined set of diverse genomic markers, including sequence variants, proteins, epigenetic markers, and glycans.

The second prospect is the implementation of the polygenic risk score (PRS) in clinical practice. PRS is based on common genetic variations from genome-wide association studies and is increasingly used for risk prediction for complex diseases. Moreover, extending this concept to the multiomics risk score (MORS) is needed to increase early identification of at-risk individuals for diseases as well as adverse drug reactions and treatment resistance, thus enabling early intervention. Prior to clinical implementation, risk scores need to be analyzed in different populations to develop population-specific and more robust scores, shared across populations and continents. MORS is a new emerging concept and term that I propose and would like to introduce here.

The *third prospect* is translation of integrated personal omics profiling introduced by the Snyder laboratory into clinical practice, for example, by combining genomic information with monitoring of physiological states by multiple high-throughput methods.

The *fourth prospect* is to develop a complete multiomics diseasome map, based on the previously developed human

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disease map by the Barabasi laboratory. Moreover, this map should also be developed for visualization of gene–trait associations in other species.

The *fifth prospect* is to establish an approach for systematic identification of knowledge gaps guiding research directions and hypothesis generation of the research community. More coordinated planning of research directions at the global level would greatly advance research. The challenge is that many researchers are busy with routine work, teaching, grant writing, and clinical or administrative work and, therefore, do not have time to follow the developments of the complete study field from a bird's eye view. Consequently, research hypotheses often focus on ''famous genes.''

The sixth prospect is to develop a central integromics database connecting all available data that can subsequently be updated on a dynamic and ongoing basis. For this goal, large amounts of old data will have to be recycled, cleaned, and supplemented with identification numbers. In addition to the production of new data, the organization of previously published data is also important. Therefore, an effort by the global scientific community is needed. Such a comprehensive database would greatly facilitate the discovery of genetic causes of diseases and therapeutic targets.

The *seventh prospect* is to develop a template for writing critically informed review articles with deep insights, in a standardized format that would enable direct transfer of tables and catalogues into databases.

The *eighth prospect* is to develop initiatives for reporting standardization in genomics, including the multiomics field. Moreover, it will also be necessary to establish guidelines for the unification of initiatives for reporting standardization, as there are many areas that need to sort and classify published data.

The *ninth prospect* is to establish better knowledge transfer between different study fields, including human, animal, and plant genomics.

The *tenth prospect* is to initiate a large-scale computational and wet laboratory ''*in silico* human'' initiative with the aim to develop an integrated and dynamic view of the body, organs, tissues, and cells in health and disease states. In addition, this initiative could be followed by other similar projects, including *in silico* mouse, *in silico* cow, and different *in silico* plant initiatives.

Prof. Özdemir: What about challenges in multiomics research?

Prof. Kunej: Data fragmentation and incompleteness hinder research progress and limit our ability to understand the molecular mechanisms of diseases. Data are dispersed across research articles, supplementary materials, and databases. Many efforts have already greatly contributed to development of the scientific field, for example, findability, accessibility, interoperability, and reusability guiding principles for scientific data management and intensively curated genomic resources such as Ensembl and the University of California, Santa Cruz genome browser, the Worldwide protein data bank, UniProt, and the National Center for Biotechnology Information. However, gene lists and databases associated with diseases and phenotypic traits are not yet available or are incomplete. Laboratories could develop their own databases related to their field of expertise, allowing further integration with existing databases.

Prof. Özdemir: What are your thoughts on teaching in the multiomics era?

Prof. Kunej: The genomics field is developing very quickly and, therefore, lecturers are challenged to maintain an overview across all known and emerging omics levels. Textbooks that contain descriptions of large numbers of omics levels are not yet available. Most of the current textbooks are focused on one or a few omics levels. It is also a challenge to describe each omics level in a consistent manner. In addition, the multiomics taxonomy is not yet complete. It would be optimal for lecturers to teach and conduct research at multiple omics levels, as well as in systems biology and multiomics data integration.

Students could also contribute to the development of the study field. During courses, students could develop genomics databases and extract published data, sort the data according to a specific omics level, thus simultaneously learning and also contributing to the genomics field.

