ACS NANO

www.acsnano.org

EDITORIAL

What Do We Mean When We Say Nanomedicine?

Cite This: *ACS Nano* 2022, 16, 13257–13259

Read Online

ACCESS | Metrics & More | Article Recommendations

Nanomedicine can be broadly defined as the branch of medicine[1] that makes use of nanotechnology[2] for disease prevention, monitoring, and intervention through new modalities for imaging, diagnosis, treatment, repair, and regeneration of biological systems. Whether this relates to new (or improved) therapies or diagnostic methods, or the development of more efficient biomaterials for tissue regeneration, the goal of nanomedicine research is to reach the clinic and improve the patient's health or quality of life.

Since the first issue of *ACS Nano*, we have actively engaged in publishing the most novel and significant nanomedicine developments—from a broad perspective—that have the potential for clinical translation. Selected recent highlights include hyperthermal and photodynamic therapies,[3,4] multifunctional probes,[5] nanozymes,[6] COVID biosensors,[7] respiratory masks,[8] as well as highly influential reviews.[9−11]

A survey of the main areas where *ACS Nano* has focused to date indicates that understanding of the nano-bio interface (*i.e.*, what happens when nanomaterials contact biological systems) has been an engaged field, which has sparked the discovery of multiple new phenomena. This includes processes involved in the formation, structure, and composition of nanomaterials in biological media *in vitro* and *in vivo* (*e.g.*, formation of a protein corona), which are affected by many parameters, including temperature, nanomaterial size, shape, composition, surface chemistry, *etc.*, that may strongly influence the nano/bio interactions.

The nanoparticle physico-chemical properties can relate to biodistribution, another major topic that addresses key questions in nanomedicine. How do nanoparticles travel through the body? Where do they accumulate? Can we affect the fate of nanomaterials by engineering their surface chemistry? Can we improve their targeting to sites of interest by anchoring specific bioreceptors to the nanoparticle surface? All of these questions have been addressed by our authors, and our knowledge has thereby increased enormously.

Nanomaterial composition and *in vivo* stability are of critical importance in the study of these effects since labels are required to track their location and monitor their activity *in vivo* (therapeutic or otherwise) and assess the extent to which they are sequestered by the mononuclear phagocyte system. Different materials can produce nanoparticles with specific properties that are suitable for therapy, diagnosis, or regeneration (or combinations thereof). A plethora of chemical compositions and combinations of materials have thus been developed as nanoparticles, characterized, and thoroughly reported to describe their nanomedicine-related activities. However, among this long list of materials, few have entered the marketplace for reasons discussed below and therefore clearly qualify in terms of the consideration of what constitutes relevance against the backdrop of innovation.

Nowadays, a typical nanomedicine manuscript submitted to *ACS Nano* often tends to be formulaic, which could lead to overlooking biological complexity. It begins with the design of a novel material or (more typically) a combination of materials that can be formulated to produce a biocompatible particle that can function, for example, to diagnose or cure a particular disease. The design concept is presented in a brilliant drawing of the delivery system. The manuscript then proceeds through a predictable sequence, starting with results in cell culture and then an animal model (often without discussion of its clinical relevance), and demonstration of an amazing *in vivo* outcome (*e.g.*, complete tumor eradication by the immune system). Plugging a new drug or disease into the formula is often proposed as a novel concept and forms the basis of other submissions to *ACS Nano*.

Regardless of novelty, we often find that materials choices and synthetic protocols lack consideration of translation potential (the chance that these materials will ultimately end up in the clinic). The relevance of these findings in terms of critical healthcare needs and the pathophysiology of the disease is often missing.[12] A possible reason for this disconnect is that an emphasis on establishing the unique properties/novelty of the studied materials, chosen from a materials science perspective, is not balanced by considerations of disease outcome, often employing a biological model system that emphasizes unique material properties instead of disease-relevant effects. This may reflect the failure to consult or include individuals with clinical or pharmaceutical expertise in the study design and execution. Their expertise would provide insights into important topics, such as the selection of materials that are likely to receive approval by the U.S. Food and Drug Administration (FDA) and related agencies in other countries, the demonstration that a nanocarrier is indeed required for an

