2020/2021

NATIONAL TSING HUA UNIVERSITY

R&D REPORT

National Tsing Hua University

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About NTHU

National Tsing Hua University (NTHU) has a long and proud history. First established as the Tsing Hua Academy at Tsing Hua Garden in Beijing in 1911, the Academy was renamed as National Tsing Hua University in 1928 as its curricula expanded to that of comprehensive university.

In 1956, NTHU was reinstalled on its current campus in Hsinchu, Taiwan. Since its reinstallation, NTHU has developed from an institute focusing on nuclear science and technology to that of a comprehensive research university offering degree programs ranging from baccalaureate to doctorate in science, technology, engineering, humanities and social sciences as well as management.

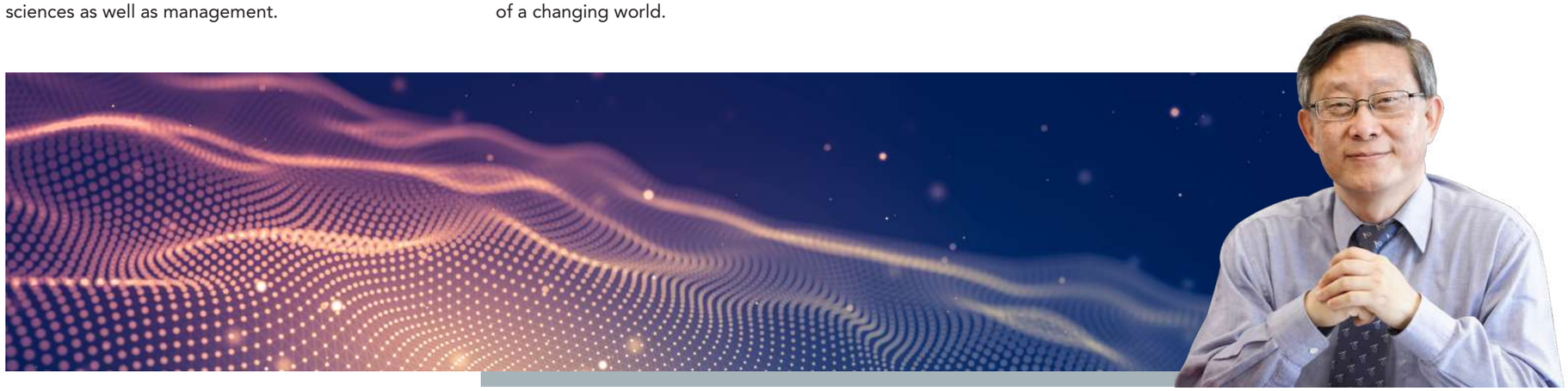
NTHU has been consistently ranked as one of the premier universities in Taiwan and is widely recognized as the best incubator for future leaders in industries as well as academics. Such stellar records are particularly exemplified by the outstanding achievements of our alumni, including two Nobel laureates in physics Drs. Cheng-Ning Yang and Tsung-Dao Lee, one Nobel laureate in chemistry Dr. Yuan-Tseh Lee and one Wolf Prize winner in mathematics Dr. Shiing-Shen Chern. On the first of November 2016, NTHU formally incorporated the National Hsinchu University of Education. This merger further diversifies and expands its curricula include arts and education to better prepare our students to take on the challenge of a changing world.

Message from the President

National Tsing Hua University (NTHU) is a research university with a long and proud tradition. Since the reestablishment in Hsinchu in 1956, NTHU has been known for excellent academic programs, stellar research output as well as outstanding alumni.

NTHU provides a stimulating and nurturing enviroment within which our faculty can offer quality teaching and conduct innovative research. Regarded as one of the toptier research universities, our research activities emphasize fundamental discoveries at the forefronts of basic sciences and exploration of breakthrough technologies with a high potential for applications. These are reflected in our publications in the world's preeminent journals, international patents received, and technology transfered. In the 2020-2021 R&D annual report, we highlight several important breakthroughts in five fields and also provide the facts and figures related to other important R&D activities. This volume is undoubtedly too limited to give the full scope of R&D at NTHU but a glimpse into our recent achievements. Hopefully, this can serve as a catalyst for further interactions, exchange of ideas, and establishment of collaborations.

Built on our proud heritage, NTHU will continue to promote excellent teaching and innovative research with the goal of achieving important scientific discoveries and innovative technologies. I hope that you will find this R&D annual report informative and will give us your precious opinions and suggestions.



Dr. Hong Hocheng
President

National Tsing Hua University
Hsinchu, Taiwan
November 2021

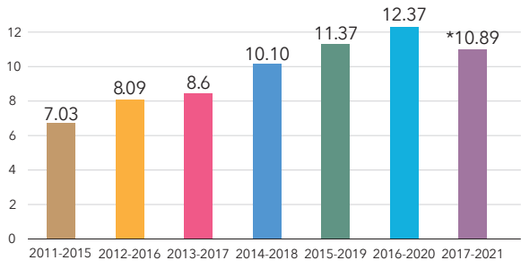
R&D Facts and Figures

2021 QS World University Rankings by Subject

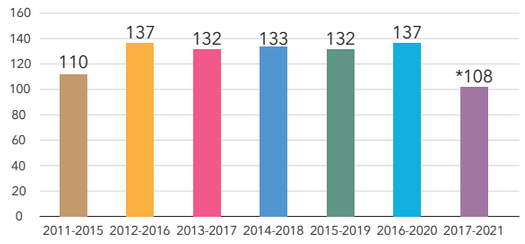
Top 50-100

Materials Science - 58
Engineering and Technology - 88
Chemical Engineering - 94
Electrical & Electronic Engineering - 100
Linguistics - 82
Mechanical - 89
Chemistry - 96

Citations Per Paper



Highly Cited Papers



* Last updated November 11, 2021
Data covers over a 10-year and 8-month period: January 1, 2011-August 30, 2021

2020 Highly Cited Researchers:

Professor. Yi-Hsien Lee (Department of Materials Science)
Professor. Horng-Tay Jeng (Department of Physics)

2020 NTHU Rankings:

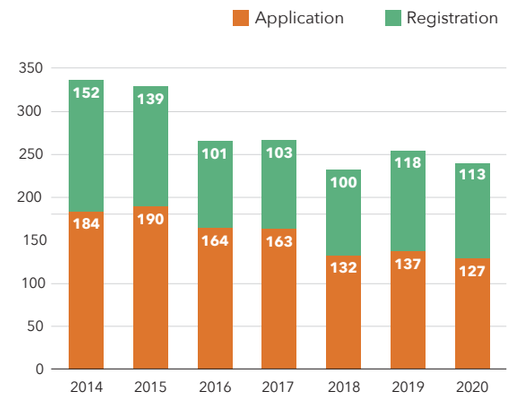
Rankings	Rank
THE Emerging Economies University Rankings	29
QS Asia University Rankings	32
THE Asia University Rankings	46
THE World Reputation Rankings	151-175

2020 Ranking of Top U.S. patent

Taiwan Ranking NO.1
2014 - 2020

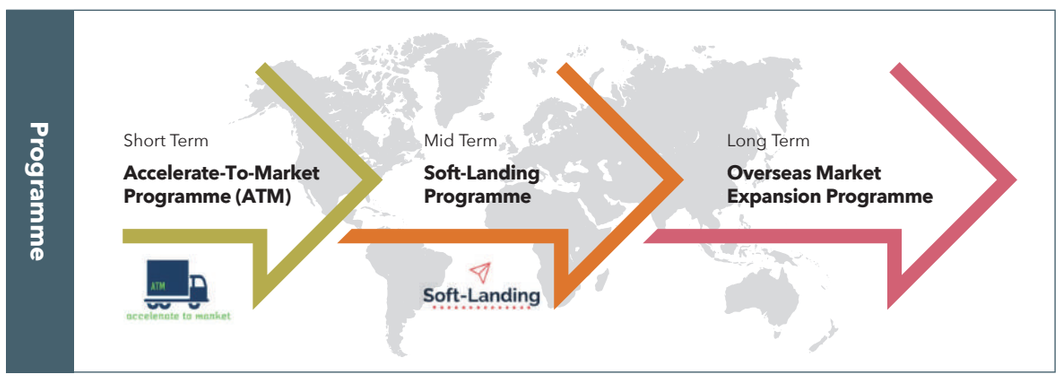
2014	2015	2016	2017	2018	2019	2020
World Ranking						
11	15	25	23	24	31	38
Taiwan Ranking						
No.1						

International Patent Application and Registration (2014-2020)



Incubation Programme *Grow fast, Grow global*

Number of Startups in 2021	Accumulative Startups	Survival Rate in 3 Years	Faculties & Students ratio	Number of IPO
56	since 2000 231	91.7%	33.9%	8



