Highlights from Stanford Drug Discovery Symposium 2021

Amanda J. Chase¹, Sanjay V. Malhotra ²,3, Mark Mercola ⁴,1,4, Kuldev Singh⁵, and Joseph C. Wu ⁴*,6,7

¹Stanford Cardiovascular Institute, Stanford, CA, USA; ²Department of Cell, Development and Cancer Biology, Oregon Health & Science University, Portland, OR, USA; ³Center for Experimental Therapeutics, Knight Cancer Institute, Oregon Health & Science University, Portland, OR, USA; ⁴Department of Medicine, Stanford University, Stanford CA; ⁵Department of Ophthalmology, Stanford University School of Medicine, Stanford, CA, USA; ⁶Department of Medicine, Division of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, CA, USA; and ⁷Department of Radiology, Stanford University School of Medicine, Stanford, CA, USA

Keywords Drug discovery • COVID-19 • Drug development • Vaccine • Translation

The Stanford Drug Discovery Symposium (SDDS), now in its 5th year, provides a unique and highly valuable platform for inspiring interdisciplinary exchange at the forefront of drug research. Over the last 6 years, SDDS has grown in size and in scope while continuing to provide a critical resource and opportunity for networking among researchers, pharmaceutical companies, investment groups, and others in the wider biomedical community. As with many things, the COVID-19 pandemic moved SDDS into the virtual space, allowing a far broader audience to participate. This year, SDDS had 45 speakers, moderators, and panelists that together represented pharmaceutical and biotech companies, government policymakers, Nobel laureates, academic leaders, scientists, editors from major journals, and venture capitalists. They not only presented their advances in drug discovery, as further discussed below, but also participated in lively panel discussions, including questions from the broader audience of over 7000 participants.

Each year, SDDS recognizes a scientist whose body of scientific work has enabled change that improves human health through a Lifetime Achievement Award. This year, Drs Douglas Lowy and John Schiller were jointly recognized for their combined work that formed the basis of the biology behind the human papillomavirus (HPV) vaccine. The vaccine has been shown to reduce rates of HPV infection and the presence of precancerous cells in people who received the vaccine and represents a significant advance in public health. They shared their work showing that HPV capsids, a combination of virus-like particles and pseudovirions, bind and infect most tumour-derived cell lines, and how this is now being leveraged to treat cancers.¹ They also presented their current work moving into therapies for a broader spectrum of cancers. The past and current works of the Drs Lowy and Schiller exemplify how human health can benefit from vaccination, and how the commitment of scientists can continuously advance their field. This is further embodied by the amazingly rapid advances we saw in COVID-19 research and the development of novel vaccines against SARS-CoV-2.

2020 was a challenging year in many ways, but it was also one of the most innovative times in health research. Many speakers at SDDS presented the work aimed at improving treatment options for COVID-19, covering not only the creation of the vaccines but also those we have learned from the pandemic and the evolving role played by scientific journals and media. The science behind the impressive timelines that yielded such effective vaccines was shared from the Pfizer, Moderna, and Johnson & Johnson perspectives.²⁻⁴ Also shared was the basis for a future single-dose COVID-19 vaccine that is stable at room temperature and is protein-based.⁵ In addition to vaccines, there was the development of REGEN-COV, an antibody cocktail effective in the treatment of SARS-CoV-2 infections.⁶ The speakers also shared how an unprecedented collaboration across big pharma, biotech, CMC manufacturers, and regulatory agencies helped to accelerate the development of COVID-19 therapies. Along with scientific and therapeutic advancements, researchers have been further learning from the pandemic, including examining and refining the clinical trial process, with a call for improved efficiency in clinical trials.⁷ Incorporating digital tools and data science into clinical trials will be instrumental to those efforts.

The importance of data science was a recurring theme throughout SDDS. The use of machine learning and artificial intelligence in drug discovery provides an unprecedented means to decrease the cost and time needed to create new therapies. Machine learning has a pivotal role in improving the clinical trial design, such as by helping to select the best primary endpoint for COVID-19 vaccine trials. Increasingly machine learning is being used not only for clinical trial optimization but also for understanding biological mechanisms, developing new therapies, and improving patient care. For instance, pulmonary arterial hypertension (PAH) is a rare, progressive disorder that is hard to diagnose. Electronic health records and machine learning have been combined to create an electrocardiogram-based model algorithm that can detect PAH before diagnosis so that medications can be used to slow progression.

