ISSUE
05
DECEMBER
2021

VANDA
A SINERGY NEWSLETTER

At a Glance

7
Academic and Research Institutes

22
Industry Partners

28
Collaborative Projects

Director's Message

Dear Colleagues,

2021 is reaching its end, and SINERGY is preparing for 2022. As restrictions are being lifted worldwide, we hope that we can resume physical interactions and organize face to face events soon. Nevertheless, we are ready to adapt to any eventualities and bring the community together no matter the circumstances. We would very much like to hear your suggestions for upcoming events or initiatives, please contact our friendly SINERGY team.

Currently, we are evaluating the Seed Grant applications for our 3rd funding round. Our next Seed Grant funding round will be in March 2022 (submission deadline **31 March 2022**).

In this issue, we are happy to introduce you to **Meng How Tan**, Associate Professor, School of Chemical and Biomedical Engineering at the Nanyang Technological University. Learn more about Meng How's research and Synthetic Biology vision on P.2. Our featured industry partner is **Engine Biosciences,** a start-up company that uses CRISPR and machine learning to design and developed targeted therapies. Learn more about Engine Biosciences on P.3

I would also like to introduce our new SINERGY partners. **Hoow Foods** is a local food company that uses its expertise in pharmaceutical and food sciences to create healthy foods that don't compromise in taste. **Sophie's Bionutrients** is a local start-up active in the alternative protein space that uses algae to create dairy alternatives. **CauseAlgae** is a student-led start-up aiming to use microalgae for carbon sequestration applications. **Officinae Bio** is an Italian company active in high-throughput, integrated biodesign and biomanufacturing. A warm welcome to all!

ESCO ASTER · CauseAlgae · SOPHIE'S BIONUTRIENTS · HOOW FOODS Making healthy food delicious again · OFFICINAE BIO

Sinergy
Singapore Consortium for Synthetic Biology

Matthew Chang
Sinergy Director

Researcher Spotlight

Meng How Tan: Editing DNA and RNA in living cells

Meng How Tan is currently an Associate Professor in the School of Chemical and Biomedical Engineering, Nanyang Technological University (NTU). Prior to setting up his laboratory in Singapore, he received a B.Sc. degree in mechanical engineering and a B.A. degree in economics from University of California, Berkeley, a M.Sc. degree in aeronautics from California Institute of Technology, a M.Sc. degree in biomedical engineering from NTU, and a Ph.D. in developmental biology from Stanford University. We asked Meng How Tan to tell us about his research, his views on synthetic biology in Singapore, and his collaboration with Engine Biosciences, our featured industry partner for this Vanda issue.

Biological information, hardwired in the genome of a living cell, can be altered. If the changes are introduced into DNA, they are permanent and will be passed on to subsequent generations of daughter cells. If the changes are introduced into RNA, they are transient and can allow dynamic responses to external stimuli or environmental cues. We are interested in understanding how DNA and RNA in living cells can be edited.

The ability to modify selected information stored in cellular DNA holds tremendous potential for myriad applications. On the basic science front, it will enable us to generate more accurate cell or animal models to study various biological processes. On a more translational front, it will enable us to permanently cure well-defined genetic diseases. Beyond therapeutics, we can also engineer next-generation crops or redesign living cells to produce

value-added chemicals, biomaterials, and biologics. We are interested in developing and applying novel genome engineering tools, including those based on CRISPR-Cas systems.

Besides DNA, our laboratory is also interested in understanding how RNA can be selectively modified. In eukaryotic organisms, RNA editing serves as an important post-transcriptional gene regulatory mechanism and can exert profound effects on other cellular processes. We study the functions and regulation of RNA editing in normal development and human diseases, including cancer, neurodegenerative diseases, and immune disorders. Beyond basic science, we are ex-ploring how RNA editing can be programmed. This can be achieved for example by selectively recruiting endogenous RNA deaminases to target sites or by using CRISPR-Cas to tether exoge-nous deaminases at target RNA species. More broadly, we are actively developing novel tools for transcriptome engineering.

Key research achievements:

- One of the fastest chemical-inducible Cas9 enzyme for tight control of genome editing (2016, Nature Chemical Biology)
- First comprehensive atlas of RNA editing in mammals (2017, Nature)
- First systematic study of multiple Cas enzymes for genome editing (2018, Genome Biology)
- Comprehensive genetic toolkit for engineering Acetobacteraceae, an emerging class of host chassis (2019, ACS Synthetic Biology)
- Rapid CRISPR diagnostic assay for COVID-19 that is sensitive and robust to viral mutations (2021, Nature Communications)

Where do you see Singapore's biggest strength in synthetic biology?

One area that Singapore has focused on is the engineering of microbes for bioproduction of chemical compounds, small molecules, etc. Some notable successes have been achieved so far, such as the production of carotenoids and fragrance molecules. This area will continue to be important in the coming years as we transform ourselves into a green economy.

Another area that will have big impact is the development of new platform technologies and engineering tools. This is because they cut across multiple application areas and can be adapted to work in various host chassis.

Yet another area that is not really "synthetic biology" per se but will have big impact is biodiversity. Nature has had millions of years to evolve all sorts of cool enzymes and pathways. Fortunately for us, the rapid development of high throughput sequencing technologies in the 21st century is nowallowing us to probe more deeply into what Nature has to offer.

Can you tell us about the collaboration with Engine Bioscience?