Natural Science

Professor Vladimir Manucharyan (University of Maryland) & Professor Yen-Hsiang Lin
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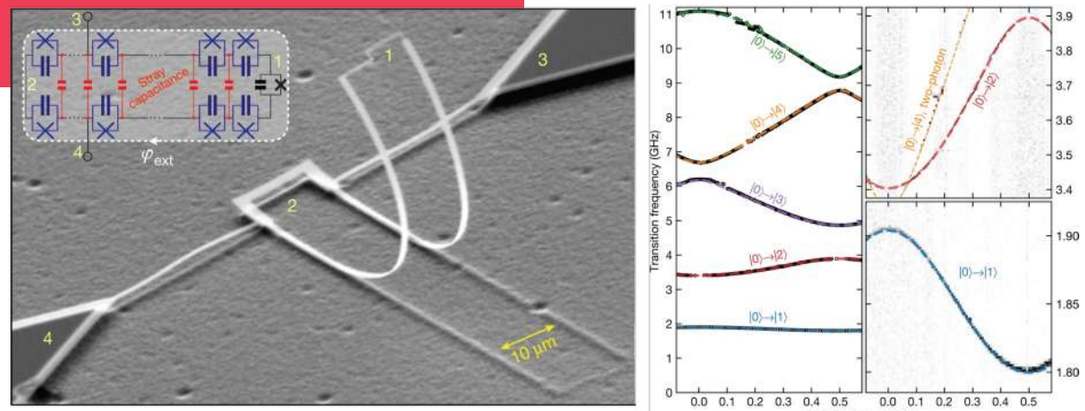
A new type of superconducting qubit: blochnium



(Left)Scanning electron micrographs of a fabricated Blochnium superconducting qubit released from the substrate to reduce the stray capacitance. The released Josephson chain curls upwards and elevates the small junction by a few tens of micrometers above the substrate. The inset shows a circuit model of the device in the form of a superconducting loop interrupted by a small-area junction (black) and the larger-area chain junctions (dark blue). The stray capacitances are marked in red. (Middle) Transition frequencies (black markers) extracted from the two-tone spectroscopy data as a function of the external flux through the loop, and the fit (dashed lines) to the spectrum. (Right) Raw data zoom-in on the |0> → |2> and the two-photon |0> → |4> transitions (top) and the qubit transition |0> → |1> (bottom). The experimental error is much smaller than the marker size. Note that the modulation of the qubit flux is only about 100 MHz.

Superconducting qubits has been attracted lots of attention for developing new quantum technology in recent years. The non-dissipative nonlinearity of Josephson junctions converts macroscopic superconducting circuits into artificial atoms, enabling some of the best-controlled qubits today. Three fundamental types of superconducting qubit are known, each reflecting a distinct behavior of quantum fluctuations in a Cooper pair condensate: single-charge tunnelling (charge qubit), single-flux tunnelling (flux qubit) and phase oscillations (phase qubit or transmon). Yet, the dual nature of charge and flux suggests that circuit atoms must come in pairs.

Here we introduce the missing superconducting qubit, "blochnium", which exploits a coherent insulating response of a single Josephson junction that emerges from the extension of phase fluctuations beyond 2π. Evidence for such an effect has been found in out-of-equilibrium direct-current transport through junctions connected to high-impedance leads, although a full consensus on the existence of extended phase fluctuations is so far absent. We shunt a weak junction with an extremely high inductance—the key technological innovation in our experiment—and measure the radiofrequency excitation spectrum as a function of external magnetic flux through the resulting loop.

Research team of Prof. Vladimir Mancharyan (middle, sixth from left). The other contributed authors are Dr. Ivan V. Pechenezhskiy(third from left), Raymond Mencia (fifth from right), Dr. Long Nguyen(second from right), and Prof. Yen-Hsiang Lin (fifth from left).

The insulating character of the junction is manifested by the vanishing flux sensitivity of the qubit transition between the ground state and the first excited state, which recovers rapidly for transitions to higher-energy states. The spectrum agrees with a duality mapping of blochnium onto a transmon, which replaces the external flux by the offset charge and introduces a new collective quasicharge variable instead of the superconducting phase. Our findings may motivate the exploration of macroscopic quantum dynamics in ultrahigh-impedance circuits, with potential applications in quantum computing and metrology.

US National Science Foundation PFC at JQI research grants.

Research Highlights

- Alfred P. Sloan Foundation research grants
- ARO-LPS HiPS programme research grants.

Research Output

- Ivan V. Pechenezhskiy, Raymond A. Mencia, Long B. Nguyen, Yen-Hsiang Lin & Vladimir E. Manucharyan, "The superconducting quasicharge qubit", Nature 585, 368–371 (2020)
- "Long B. Nguyen, Yen-Hsiang Lin, Aaron Somoroff, Raymond Mencia, Nick Grabon, Vladimir Manucharyan, The high-coherence fluxonium qubit", Phys. Rev. X 9, 041041(2019)
- Yen-Hsiang Lin, Long B. Nguyen, Nick Grabon, Jon San Migue, Vladimir Manucharyan, "Demonstration of protection of a superconducting qubit from energy decay" Phys. Rev Lett. 120, 150503(2018)

Discovery of a cosmic neutrino from a star-destroying black hole

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Since 2016, National Tsing Hua University has joined the Zwicky Transient Facility (ZTF) as the founding members under the support of the Ministry of Science and Technology. ZTF is a 1.2m robotic telescope with a very wide-field camera (currently the world's largest camera in use) owned by Caltech. This is a very significant improvement over all other similar facilities and ZTF has been playing a key role in optical follow-up of gravitational wave events and transients in general. In addition to the famous gravitational wave event, the double neutron star merger GW170817/GRB170817A for which ZTF makes significant contribution.ZTF also follows up other cosmic transients.

In 2019, ZTF discovered a tidal disruption event which is a rare transient event when a star passes close to a supermassive black hole. This event is from a galaxy 700 million light years away from us and the central black hole is as massive as 30 million suns. About 6 months later, an extremely energetic neutrino event found by the IceCube neutrino detector in Antarctica was associated with this tidal disruption event. This is the first ever neutrino discovered from a tidal disruption event, and is also the second cosmic neutrino event coming outside the local group of galaxies. The detection of the first neutrino linked to a tidal disruption event points to the existence of a central, powerful engine near the accretion disk, spewing out fast particles. By analysing the X-ray follow-up data, the NTHU team found that the X-ray emission decays rapidly indicating that the accretion disk cools swiftly, or the X-rays are absorbed by surrounding materials. Sufficient X-ray photons have to be accumulated at specific regions around the central black hole in order to interact with particles for producing high-energy neutrinos. Therefore, a delay for the neutrino detection is expected. This confirms that a tidal disruption event can be a powerful cosmic particle accelerator and a new multi-messenger observing window is opened.

An artist concept picture of a tidally disrupted star surrounding a supermassive black hole. The stellar remnants are orbiting around the black hole in the form of an accretion disk. A jet-like structure is also seen above the black hole. Image credit: DESY, Science Communications Lab.

Professor Albert Kong

Research Highlights

- First ever discovery of a high-energy neutrino from a tidal disruption event
- NTHU as a partner of the Zwicky Transient Facility collaboration to search for cosmic transients

Research Output

- Stein, R. et al. (including A.K.H. Kong), "A tidal disruption event coincident with a high-energy neutrino", Nature Astronomy, 5, 510-518 (2021)

> *Leading Taiwan to participate the first gravitational wave observation with the underground gravitational wave detector KAGRA in Japan*

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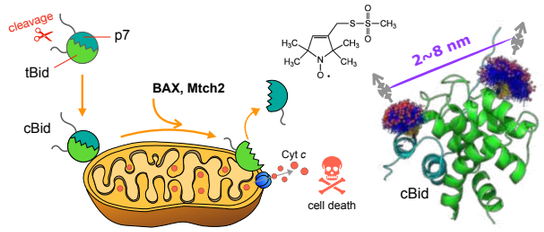
Electron Spin Resonance Reveals the Stepwise Apoptotic Activation on Mitochondrial Membranes

Bid protein cleavage by Caspase-8 represents a lethal event in the mitochondria-mediated apoptosis. Cleaved Bid (cBid) subsequently associates with BAX protein and membranes, leading to mitochondria outer membrane permeabilization (MOMP) and cell death. However, it remains largely unclear by what mechanism cBid interacts with BAX on mitochondrial membrane to bring about MOMP. The current structural models of Bid are established primarily based on the results of model membranes. The conformational changes in cBid during the association with real mitochondrial membranes have not been sufficiently characterized. Without the use of real mitochondria, the possible contributions of other factors that affect the regulation of Bid could be overlooked.