Alongside the impressive advances in COVID-19 treatments and vaccines and the increased use of data science in drug discovery, other SDDS speakers shared their recent works on RNA modulators, anti-sense oligonucleotides, cell and gene therapies, conjugates, and therapeutic peptides. They also shared how genome-association studies and omics are being leveraged in drug discovery and development to both find new candidates and to determine biological mechanisms of action.

*Corresponding author. Tel: 650-736-2246, E-mail: joewu@stanford.edu
Published on behalf of the European Society of Cardiology. All rights reserved. © The Author(s) 2021. For permissions, please email: journals.permissions@oup.com.
Drug discovery is an exciting and rapidly evolving field. The annual SDDS provides a unique opportunity for all stakeholders to come together and engage in discussions and networking. SDDS 2021 showcased just how fast the health field can build upon previous progress to advance the field and develop life-saving vaccines and therapies that improves public or even global health (https://med.stanford.edu/cvi/events/2021-drug-discovery-conference.html). Our Symposium this year further showcased earlier stage companies that are poised to impact the field in coming years, while other companies and venture capitalists shared their visions for the future of drug discovery. We expect that SDDS 2022 will be another valuable opportunity to share and discuss even more advances that are resulting from this fantastic period of advancements and growth in drug discovery.

Data availability statement

No new data were generated or analyzed in support of this research.

References

1. Kines RC, Cerno RJ, Roberts JN, Thompson CD, de Las Pinos E, Lowy DR, Schiller JT. Human papillomavirus capsids preferentially bind and infect tumor cells. Int J Cancer 2016;138:901–911.

2. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, Diemert D, Spector SA, Rouphael N, Creix JM, Khetan S, Segall N, Solomon S, Brosz A, Fierro C, Schwartz H, Neuville C, Corey L, Gilbert P, Janes H, Follmann D, Marovich M, Mascia C, Polansky L, Ledgerwood J, Graham BS, Bennett H, Rabin R, Knightly C, Leary B, Dang W, Zhou H, Han S, Irvinson M, Miller J, Zaks T, COVE Study Group. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med 2021;384:403–416.

3. Polack FP, Thomas SJ, Kitchin N, Abalon J, Curtin A, Lockhart S, Perez JL, Perez-Marc G, Moreira ED, Zerbini C, Bailey R, Swanson KA, Raychaudhury S, Koury K, Li P, Kalina WV, Cooper D, French RW Jr, Hammit LL, Tureci O, Nell H, Schaefer A, Unal S, Tresnan DB, Masther S, Domrutzki PR, Sahn U, Janse KJ, Gruber WC, C4591001 Clinical Trial Group. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med 2020;383:2603–2615.

4. Stephenson KE, Le Gars M, Sadoff J, de Groot AM, Heerwegh D, Tryres C, Ayezi C, Loos C, Chandrashekhar A, McMahan K, Tostanoski LH, Yu J, Gebre MS, Jacob-Dolany C, Li Z, Patel S, Peter L, Liu J, Borduetsch EJ, Nicola D, Souza M, Tan JS, Zahi R, Julig B, Nathavitharan R, Shapiro RL, Aann AA, Alonso CD, Jaggie K, Ansel JL, Kanjilal DG, Guiney CJ, Bradshaw C, Tyler A, Makwana T, Yanosick KE, Seaman MS, Lauffenburger DA, Alter G, straps F, Douougi M, Van Hoof J, Southemaker H, Barouch DH. Immunogenicity of the Ad26.COV2.S vaccine for COVID-19. JAMA 2021;325:1535–1544.

5. Powell AE, Zhang K, Sanyal M, Tong S, Weidenbacher PA, Li S, Pham TD, Pak KE, Chiu W, Kim P. A single immunization with spike-functionalized ferritin vaccines elicits neutralizing antibody responses against SARS-CoV-2 in mice. ACS Cent Sci 2021;7:183–199.

6. Weinreich DM, Sivaplasangam S, Norton T, Ali A, Gao H, Bhore R, Musser BJ, Sso Y, Rofail D, Im J, Perry C, Panc C, Hosain R, Mahmood A, Davis JD, Turner KC, Hooper AT, Hamilton JD, Baum A, Kyratsos CA, Kim Y, Cook A, Kampman W, Kohli A, Satcheva Y, Graber X, Kowal B, DiCicco T, Stall N, Lipsch L, Brausen N, Herman G, Yanacopoulos GD, Trial Investigators. REGN-COVID, a neutralizing antibody cocktail, in outpatients with Covid-19. N Engl J Med 2021;384:403–416.