Genome-wide screening is a powerful methodology to uncover new biology and drug targets etc. For example, we may be interested in understanding which metabolic genes play important roles in the synthesis of certain compounds-of-interest. However, traditional screening methods are based on single-gene knockdowns or knockouts. In our collaboration with Engine Bioscience, we wish to explore new screening modalities that will allow us to discover richer information. We hope to achieve some successful proofs-of-concept at the end of the collaboration.

Featured Industry Partner

Engine Biosciences: Deciphering Biological Complexity to Unleash Many Impactful Medicines

Contributed by Engine Biosciences

Engine Biosciences was founded out of MIT, Harvard, Mayo Clinic, and UCSD by leading synthetic biology, computational biology, and genome engineering pioneers with a mission todecipher complex disease biology and unleash new therapeutics. Engine's approach focuses on mapping and mining gene networks using its integrative machine learning and combinatorial CRISPR screening experimental platforms for compelling targets and biomarkers, then designing and developing new targeted therapies with internal chemistry and drug discovery expertise. Engine has built a team of over 40 people across its sites in Singapore and the SF Bay Area, comprising industry drug discovery veterans, biologists, computational scientists, chemists, engineers, and business leaders.

When asked about the advantages of having a company present both in Singapore and in the US, Jeffrey Lu, CEO & Co-Founder of Engine, notes that *"Singapore has world-class scientists and researchers, a closely-knit and accessible scientific and clinical network, strategic support for the biotech sector from the government with a compelling long-term vision, offers differentiated clinical data relevant to Asian populations, and is truly an international business hub. Meanwhile, the US continues to be the epicenter of biotech and drug discovery innovation (both industry and academic), as well as being the largest commercial market for new therapeutics".*

Engine's discovery platform, **NetMAPPR**, is driving new discoveries, drug development pipeline programs, and collaborations in multiple diseases including cancer, neurodegeneration, and dermatology. With its internal functional genomics platform generating proprietary experimental data, access to clinical data across Asia and USA, and AI-powered data mining and curation, Engine has amassed unique databases to power novel R&D. Engine is currently advancing its growing pipeline of novel precision cancer medicines towards the clinic, which include programs treating genetically defined patient populations in liver, ovarian, colorectal cancers, among others.

Since 2018, Engine has raised over US$53 million in Seed and Series A financing from renowned VCs, strategic investors, and private equity investors across US, Singapore, and North Asia, including Polaris Partners, 6 Dimensions Capital, Invus, EDBI, WuXi AppTec, DHVC, and others. *"It's critical to think about the execution plan for your vision and importantly, the team that is needed to make it happen",* Lu advises prospective bioentrepreneurs. *"Attaining success in a biotech company requires executing on many distinct areas that require specific expertise and networks, and no single person has either the capabilities or the bandwidth to do it all".*

The Engine Biosciences Singapore team. Photo by Engine Biosciences

During this time, Engine has worked closely with many leading companies, academic institutions and clinical centers, including but not limited to a US Fortune 500 company, MIT, A*STAR, NTU, National Cancer Centre Singapore, and others. Engine Biosciences has been awarded a SINERGY Seed Grant in 2021, together with Associate Prof Meng How Tan. *"We have been impressed by Singapore's vision and commitments to becoming an influential global leader in the synthetic biology field. Engineering biology is re-defining the world in so many ways, but this will take time, talent, risk-taking, and capital over a long period to truly realize the game-changing opportunities that are increasingly evident. We are seeing more innovators building platforms and capabilities and conducting R&D for exciting products across sectors",* Lu said.

SINERGY Seed Grant Calling for Submissions

SINERGY provides a one-year S $50,000 seed grant for selected academic-industry collaboration research projects. The grant call is open throughout the year with submission deadlines on 31 March and 31 October respectively. Interested PIs and companies can find details at sinergy. **sg/#grant** and submit to **sinergy@nus.edu.sg**

SINERGY Memberships

As a SINERGY member, an industry partner is entitled to apply for NRF grants, access select lab facilities at members' rate, and has other benefitssuch as marketing and licensing opportunities, advice and consultancy from topnotch scientists, among others.

For inquiries, please contact **sinergy@nus. edu.sg**

"Promotion (Olink Proteomics): "

Olink®
Accelerating proteomics together

Promotion (Genscript Asia Pacific):

GenScript
Make Research Easy

30% off for gRNA library construction service until 31st Dec 2021

Pooled CRISPR guide RNA libraries, or gRNA libraries, are ideal for high-throughput screening of important molecular targets. These libraries leverage the efficiency and specificity of the CRISPR gene editing technology to either knock-out gene expression or transcriptionally activate genes in the genome.
GenScript offers a variety of Broad Institute pre-validated gRNA library options, including GeCKO libraries for genome-wide knockout of human and mouse genes, and CRISPR Synergistic Activating Mediator (SAM) libraries for transcriptional activation of every gene in the human and mouse genome.
We also offers fully customized gRNA libraries, with complete coverage and uniform distribution, for CRISPR knockout, CRISPRa, and CRISPRi.

Recruitment (Genscript Asia Pacific):

Genscript Asia Pacific is looking for:

1. Sales Manager (IVD portfolio), APAC
2. Market Intelligence Manager, APAC

Write in to ap.marketing@genscript.com for more information.

The **Singapore Biofoundry @ NUS**

SynCTI Sinergy BioFoundry Singapore

The **Singapore BioFoundry @ NUS** is a state - of - the - art facility that enables the Engineering of Biology at Scale