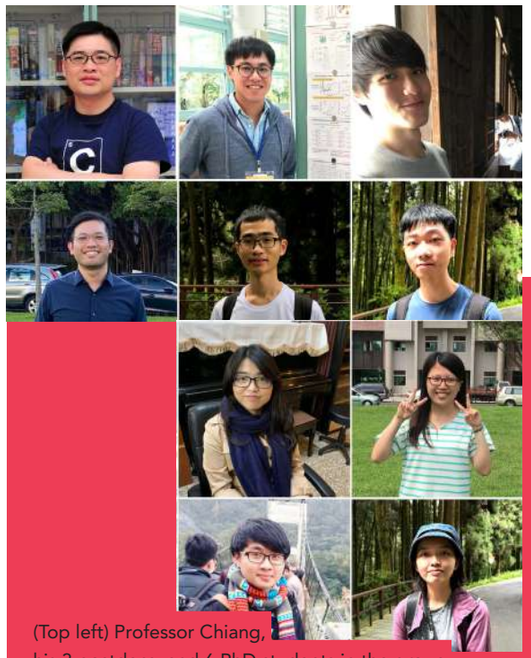
The team led by Prof. Yun-Wei Chiang at NTHU has recently made a breakthrough in identifying the conformational changes of cBid that occur during the process of cBid-induced BAX oligomerization and MOMP, using techniques including spin-label electron spin resonance (ESR) and PEGylation-based gel shift assay. The double electron-electron resonance (DEER) ESR technique is a powerful tool for determining protein structure and topology in a complex membrane environment. The DEER data provide interspin distance distributions in the range of 2–8 nm and the distance constraints that can be used to determine assembly and individual structures of protein subunits in a complex membrane environment. The team performed DEER to identify the conformational changes in cBid and explore the interactions of Bid with the mitochondrial carrier homolog 2 (Mtch2), a key protein known to play a role in facilitating the recruitment of tBid to mitochondria.



Stepwise activation of the pro-apoptotic Bid protein at mitochondrial membrane is revealed using electron spin resonance spectroscopy.

Various single-/double-/triple-cysteine variants of Bid were prepared for spin-label ESR as well as PEGylation studies. Triply spin-labeled samples were used to study the structural integrity of cBid during the cBid-induced BAX activation. Doubly spin-labeled cBid samples can be further divided into two groups: p7/tBid- breakup and intra-tBid groups; samples of the former allow one to explore when the breakup of cBid (i.e., p7/tBid) occur, and samples of the latter were used to identify the conformational changes in the tBid fragment at the mitochondrial membranes. New insights into the details of cBid-induced BAX activation at real mitochondrial membranes were thus revealed in this study.

In summary, the Chiang group reveals molecular details of the Bid activation at real mitochondrial membranes in a stepwise manner. The association of cBid with membranes and Mtch2 initiates structural rearrangements that unmask the BH3 domain, priming it for engagement with BAX to induce BAX-mediated MOMP. It is the interactions among cBid, BAX, and Mtch2 at mitochondrial membranes that further trigger the fragmentation of cBid and drive the conformation of tBid from a compact ensemble to an ensemble of highly extended conformations. However, the activated tBid fragments do not assemble into an aggregate in mitochondrial membranes. This study provides a better understanding of the cBid-induced BAX activation, and the refined model might lead to an effective treatment that can specifically target different functional states of Bid to suppress the cBid-induced BAX activation.



(Top left) Professor Chiang, his 3 postdocs, and 6 PhD students in the group.

> *"The study answers a long-standing question about how Bid triggers the BAX-mediated apoptosis on mitochondrial membranes, providing key information for the development of more efficient molecules to regulate apoptosis."*

Research Highlights

- Ta-You Wu Memorial Award Research Grant" by Ministry of Science and Technology (MOST), 2019-2022
- Outstanding Young Scholar Research Grant" by MOST, 2013-2019

Research Output

- C.L. Hung, H.H. Chang, S.W. Lee, Y.W. Chiang*, Stepwise activation of the pro-apoptotic protein Bid at mitochondrial membranes, Cell Death & Differentiation, 28 (2021) 1910-1925.
- C.C. Li, T.Y. Kao, C.C. Cheng, Y.W. Chiang*, Structure and regulation of the BsYetJ calcium channel in lipid nanodiscs, Proceedings of the National Academy of Sciences (PNAS), 117 (2020) 30126-30134.
- Y.J. Lan, P.S. Yeh, T.Y. Kao, Y.C. Lo, S.C. Sue, Y.W. Chen, D.W. Hwang*, Y.W. Chiang*, Anti-apoptotic BCL-2 regulation by changes in dynamics of its long unstructured loop, Communications Biology, 3 (2020) 668.
- R.F. Tsai, N.C. Lin, T.Y. Kao, Y.H. Kuo, F.C. Lo, W.F. Liaw, Y.W. Chiang*, Nitrosylation of the Diiron Core Mediated by the N Domain of YtfE, Journal of Physical Chemistry Letters, 11 (2020) 8538-8542.
- Y.H. Kuo and Y.W. Chiang*, Slow Dynamics around a Protein and Its Coupling to Solvent, ACS Central Science, 4 (2018) 645-655.

Dinitrosyl Iron Complex [K-18-crown-6-ether][$(NO)_2Fe(^{Me}PyrCO_2)$]: Intermediate for Capture and Reduction of Carbon Dioxide

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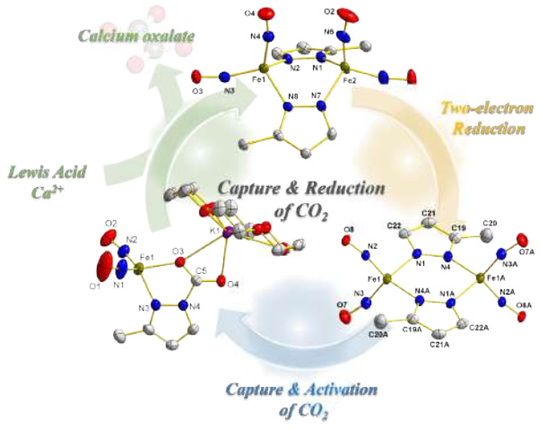
Professors Wen-Feng Liaw
wfliaw@mx.nthu.edu.tw



Through sequential reaction of $[(NO)_2Fe(\mu\text{-}^{Me}Pyr)_2Fe(NO)_2]^{2-}$ (2, ^{Me}Pyr = 3-methylpyrazolate) with carbon dioxide, $Ca(OTf)_2$, and KC_8, a synthetic cycle, 2 → $[(NO)_2Fe(^{Me}Pyr\text{-}CO_2)]-$ → $[(NO)_2Fe(\mu\text{-}^{Me}Pyr)_2Fe(NO)_2]$ → 2, was established for effective capture and selective reduction of carbon dioxide into calciumoxalate.

Carbon dioxide, the waste from human activity embodying the nature of high thermodynamic stability and chemical inertness, is a kind of greenhouse gases inducing the continued global warming. In addition to reducing the level of carbon dioxide on earth, extensive efforts were made on utilization of carbon dioxide as an inexpensive and potential feedstock of C_1 sources for the regeneration of valuable chemicals and fuel. Based on the bioinorganic study of biological dinitrosyl iron unit $[Fe(NO)_2]$ and bioinspired dinitrosyl iron complexes (DNICs) for 20 years, the research team developed a series of DNICs for translational application to effective capture and selective reduction of carbon dioxide into calcium oxalate. After two-electron reduction of DNIC $[(NO)_2Fe(\mu\text{-}^{Me}Pyr)_2Fe(NO)_2]$ (1, ^{Me}Pyr = 3-methylpyrazolate), nucleophilic activation of carbon dioxide by complex $[(NO)_2Fe(\mu\text{-}^{Me}Pyr)_2Fe(NO)_2]^{2-}$ (2) results in the formation of CO_2-captured complex $[(NO)_2Fe(^{Me}PyrCO_2)]$-(2-CO_2, $^{Me}PyrCO_2$ = 3-methyl-pyrazole-1-carboxylate). In complex 2, nucleophilic pyrazolate ligand, neutral $\{Fe(NO)_2\}^{10}$ unit, and [K-18-crown-6-ether]+ counter cation work in concert to capture and activate carbon dioxide via the assembly of 2-CO_2. Moreover, single-crystal structure, spectroscopic, reactivity, and computational study unravels 2-CO_2 as a unique intermediate for reductive transformation of CO_2 promoted by Ca^{2+}. Relying on one-electron reduction power of $\{Fe(NO)_2\}^{10}$ core in complex 2-CO_2, addition of dicationic Ca^{2+} further initiates the C-C coupling between activated/reduced carbon dioxide and yields precipitated calcium oxalate. Bridging nature of pyrazolate ligand, moreover, promotes the re-assembly of complex 1, which holds the potential to recover complex 2 for continued capture and activation of carbon dioxide at a low reduction potential of -1.18 V (vs. Fc/Fc^+). Consequently, sequential reaction of 2 with carbon dioxide, $Ca(OTf)_2$, and KC8 established a synthetic cycle, 2 → 2-CO_2 → 1 → 2, for selective conversion of carbon dioxide into oxalate. Discovery of carbamate-bound 2-CO_2 as a critical intermediate may open an avenue for development of (photo-/electro-)catalytic processes for capture of carbon dioxide from ambient air/flue gas and for reductive transformation of captured carbon dioxide into value-added chemicals.