7. Bugn K, Woodcock J. Trends in COVID-19 therapeutic clinical trials. Nat Rev Drug Discov 2021;20:254–255.

Authors

Biography: Dr Amanda J. Chase, PhD, is an Associate Director of Strategic Research Development for the Stanford Cardiovascular Institute (CVI). Prior to Stanford, she received her PhD in virology from the University of California, Irvine, completed her postdoctoral fellowship in cell biology and virology at the University Hospital Heidelberg, Germany, and was a Scientific Communications Manager at the European Molecular Biology Laboratory in Heidelberg, Germany.

Biography: Dr Sanjay V. Malhotra, PhD, is a Professor and Endowed Chair in Cancer Research, and Director, Center for Experimental Therapeutics at the Knight Cancer Institute, OHSU. Previously, he was a faculty in the departments of Radiation Oncology (Cancer and Radiation Biology), Radiology (Molecular Imaging Program), and Medicine at the Stanford University School of Medicine. He also served as Director, Stanford-SRI Drug Discovery & Development Program, Stanford Cancer Institute. Before Stanford, he was a Principal Investigator & Head of the ‘Small Molecule Drug Discovery Laboratory’ at the Frederick National Laboratory of Cancer Research (FNLCR), NIH, and served as the Director, Chemical Diversity Division of the Chemical Biology Consortium/NCI. He has over 20 years of experience in basic and translational research. His work is focused on the design/discovery/development of synthetic and natural product inspired small molecules as probes to understand biological phenomena, and translational research in drug discovery, development, imaging, and radiation. Dr Malhotra’s work has led to the preclinical and clinical advancement of several molecules. He has edited five books and authored >150 research articles. He is a Fulbright Specialist and Fellow of the Royal Society of Chemistry, UK.
Biography: Dr Mark Mercola, PhD, is a Professor of Cardiovascular Medicine at Stanford University and a member of the Stanford Cardiovascular Institute. Prior to Stanford, he was a Professor of Bioengineering at the University of California, San Diego and jointly at the Sanford-Burnham-Prebys Medical Discovery Institute where he co-founded the Prebys Center for Drug Discovery, which is one of the largest academic drug discovery and development centres. Previously, he was an Associate and Assistant Professor at Harvard Medical School where he also did postdoctoral training. He laid the groundwork for the efficient production of heart cells from pluripotent stem cells and has done foundational work on the creation of induced pluripotent stem cell models of heart disease and their use in therapeutic target discovery and development. His research is funded by the National Institutes of Health, the California Institute for Regenerative Medicine, the PLN Foundation, and the Fondation Leducq.

Biography: Dr Kuldev Singh, MD, is a Professor of Ophthalmology and Director of the Glaucoma Service. Dr Singh joined Stanford faculty after he was a Dana Foundation Fellow at the Wilmer Eye Institute, Johns Hopkins Hospital and completed residency training at the Casey Eye Institute and a Heed Foundation Fellowship at the Bascom Palmer Eye Institute. He has published over 200 original peer-reviewed articles, delivered over 350 invited lectures including over 70 named or keynote lectures, edited 3 textbooks, and served on the editorial board of 11 ophthalmic publications. Dr Singh is an investigator in the National Institutes of Health-funded NEI Glaucoma Human Genetics Collaboration and is funded by the FDA to study patient-related outcomes with minimally invasive glaucoma surgery. His clinical practice focuses on the medical, laser, and surgical management of glaucoma and cataract.

Biography: Dr Joseph C. Wu, MD, PhD, is a Director of the Stanford Cardiovascular Institute (CVI) and the Simon H. Stertzer, MD, Professor of Medicine and Radiology. His lab works on cardiovascular genomics and induced pluripotent stem cells. The main goals are to (i) understand basic disease mechanisms, (ii) accelerate drug discovery and screening, (iii) develop ‘clinical trial in a dish’ concept, and (iv) implement precision medicine for patients. Dr Wu has published >400 manuscripts with H-index of 108 on Google scholar. He is listed as top 1% of highly cited researchers by Web of Science (2018, 2019, and 2020). He serves on the FDA Cellular, Tissue, and Gene Therapies Advisory Committee. Dr Wu is an elected member of Association of University Cardiologists (AUC), American Institute for Medical and Biological Engineering (AIMBE), American Association for the Advancement of Science (AAAS), American Association of Physicians (AAP), and National Academy of Medicine (NAM).