Published: September 27, 2022

https://doi.org/10.1021/acsnano.2c08675
ACS Nano 2022, 16, 13257−13259

effect, as opposed to existing pharmaceuticals, and consideration of pharmacokinetics, dosimetry, cost, safety, and significance concerning the actual complexities of the disease model. Further, given the extent of the published literature, new work should be benchmarked against existing studies. A "new" material that does not improve upon the functionality or performance observed with previously published materials is not likely to advance the field. Novelty can be achieved by either describing a new effect associated with a material or demonstrating the quantitative performance of this material exceeding the performance of competing materials.

Thus, to develop a more balanced approach, *ACS Nano* nanomedicine submissions would benefit from moving beyond fundamental research and formulaic approaches that emphasize material design strategies for proof-of-principle testing to addressing more clinically relevant challenges that involve the pathophysiology of disease, clinical relevance, and consideration of pharmacology. This should include consideration of production scalability, dosimetry, delivery efficacy, pharmacokinetics, degradability, ADME (absorption, distribution, metabolism, and excretion), reproducibility, cost-benefit analysis, and the feasibility of obtaining FDA approval. A thorough discussion of study limitations should also be included to provide our readership with a balanced assessment of barriers to clinical translation/acceptance and remaining work that should be addressed. We strongly encourage involving clinicians to participate in therapeutics development, imaging, diagnostics, and pharmacology to ensure clinical relevance, as opposed to promoting an uncritical acceptance that a cleverly designed nanomaterial resulting in an amazing therapeutic outcome will automatically be beneficial, as portrayed in table of content (TOC) drawings. In reverse, we propose that the use of nanoenabled concepts could be equally significant to biologists and clinicians, informed of the importance of implementing an engineered approach to disease management vis-à-vis the classical biological approach of basing research progress on hypotheses only. What is often missing in the latter approach is the consideration that a seemingly "impenetrable" tumor with a robust stroma may still contain a gate that can be opened through the eyes of an engineer. This includes the accomplishment of some biological outcomes that are only achievable using nanotechnology, as witnessed in meeting the pandemic vaccine requirements for COVID-19.

ACS Nano nanomedicine submissions would benefit from moving beyond fundamental research and formulaic approaches that emphasize material design strategies for proof-of-principle testing to addressing more clinically relevant challenges that involve the pathophysiology of disease, clinical relevance, and consideration of pharmacology.

Clinical relevance requires early stakeholder engagement from clinicians, medical practitioners, or pharmaceutical experts with researchers in the design and execution phases. Collaboration between those with vested interests in developing nanomedicine could benefit from practical considerations such as the selection of regulated FDA-approved materials, evidence for the need of a specific nanocarrier, pharmacokinetics, dosimetry, cost, safety, and significant understanding of the complexities of the disease model. With the awareness among clinicians of what nanotechnology can contribute, nanomedicine is poised to impact all aspects of public health and all fields of medicine. Steering research in a direction that will most efficiently shape the future of nanoenabled therapies will impact public health and enhance the effectiveness of an interdisciplinary collaboration between stakeholders from industry, government, and academia for clinical and population-based implementation.

With the awareness among clinicians of what nanotechnology can contribute, nanomedicine is poised to impact all aspects of public health and all fields of medicine.

Luis M. Liz-Marzán, Executive Editor orcid.org/0000-0002-6647-1353
Andre E. Nel, Associate Editor orcid.org/0000-0002-5232-4686
C. Jeffrey Brinker, Associate Editor orcid.org/0000-0002-7145-9324
Warren C. W. Chan, Executive Editor orcid.org/0000-0001-5435-4785
Chunying Chen, Associate Editor orcid.org/0000-0002-6027-0315
Xiaodong Chen, Editor-in-Chief orcid.org/0000-0002-3312-1664
Dean Ho, Associate Editor orcid.org/0000-0002-7337-296X
Tony Hu, Associate Editor orcid.org/0000-0002-5166-4937
Kazunori Kataoka, Associate Editor orcid.org/0000-0002-8591-413X
Nicholas A. Kotov, Associate Editor orcid.org/0000-0002-6864-5804
Wolfgang J. Parak, Associate Editor orcid.org/0000-0003-1672-6650
Molly M. Stevens, Associate Editor orcid.org/0000-0002-7335-266X