Research Highlights

- Graeme-Hanson-AsBIC Early Career Researcher Award, Society of Biological Inorganic Chemistry (Tsai-Te Lu)
- The Academic Award of Ministry of Education (Wen-Feng Liaw)

Research Output

- Yu-Ting Tseng, Wei-Min Ching, Wen-Feng Liaw,* Tsai-Te Lu* "Dinitrosyl Iron Complex [K-18-crown-6-ether][$(NO)_2Fe(^{Me}PyrCO_2)$]: Intermediate for Capture and Reduction of Carbon Dioxide." Angew. Chem. 2020, 59, 11819-11823.
- Tzung-Wen Chiou,* Yen-Ming Tseng, Tsai-Te Lu, Tsu-Chien Weng, Dimosthenes Sokaras, Wei-Chieh Ho, Ting-Shen Kuo, Ling-Yun Jang, Jyh-Fu Lee, Wen-Feng Liaw* "[Ni^{III}(OMe)]-mediated reductive activation of CO_2 affording a Ni(κ^1-OCO) complex." Chem. Sci. 2016, 7, 3640-3644
- DINITROSYL IRON COMPLEX FOR CAPTURE AND REDUCTION OF CARBON DIOXIDE. U.S. Pat. US 63/173723

(from left) Professor Wen-Feng Liaw, Dr. Yu-Ting Tseng, Professor Tsai-Te Lu.

Engineering

Plasmonic topological quasiparticle on the nanometre and femtosecond scales

CMOS-integrated memristive non-volatile computing-in-memory for AI edge processors

Low-power 2D complementary integrated circuits

Interrogation of single-cell cellular compositions using electrorotation

Inkjet-Printed Salt-Encapsulated Quantum Dot Film for UV-Based RGB Color-Converted Micro-Light Emitting Diode Displays

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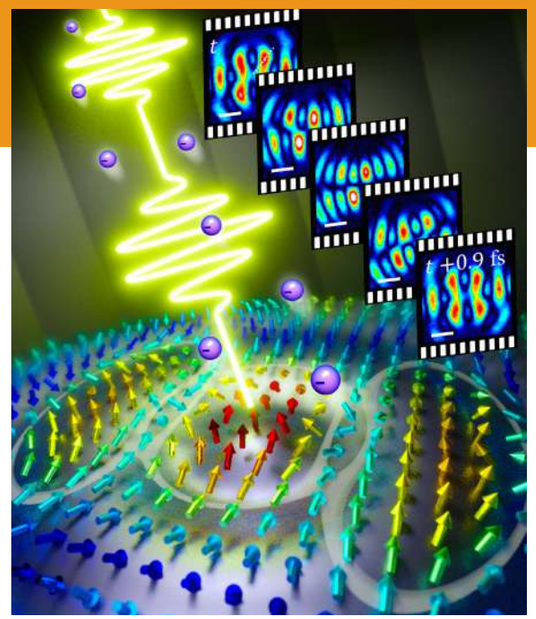
Plasmonic topological quasiparticle on the nanometre and femtosecond scales



An interferometric photoemission electron microscope is used to time-resolve the vectorial surface plasmon vortex fields and reveal the corresponding spin textures.

"Using time-resolved two-photon photoemission electron microscopy (PEEM), we experimentally recorded attosecond videos revealing evanescent vortex creations in a chiral plasmonic device even under linearly-polarized optical excitation. Moreover, the resulting vortex fields generate topological quasiparticles at the metal surface similar to magnetic skyrmions. We discover the stable creation of three plasmonic merons at the vortex core in the nano-femto scale."

At interface of the classical and quantum physics Maxwell's and Schrödinger equations describe how optical fields drive and control electronic phenomena at THz or PHz frequencies and on ultra-small scales to enable nanophotonics. Light field striking a metallic surface triggers electron-wave interactions and coherently transfers its attributes on the attosecond time scale. In this work, we create and image a new spin quasiparticle as the result of light-electron interactions through the use of state-of-the-art ultrafast photoemission electron microscopy. The plasmonic device geometrical phase alone formed a plasmonic topological spin angular momentum texture. The observed spin texture resembles that of magnetic meron quasiparticle, being localized within ½ wavelength of surface plasmon polaritons, and exists on ~20 fs (2×10^{-14} s) time scale of the plasmonic field.

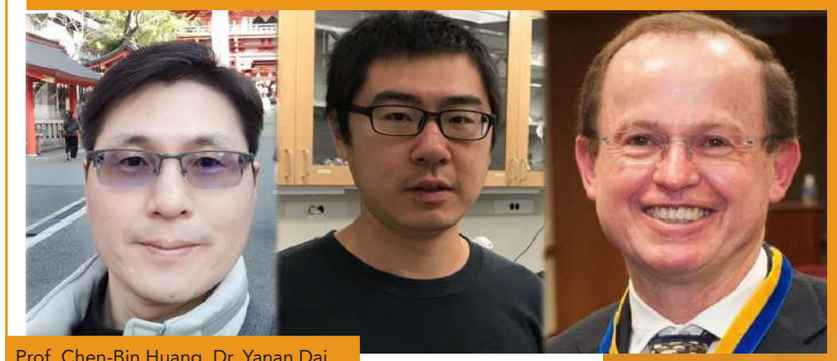
The quasiparticle is created in a nanostructured silver film, which converts coherent linearly polarized laser pulse into an evanescent surface plasmon polariton wave packet with a tailored geometric phase to form a plasmonic vortex. Ultrafast coherent microscopy imaging of electromagnetic waves propagating at the local speed of light of 255 nm/fs, electromagnetic simulations. From these three-dimensional (3D) data we extract the linear polarization L-line singularity distribution with sub-diffraction limited resolution, and thereby define the meron boundaries. We reveal how vectorial optical fields impress topological spin texture arrays that break the time-reversal symmetry. We established an analytic theory in finding a new spin quasiparticle within the vortex core, with topological spin properties of three aggregated merons.

Research Highlights

- First time-resolved experimental observation of pure geometric chirality induced orbital angular momenta
- First discovery of plasmonic spin merons

Research Output

- Y. Dai, Z. Zhou, A. Ghosh, R. S. K. Mong, A. Kubo, C.-B. Huang, and H. Petek, "Plasmonic topological quasiparticle on the nanometre and femtosecond scales," Nature 588, 616-619 (2020).
- Y. Dai, Z. Zhou, A. Ghosh, S. Yang, C.-B. Huang, and H. Petek*, "Ultrafast nanofemto photoemission electron microscopy of vectorial plasmonic fields," MRS Bulletin 46, 738-746 (2021).



Prof. Chen-Bin Huang, Dr. Yanan Dai, Prof. Hrvoje Petek

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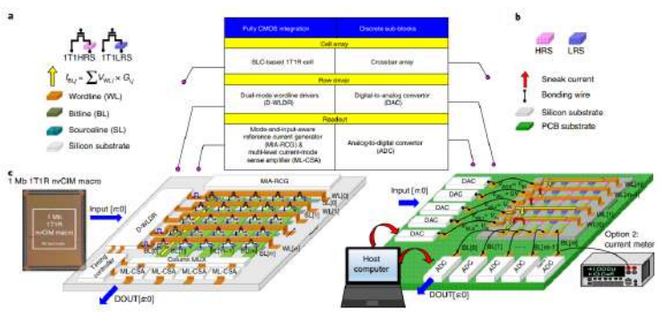
CMOS-integrated memristive non-volatile computing-in-memory for AI edge processors



Features of the CMOS-integrated nvCIM macro. a, Structure of the proposed fully CMOS-integrated nvCIM macro based on the SLC 1T1R resistive memory cell array and on-chip peripheral circuits. b, Previous nvCIM based on crossbar cell arrays and discrete off-chip peripheral circuit components (ADCs and DACs) or high-precision testing equipment. c, Die photo of the fabricated 1 Mb nvCIM chip. The on-chip periphery circuits in the proposed nvCIM macro include D-WLDRs, a timing controller, column multiplexors, write circuits, ML-CSAs and MIA-RCG. The table summarizes the differences between previous works and our fully CMOS-integrated scheme for the key sub-blocks: cell array, row drivers, timing control and readout circuits. Here, $I_{BL,j}$ and $V_{WL,i}$ refer to the bitline (BL) current of the *jth* column and the WL voltage of the *ith* row, respectively. $G_{i,j}$ is the conductance of the cell in the *ith* row and *jth* column. HRS, high-resistance-state; LRS, low-resistance-state.

Artificial intelligence (AI) processors for edge platforms based on conventional von Neumann architecture face challenges in terms of energy efficiency and computing latency due to the large volume of intermediate data and the massive movement of data between the various levels of the memory-hierarchy and process elements. Non-volatile computing-in-memory (nvCIM) was developed to overcome the memory wall encountered in the von Neumann architecture. This can (1) avoid the long latency in the movement of data across multilayer memory hierarchies through the on-chip storage of most or all of the data and/or weights; (2) reduce the amount of intermediate data generated in multiply-and-accumulate (MAC) operations; (3) shorten the latency of multiple logic or MAC operations by executing parallel operations within a single CIM-cycle.

Our fully integrated ReRAM-nvCIM macro, including a 1T1R ReRAM (memristor) cell array, digital dual-mode wordline (WL) drivers (D-WLDRs), small-offset multi-level current-mode sense amplifiers (ML-CSAs), a mode-and-input-aware reference current generator (MIA-RCG) and a system using split binary input ternary weights (SBITWs).