For example, in the ''Genomics'' and ''Animal genomics'' courses of the Master degree programmes of Biotechonology and Animal Science at the University of Ljubljana, Biotechnical faculty, students choose a topic for a seminar article, that is, for example, related to a pathway, omics level, method, disease or trait. The seminar chapters are recommended to be organized according to multiomics taxonomy or contextualized at a wider multiomics insight. Students must follow the proposed initiatives for reporting standardization and complement the data with identification numbers and perform basic biocuration. This project work enables students to gain multiomics insight early in their careers. In addition, students also gain skills in scientific writing, as they are required to follow the instructions for writing a scientific article. Usually, their MSc theses focus on a single mechanism, however, they still acquire broader knowledge to be able to communicate their results to a wider audience with multiomics insights. To date, we have published eight seminar books including >200 seminar articles.

Prof. Özdemir: What are your most significant three articles or research contributions that relate to where the field of systems science is currently advancing, particularly in the present era of the COVID-19 pandemic?

Prof. Kunej: I would like to point out the articles that introduced the taxonomy for multiomics science, for example, (https://www.liebertpub.com/doi/10.1089/omi.2016.0144) and (https://www.liebertpub.com/doi/10.1089/omi.2017.0181). Genome-wide study approaches were extracted from several published studies and sorted into 13 omics levels: genomics (DNA level), transcriptomics, proteomics, interactomics, metabolomics, epigenomics, miRNomics/ncRNomics, glycomics, lipidomics, integrated omics, phenomics, environmental omics, and pharmacogenomics. These studies present a baseline for future development of taxonomy with novel technologies and contribute to the terminology development. The project will enable more efficient and controlled multiomics integration and development of biomarkers with multiomics design.

The second group of articles is related to the integration of multiomics data for the identification of novel biomarkers in agriculture and biomedicine. This approach has also enabled molecular explanation of disease comorbidity, for example, the copresence of cryptorchidism and cardiomyopathy, which is common in several syndromes such as RASopathies (https://bmcmedgenomics.biomedcentral.com/articles/10.1186/1755-8794-6-5). The applied network-based systems biology

approach presents a baseline for the development of a complete map of genome–phenome associations in this knowledge domain.

The third group of articles is related to reporting standardization in genomics, for example, the reporting of microRNA–target interactions (https://www.liebertpub.com/doi/10.1089/omi.2017.0023). Reporting standardization facilitates database development and enables more efficient biocuration and, multiomics integration. Moreover, one of the initiatives developed is included in the instructions for authors of the journal and serves as a template for formatting research articles reporting genetic causes of male infertility (https://www.tandfonline.com/doi/full/10.1080/19396368.2016.1250181).

The mentioned projects are also relevant to COVID-19 systems science. Namely, the integrative omics approach and network-based systems biology are highly important for understanding the molecular changes that drive the host COVID-19 response. Studies have revealed that COVID-19 severity depends mainly on the host, rather than viral factors supporting the need for systematic research of the individuals' responses at all omics levels.

Prof. Özdemir: Thanks so much for sharing your thoughts with the *OMICS* readership, and reaching out to integrative biologists and biomedical scientists, physicians, nurses, and health professionals. Your biography is available at the end of this interview for the interested readers who may want to learn more. Any final thoughts you wish to add?

Prof. Kunej: Thank you very much Prof. Özdemir for your work as editor for the *OMICS* journal for the important contribution to the development of the multiomics and integrative biology field, which is expected to continue its rapid and interdisciplinary growth in science and society in the future.

Disclaimer

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Abbreviations Used

MORS = multiomics risk score
PRS = polygenic risk score

BIOGRAPHY: TANJA KUNEJ, PHD

Tanja Kunej is a professor of genetics at the University of Ljubljana, Biotechnical Faculty, Department of Animal Science. She is a coauthor of >700 bibliographic records, including 100 scientific publications, 2 book chapters, and 2 patents. Her main research interest is integration of genomics data and biomarker development in agriculture and biomedicine.

She is a lecturer of undergraduate courses ''Genomics'' and ''Animal genomics'' and postgraduate courses ''Concepts of genomics data integration'' and ''Analysis of non-coding RNAs.'' She has mentored >80 students at PhD, MSc, and undergraduate levels.

In 2010 and 2013, she received award of the Slovenian Research Agency for one of the most important achievements of Slovenian scientists. In 2018, she received the ''Best Teacher at the Study of Biotechnology'' award by the University of Ljubljana Biotechnical Faculty. In 2017–2019, she received six Publons Peer Review Awards.

The complete bibliography is available at: https://bib.cobiss.net/biblioweb/direct/si/eng/cris/16361.