AUTHOR INFORMATION

Complete contact information is available at:
https://pubs.acs.org/10.1021/acsnano.2c08675

Notes

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

REFERENCES

(1) https://www.britannica.com/science/medicine.
(2) https://www.britannica.com/technology/nanotechnology.
(3) Espinosa, A.; Di Corato, R.; Kolosnjaj-Tabi, J.; Flaud, P.; Pellegrino, T.; Wilhelm, C. Duality of Iron Oxide Nanoparticles in Cancer Therapy: Amplification of Heating Efficiency by Magnetic

Hyperthermia and Photothermal Bimodal Treatment. *ACS Nano* **2016**, *10*, 2436−2446.
(4) Li, S. Y.; Cheng, H.; Xie, B.-R.; Qiu, W.-X.; Zeng, J.-Y.; Li, C.-X.; Wan, S.-S.; Zhang, L.; Liu, W.-L.; Zhang, X.-Z. Cancer Cell Membrane Camouflaged Cascade Bioreactor for Cancer Targeted Starvation and Photodynamic Therapy. *ACS Nano* **2017**, *11*, 7006−7018.
(5) Liong, M.; Lu, J.; Kovochich, M.; Xia, T.; Ruehm, S. G.; Nel, A. E.; Tamanoi, F.; Zink, J. I. Multifunctional Inorganic Nanoparticles for Imaging, Targeting, and Drug Delivery. *ACS Nano* **2008**, *2*, 889−896.
(6) Zhang, Y.; Wang, F.; Liu, C.; Wang, Z.; Kang, L.; Huang, Y.; Dong, K.; Ren, J.; Qu, X. Nanozyme Decorated Metal-Organic Frameworks for Enhanced Photodynamic Therapy. *ACS Nano* **2018**, *12*, 651−661.
(7) Qiu, G.; Gai, Z.; Tao, Y.; Schmitt, J.; Kullak-Ublick, G. A.; Wang, J. Dual-Functional Plasmonic Photothermal Biosensors for Highly Accurate Severe Acute Respiratory Syndrome Coronavirus 2 Detection. *ACS Nano* **2020**, *14*, 5268−5277.
(8) Konda, A.; Prakash, A.; Moss, G. A.; Schmoldt, M.; Grant, G. D.; Guha, S. Aerosol Filtration Efficiency of Common Fabrics Used in Respiratory Cloth Masks. *ACS Nano* **2020**, *14*, 6339−6347.
(9) Pelaz, B.; Alexiou, C.; Alvarez-Puebla, R. A.; Alves, F.; Andrews, A. M.; Ashraf, S.; Balogh, L. P.; Ballerini, L.; Bestetti, A.; et al. Diverse Applications of Nanomedicine. *ACS Nano* **2017**, *11*, 2313−2381.
(10) Udugama, B.; Kadhiresan, P.; Kozlowski, H. N.; Malekjahani, A.; Osborne, M.; Li, V. Y. C.; Chen, H.; Mubareka, S.; Gubbay, J. B.; Chan, W. C. W. Diagnosing COVID-19: The Disease and Tools for Detection. *ACS Nano* **2020**, *14*, 3822−3835.
(11) Liu, Y.; Pharr, M.; Salvatore, G. A. Lab-on-Skin: A Review of Flexible and Stretchable Electronics for Wearable Health Monitoring. *ACS Nano* **2017**, *11*, 9614−9635.
(12) Nel, A. E. Transformational Impact of Nanomedicine: Reconciling Outcome with Promise. *Nano Lett.* **2020**, *20*, 5601−5603.

https://doi.org/10.1021/acsnano.2c08675
ACS Nano 2022, 16, 13257−13259