We used three-terminal 1T1R single-level cell (SLC) memristive devices to overcome the disadvantages of conventional crossbar arrays that use two-terminal memristor cells. First, the 1T1R array structure uses a standard-voltage NMOS transistor as the selector to eliminate the row-to-column current and sneak current, which could degrade the signal margin and limit the size of the crossbar cell array. Second, compared with multi-level cell (MLC) or analog cells, SLC cells have a larger readout margin and longer data-retention time for CIM operations to tolerant process variation, resistance drift effects and read weak-disturb effects.

Unlike in a crossbar cell array, the 1T1R cell array does not involve the flow of current from an activated row (that is, the SL) to all of its connected columns (that is, the BL). Thus, it is possible to use a small-area digital buffer as a row driver, rather than using a DAC to provide stable analog voltage against large current load in crossbar arrays. The DAC in a crossbar array imposes a large area and power consumption as well as long latency. In this work, we used D-WLDRs to control the gates of the NMOS transistors of 1T1R cells sharing the same row. The D-WLDR activates only one WL in memory mode and multiple WLs in CIM mode for logic or MAC operations. As mentioned above, the lack of current load (as in a crossbar structure) makes it possible to fit a small area D-WLDR into the small cell-height pinch of each 1T1R cell to improve the macro area efficiency and lessen the mismatch in parasitic load between rows.
MIA-RCG is meant to generate mode-dependent reference currents to enlarge the BL signal margin across computing states for both logic and MAC operation modes. Mismatch between CMOS devices due to process variation can result in sense amplifier (SA) offset, which limits the minimum sense signal that can be correctly detected. The small-offset ML-CSA was developed to tolerate a small sensing margin with small area, low power consumption and short latency for readout operations. The combination of MIA-RCG and ML-CSA allows the integration of many more parallel readout operations on the same macro, while providing readout speeds faster than those in previous works.

Two ReRAM sub-arrays (nvCIM-P and nvCIM-N) are used to store positive (P) and negative (N) weights separately. Each subarray then computes the partial MAC value (MACV) separately for the employed binary-input ternary-weight (SBITW) model. The PE subsequently combines the partial MACV of the nvCIM-P (MACV-P) and nvCIM-N (MACV-N) to generate the final MACV for DNN operations.

The results reveal a trade-off between inference accuracy and energy efficiency associated with the precision of the readout circuit. This could be used as a design guideline in optimizing the performance and power of inference systems for different applications. Furthermore, this system-level test verified the high accuracy and high energy efficiency that can be achieved using a fully CMOS-integrated ReRAM nvCIM macro.

(from left) Professor Ren-Shuo Liu, Professor Meng-Fan Chang, Professor Kea-Tiong Tang, Professor Chih-Cheng Hsieh, Professor Chung-Chuan Lo

Research Highlights

- Nature Electronics volume 2, pages420–428 (2019)

Low-power 2D complementary integrated circuits

Professor Po-Wen Chiu
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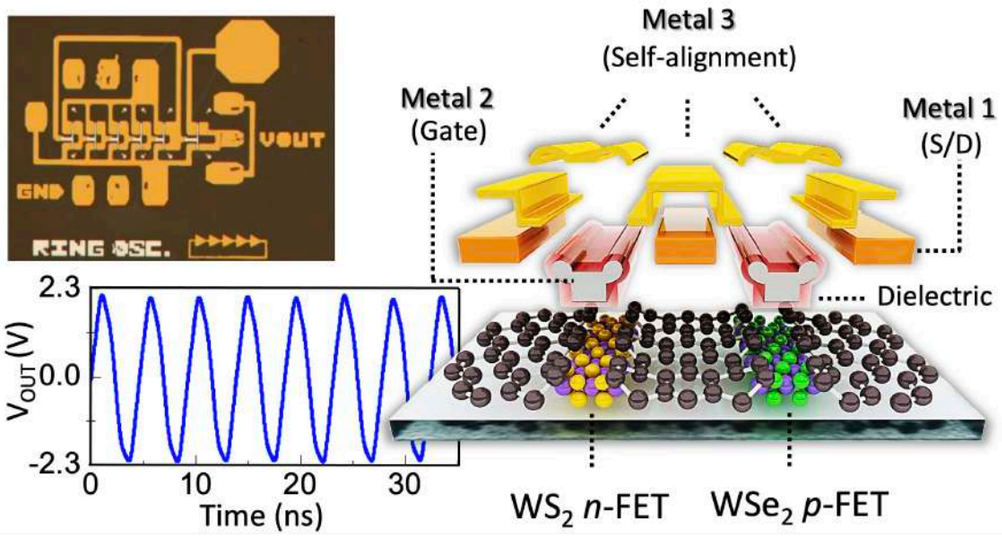

Schematic illustration of 2D FET architecture and measurement property of a ring oscillator thus made

In this work, we report an in-plane epitaxial route for the growth of interlaced 2D semiconductor monolayers using chemical vapor deposition with a gas-confined scheme, in which patterned graphene (Gr) serves as a guiding template for site-selective growth of Gr-WS2-Gr and Gr-WSe2-Gr heterostructures. The Gr/2D semiconductor interface exhibits a transparent contact with a nearly ideal pinning factor of 0.95 for the n-channel WS2 and 0.92 for the p-channel WSe2. The effective depinning of Fermi level gives an ultralow contact resistance of 0.75 and 1.20 kΩ.μm for WS2 and WSe2, respectively. Integrated logic circuits including inverter, NAND gate, static random access memory, and five-stage ring oscillator are constructed using the complementary Gr-WS2-Gr-WSe2-Gr heterojunctions as a fundamental building block, featuring the prominent performance metrics of high operation frequency (>0.2 GHz), low-power consumption, large noise margins, and high operational stability. The technology presented here provides a speculative look to the electronic circuitry built on atomic-scale semiconductors in the near future.

Research Highlights

- Outstanding research award 2021 (Ministry of Science and Technology)
- Y. Z. Hsu scientific paper award 2021

Research Output

- Y. C. Lin et al., Advanced Materials, 2007819, (2021).
- C. H. Yeh et al. ACS Nano, 14, 985-992 (2020).
- M. C. Chang et al. Nature Comm., 11, 3682, (2020).
- T. H. Tsai et al. ACS Nano, 14, 4559-4566 (2020).

> *National semiconductor project:*
> *Angstrom Semiconductor Initiative*

Group photo of Prof. Po-Wen Chiu

Interrogation of single-cell cellular compositions using electrorotation

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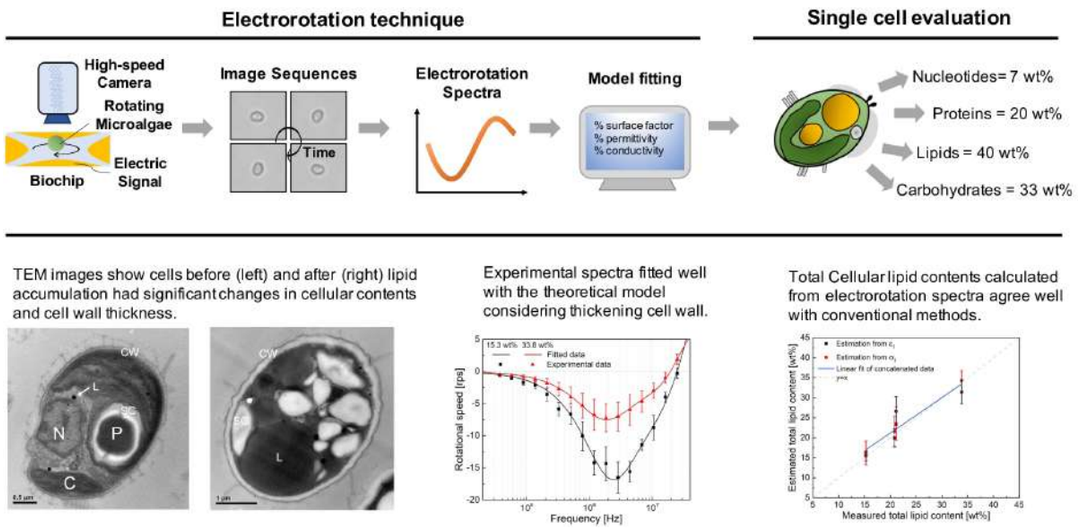

Single microalgae cells were submitted to a rotating electric field to record their electrorotation spectra. Electrorotation spectra were then fitted to the dielectric model with the thickening cell wall to evaluate the cellular composition.

Biofuel production from renewable feedstock such as microalgae has received wide attention and intense research efforts for enhancing the efficiency and productivity. Microalgal cellular contents vary significantly during the nutrient-depletion process and low productivity is highly possible if the harvest timing is not optimized. Therefore, a rapid quantification method for the total cellular lipid content is essential in ensuring a satisfactory productivity. This study demonstrated the use of electrorotation to characterize the dielectric properties of single microalgal cells and the estimation of the total cellular lipid content from these dielectric properties. The electrorotaion spectra, *i.e.*, the change of rotational speed of cells with the applied electric field frequency, were obtained and compared with the theoretical model to acquire dielectric properties of cellular compartments. *Scenedesmus abundans* cells were studied during nitrogen starvation and the results showed that both total cellular lipid contents and cell wall properties have considerable effects on the electrorotation spectra. The accurate interpretation of electrorotation spectra was achieved with the inclusion of a thickening cell wall in the double-shell ellipsoidal model. The dielectric properties of the cell inner core (a mixture of cytoplasm, lipid droplets, and nucleus) provided information for quantitative assessment of the total cellular lipid content. When the total cellular lipid content increased from 15.3 wt% to 33.8 wt%, the conductivity and relative permittivity of the inner core decreased by 21.7% and 22.5%, respectively. These dielectric properties were then applied to estimate total lipid contents by using the mixing formula and a good agreement was found between the estimated and measured values with the error as less as 0.22 wt%. The structural and compositional changes of cell wall during nitrogen starvation were also revealed by the increases in the conductivity and relative permittivity of the cell wall. To our best knowledge, this is the first study that succeeds in applying electrorotation on quantifying total cellular lipids of microalgae cells.

Research Highlights

- Partnership Program for the Connection to the Top Labs in the World (Dragon gate program), 2016~2018, funded by MOST, Taiwan
- NTHU- Université Paris-Saclay Dual Degree Program

Research Output

- Lin YS, Tsang S, Bensalem S, Tsai CC, Chen SJ, Sun CL, Lopes F, Le Pioufle B, Wang HY*. Electrorotation of single microalgae cells during lipid accumulation for assessing cellular dielectric properties and total lipid contents. Biosensors and Bioelectronics (2021), 173, 112772 [SCI, IF=10.257, Rank=8/329 in Biomedical Engineering]
- Y. Okamoto, T. Tsuchiya, C. Moslonka, Y.S. Lin, S. Tsang, F. Marty, A. Mizushima, C.L. Sun, H.Y. Wang*, A. Tixier-Mita and O. Français (2019 June). Z-Axis Controllable Mille-Feuille electrode electrorotation device utilizing levitation effect. The 20th International Conference on Solid-State Sensors, Actuators and Microsystems & Eurosensors XXXIII (TRANSDUCERS & EUROSENSORS XXXIII) (pp. 213-216). IEEE. 23-27 June, 2019, Berlin, Germany.
- Yu-Sheng Lin, Sung Tsang, Sakina Bensalem, Filipa Lopes, Chen-li Sun, Bruno Le Pioufle, Hsiang-Yu Wang. (2018 Nov) Using dielectrophoresis and electrorotation techniques to assess the dielectric properties of Scenedesmus abundans at different growth states. The Twenty Second International Conference on Miniaturized Systems for Chemistry and Life Sciences (μTAS 2018), Nov 11-15, 2018, Kaohsiung, Taiwan

(from left) Professor Bruno Le Pioufle, Professor Hsiang-Yu Angie Wang.

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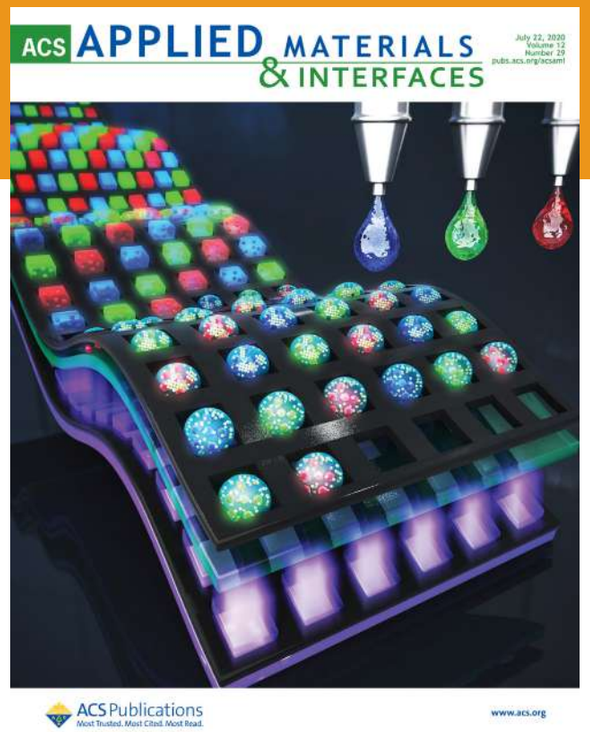
Inkjet-Printed Salt-Encapsulated Quantum Dot Film for UV-Based RGB Color-Converted Micro-Light Emitting Diode Displays



By introducing NaCl into a formulated ink, which enabled spontaneous self-encapsulation of QDs in a single NaCl crystal. An RGB QD@NaCl array with a small pixel size and uniform size distribution (diameter = 3.74 ± 0.5 μm) is obtained in the IJP process.

First, the hydrophilic QDs are obtained by exchanging the QD surface ligands from oleic acid (OA) to 3-mercaptopropionic acid (MPA), which can be well-dispersed in water or alcohols, and can be encapsulated in NaCl for forming a single QD@NaCl particle during the solvent evaporation of ink drops. Second, the entry of the QDs into the NaCl matrix is considered to be determined by the cohesion energy of NaCl ($W_{NaCl-NaCl}$, ~7 eV per pair) and the adhesion energy of QD-NaCl ($W_{QD-NaCl}$, ZnS-NaCl~20 eV (Na_2S) and ~110 eV ($ZnC1_2$)) in water, which the QD-NaCl adhesion would be very strong and thus QDs could be incorporated into the NaCl crystals. Then, A deposited drop on a hydrophobic substrate initially appears spherical because of the high contact angle (>90°). In the case, the drop retains both the shape and contact angle during solvent evaporation, and the drop edge continuously shifts inward without pinning the substrate, resulting in a decreased drop radius upon solvent evaporation. Consequently, QD-NaCl crystallization gradually proceeds in the ink concentrating process and finally generates a single QD@NaCl micron particle. In the end, a flexible QD converting film prepared by printing a QD@NaCl array with a pixel diameter of 3.74 ± 0.5 μm on a PET film has been demonstrated to be promising and feasible for full color wavelength-converted μ-LED displays.

(from left) (Master student) N. T. Jung, Dr. S. J. Ho, Professor H. S. Chen, (Master student) Y. L. Zhuang.

Research Highlights

- The cover of the Applied Materials & Interfaces (Volume 12)
- News media coverage

Research Output

- S. J. Ho, H. C. Hsu, C. W. Yeh and H. S. Chen, ACS Appl. Mater. Interfaces, 2020, 12, 33346-33351.
- S. J. Ho and H. S. Chen, J. Mater. Chem. C, 2020, 8, 4309-4313.
- P. R. Chen, K. Y. Lai and H. S. Chen, Mater. Adv., 2021.

Biomedical Technology

Loop extrusion mediates physiological Igh locus contraction for RAG scanning

Structure of the sodium-dependent phosphate transporter reveals insights into human solute carrier SLC20

Discovery of Epigenetic Biomarkers for Tailored Therapy

STAT3 phosphorylation at Ser727 and Tyr705 differentially regulates the EMT–MET switch and cancer metastasis

Professor Cheng-Sheng Lee
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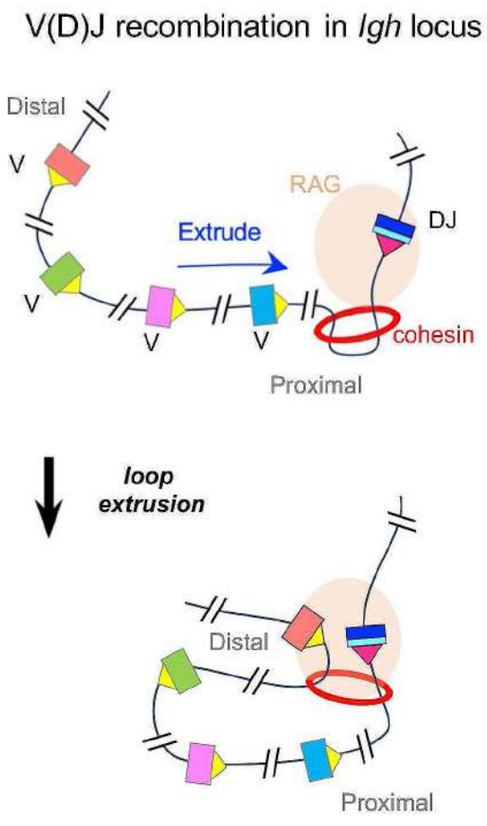
Loop extrusion mediates physiological Igh locus contraction for RAG scanning



Loop extrusion mediates physiological Igh locus contraction for RAG scanning

V(D)J recombination during B cell development is critical for the generation of antigen receptors expressed on the surface of B cells and antibodies secreted by the differentiated B cells in response to antigen challenges. In C57BL/6 mice, the V_H locus contains 109 functional V_H segments clustered in a 2.4Mb region, while D_H and J_H have much fewer segments and clustered within a relatively small region (60kb and 1.4kb respectively) downstream of the V_H locus. Each of the V_H, D_H, and J_H segments is flanked by recombination signal sequences (RSS), which can be recognized by RAG endonuclease. RAG initiates V(D)J recombination by introducing double-stranded breaks adjacent to V/D/J segments. As the result of a successful V(D)J recombination, one of the dispersed V_H segments formed one continuous exon, with a recombined DJ_H segment, to encode for the variable region of the antigen receptor and antibody. The choice of different V/D/J segments in different B cells enables combinational diversity. Together with the junctional diversity, mediated by other enzymes during V(D)J recombination, the diversity of the specificity of antigen recognition in an individual organism is greatly expanded.

To undergo V(D)J recombination, V_H segments need to get close contacts with DJ segments. A phenomenon, locus contraction, was observed to explain how distal V_H segments get involved. However, the mechanism by which Igh locus is contracted to promote the involvement of distal V_H segments in V(D)J recombination is unclear. To gain mechanistic insights, the collaborators in Boston Children's Hospital/Harvard Medical School inverted the 2.4-Mb V_H locus in mouse primary progenitor B cells. The inversion abolished the rearrangement with V_H segments, whereas the contracted configuration of Igh locus can still be observed. The inversion also abrogated the rearrangements of D-RSSs with cryptic V_H-RSSs, which are normally composed with a CAC motif convergent to D-RSSs. The detection of cryptic V_H-RSSs is normally restricted to the V_H topologically associating domain (TAD). The inversion activated new cryptic V_H-RSSs, that are normally in the opposite orientation, spreading even to the end of chromosome.

Recent studies suggest a role of cohesin in modulating the size of TADs. In v-Abl-transformed progenitor B cell lines, both contraction and RAG scanning of the V_H locus are lacked. We built a Tetracycline-inducible degron system to deplete wings apart-like protein homologue (WAPL), a cohesin-releasing factor. When we depleted WAPL, both contraction and RAG scanning of the V_H locus were activated. Distal V_H segments were able to participate V(D)J recombination and the increased combinational diversity is expected to promote the diversity of antigen recognition. Interestingly, we found the expression of WAPL is lower in primary progenitor B cells than in the v-Abl-transformed progenitor B cell lines. These findings suggest that loop extrusion controlled by the amount of cohesin on chromatin may regulate Igh locus contraction and RAG scanning. It is thus indicated that cohesin dynamics in primary progenitor B cells may promote the diversity of antigen receptor and antibody.

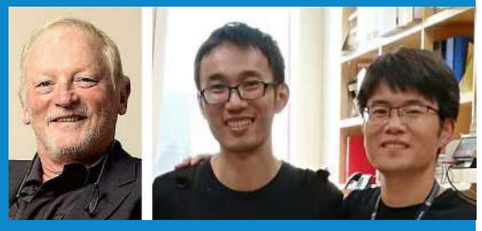
Young Scholar Fellowship (Einstein Program), Ministry of Science and Technology

Research Highlights

- Research work was recommended by Faculty Opinions

Research Output

- Dai HQ, Hu H, Lou J, Ye AY, Ba Z, Zhang X, Zhang Y, Zhao L, Yoon HS, Chapdelaine-Williams AM, Kyritsis N, Chen H, Johnson K, Lin S, Conte A, Casellas R, Lee CS, Alt FW. Loop extrusion mediates physiological Igh locus contraction for RAG scanning. Nature. (2021)



(from left) Professor Frederick W. Alt, Professor Cheng-Sheng Lee, Dr. Hai-Qiang Dai.

Professor Yuh-Ju Sun
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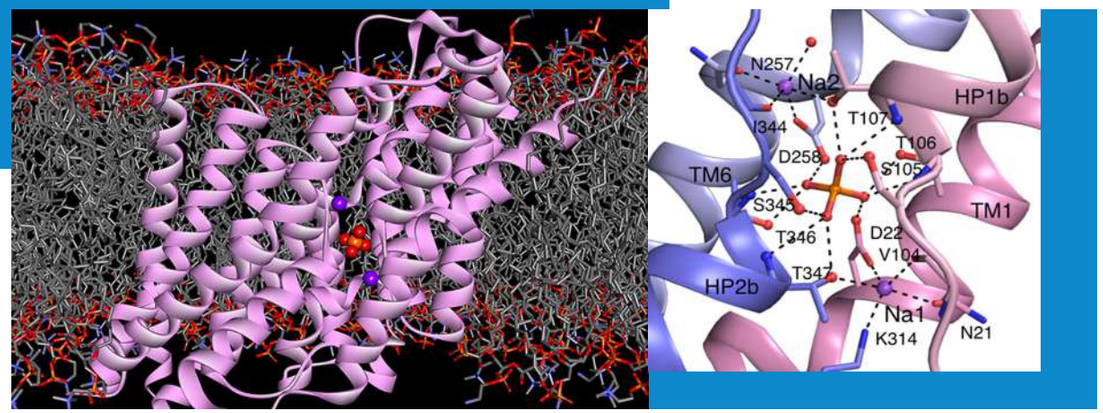
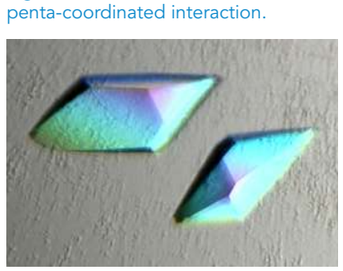
Structure of the sodium-dependent phosphate transporter reveals insights into human solute carrier SLC20



Crystallography made crystal clear. X-ray crystallographic approach is utilized to determine the phosphate transporter structure. The ribbon diagram of the TmPiT-Pi/Na complex consisting of 12 transmembrane helices with a transport domain and a scaffold domain are buried in the membrane. The Pi and Na ions are shown in CPK and as purple spheres, respectively. In the zoomed-in view of the Pi-2Na binding pocket, the Pi was tightly bound via 12 interactions with eight conserved residues and Na ions were bound within a penta-coordinated interaction.



Phosphate (Pi) is a fundamental and essential element for nucleotide biosynthesis, energy supply and cellular signalling in living organisms. In humans, Pi is translocated into cells by two major secondary active transporters. Dysfunction of human phosphate transporters causes numerous diseases, including hyperphosphatemia, vascular and brain calcification and neuropsychiatric disorders, but the molecular mechanism of these transporters remains elusive. Human phosphate transporters (hPiT1 and hPiT2) have been identified in various organs, including the kidney, liver and brain.

Specifically, several variants of hPiT2 are associated with neuropsychiatric disorders and primary familial brain calcification (PFBC), a neurodegenerative disorder with characteristic calcium deposits in the basal ganglia and other brain areas visualized on neuroimaging. Therefore, the sodium-dependent phosphate transporter can be a target protein for understanding the mechanism of the related diseases caused by its dysfunction and for future study in structure-based drug design.

To investigate the structural information for a sodium-dependent phosphate transporter, we solved the crystal structure of TmPiT, a homology of hPiT. We measured the phosphate binding affinity and determined uptake ability of TmPiT being driven by sodium. In the TmPiT-Pi/Na complex structure, three sodium ions were found; two sodium ions and one phosphate (hereafter Pi-2Na) were located at the core of TmPiT, and the third sodium Na_{fore} was situated near the inner membrane boundary. Interestingly, certain structural characteristics of TmPiT reflected those reported in disease-associated variants in hPiT. To understand how variants might affect hPiT function, we modeled the hPiT structure based on the TmPiT-Pi/Na complex structure and mapped out these hPiT mutations. We found some structural and functional correlation between our TmPiT results and clinical data from hPiT variants.

In summary, this study provides structural information that aids the understanding of important functional mutations that occur in hPiT. This work makes the scientists to conduct structural modeling, computational simulation, and molecular docking to develop and search the potential substrate analogs and modulators for phosphate transporter.

> *MOST best research paper award for postdoctoral fellows (2020) (Dr. Jia-Yin Tsai)*

(from left) Dr. J. Y. Tsai, Professor Y. J. Sun.

Research Highlights

- Excellence Biomedical Award from Tien Te Lee Biomedical Foundation (2021) (Prof. Yuh-Ju Sun)
- The Research Achievement Award, Ministry of Education (2020) (Prof. Yuh-Ju Sun)

Research Output

- Tsai, J. Y., Chu, C. H., Lin, M. G., Chou, Y. H., Hung, R. Y., Hsiao, C. D., and Sun, Y. J. (2020) Structure of the sodium-dependent phosphate transporter reveals insights into human solute carrier SLC20. Sci Adv 6, eabb4024

Discovery of Epigenetic Biomarkers for Tailored Therapy

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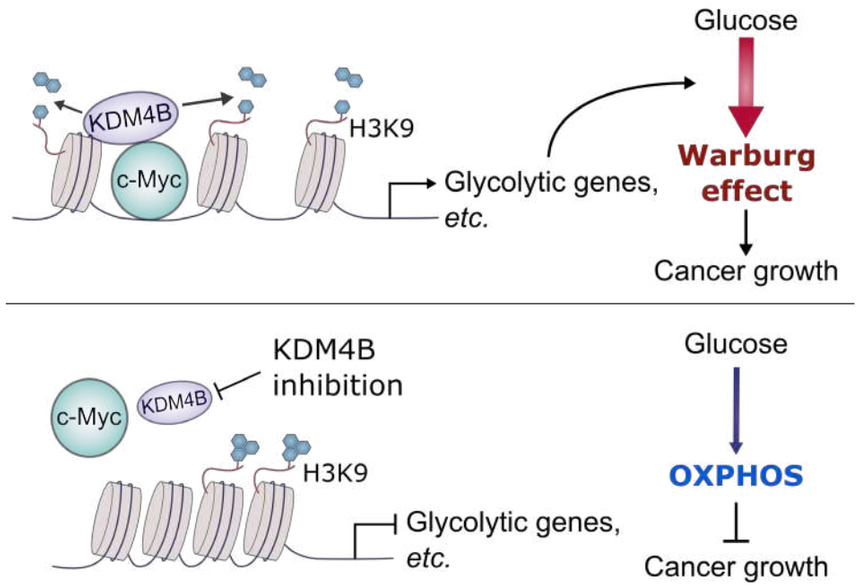
KDM4B interacts with c-Myc and regulates the metabolic genes including glycolytic genes via a demethylase-dependent manner, promoting the Warburg effect to accelerate the prostate cancer growth. Inhibition of KDM4B expression by specific shRNAs or small molecule inhibitors switches to an OXPHOS metabolism and curbs tumor growth.

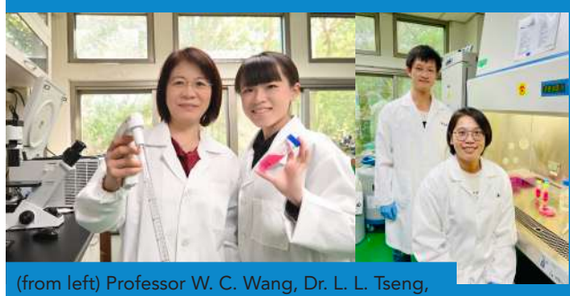


Cancer is a leading cause of mortality worldwide, accounting for approximately 10 million deaths in 2020. Aberrant epigenetic reprogramming critically mediates tumor initiation, tumor metabolism, metastatic spread, and tumor microenvironment reshaping. Notably, dynamic methylation/demethylation of histone tails by histone methyltransferases and demethylases plays an important role in cancer epigenetics. The research team employed in silico analyses to derive the epigenetic enzymes (histone lysine demethylases) and biological pathways that lead to gastric cancer progression from more than 30,000 potential genes.

The team uncovered that the PHF8 demethylase prevalent in ~40% of gastric cancer tissue causes PKCα to surge in conjunction with c-Jun, triggering the loss of the tumor suppressor PTEN, like "a brake failure". Infection with Helicobacter pylori, an etiologic agent of gastric cancer, induces the expression of KDM4B which interacts with c-Jun to drive gastric cancer progression. Inhibition of the PHF8-PKCα-PTEN axis curbs gastric cancer metastasis in an in vivo mouse model, suggesting a potential prognostic/therapeutic target pathway in metastatic gastric cancer.

In a new report by Wu et al., the team discovered that KDM4B functions to co-activate a major oncogene c-Myc in castration-resistant prostate cancer. Mechanistically, KDM4B and c-Myc are co-recruited to the c-Myc-binding sequence on the promoters of metabolic genes, such as LDHA, ENO1, and PFK. KDM4B and c-Myc synergistically promote the transactivation of the LDHA promoter in a demethylase-dependent manner. Additionally, KDM4B and c-Myc are significantly co-localized in prostate cancer and high expression of KDM4B and c-Myc are significantly associated with worse overall survival. Together, the team provides new insights into the epigenetic regulation of methylation/demethylation on the histone tail to drive metabolic adaptation and cancer progression, providing potential tailored prognostic/therapeutic strategies in malignant tumors.

> *Research Distinguished Professor of National Tsing Hua University*



(from left) Professor W. C. Wang, Dr. L. L. Tseng, Dr. T. J. Chen, Dr. M. J. Wu.

Research Highlights

- Distinguished Professor of National Tsing Hua University
- NSC Outstanding Scholar Project
- NSC Outstanding Scholar Award

Research Output

- Wu MJ, Chen CJ, Lin TY, Liu YY, Tseng LL, Cheng ML, Chuu CP, Tsai HK, Kuo WL, Kung HJ*, and Wang WC* (2021). Targeting KDM4B that coactivates c-Myc-regulated metabolism to suppress tumor growth in castration-resistant prostate cancer. Theranostics, 11(16), 7779-7796. doi:10.7150/thno.58729
- Tseng LL , Cheng HH , Yeh TS , Huang SC, Syu YY, Chuu CP, Yuh CH, Kung HJ, Wang WC* (2020). Targeting the histone demethylase PHF8-mediated PKC α -Src-PTEN axis in HER2-negative gastric cancer. Proc Natl Acad Sci USA, 117(40), 24859-24866. Epub, 23 September 2020
- Wu MC, Cheng HH, Yeh TS, Li YC, Chen TJ, Sit WY, Chuu CP, Kung HJ*, Chien S, Wang WC* (2019). KDM4B is a co-activator of c-Jun and involved in gastric carcinogenesis. Cell Death Dis., 2019. 10(2): p. 68.
- Chen TJ, Wang HJ, Liu JH, Cheng HH, Hsu SC, Wu MC, Lu CH, Wu YF, Wu JW, Liu YY, Kung HJ*, and Wang WC* (2019). PKM2 exon-10 tumor-related mutations: reduced allostery with increased nuclear translocation and association with KDM8. Commun. Biol. 2, 2019: 105 doi: 10.1038/s42003-019-0343-4

STAT3 phosphorylation at Ser727 and Tyr705 differentially regulates the EMT–MET switch and cancer metastasis

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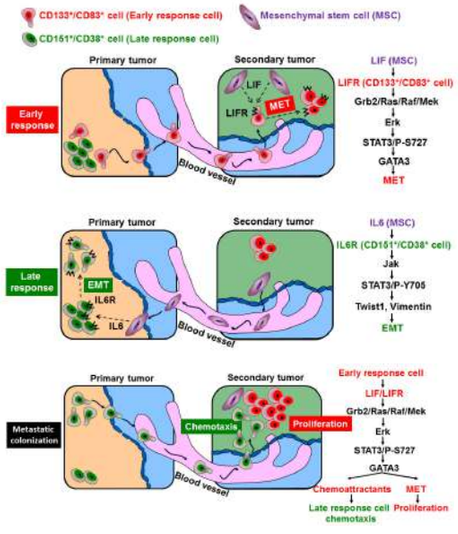
Metastasis, which causes more than 90% of cancer-related deaths, is a multistage process during which malignant cells spread from the primary tumour into distant organs. For distant metastasis to occur, primary tumour cells must acquire the ability to invade and disseminate into the circulatory system, seed at the distant site, and subsequently proliferate to establish macrometastatic colonies. The current understanding of epithelial carcinoma metastasis highlights the importance of epithelial–mesenchymal transition (EMT) in equipping tumour cells with motility and invasiveness. After undergoing EMT, tumour cells acquire a mesenchymal-like phenotype with enhanced migratory ability, a crucial trait that allows them to escape the primary site. Upon histopathological examination, however, cells in metastatic nodules often resemble those in the primary site. This observation suggests that once migrating cancer stem cells (CSCs) reach a suitable distant site, they usually need to revert to the epithelial phenotype through mesenchymal–epithelial transition (MET) to reacquire their proliferative ability and eventually form metastatic colonies. Epithelial plasticity, defined as the transition between the epithelial and mesenchymal phenotypes, is therefore crucial in the initiation and establishment of cancer metastasis. However, to date, the mechanism by which tumour cells commence and resolve the EMT-MET programme as they proceed through the metastatic cascade remains incompletely understood. Transient de-differentiation (EMT)–re-differentiation (MET) processes are proposed to be a driving force of cancer metastasis; however, considerable uncertainty regarding the EMT-MET switch remains: 1) Although many clinical reports13 have advanced the concept of transient EMT-MET switches in metastasis, there are only a few experimental proofs. 2) EMT is proposed to provide cancer cells with several prometastatic traits, including motility and stemness. One argument that has been raised against a role for EMT in cancer progression is that metastatic tumours examined histologically often exhibit an epithelial-like phenotype and resemble the primary tumour. 3) Many studies support the need for re-differentiation (MET) to support the colonization and metastasis of differentiated carcinomas and show that EMT-associated growth arrest is a reason underlying this need. However, how do metastases re-differentiate? 4) Future therapeutic strategies against metastasis will have clinical impacts. Inducing differentiation and targeting EMT alone might be counterproductive by inducing the proliferation of disseminated cells. How should this problem be solved? The conclusion of our study, based on microarray analysis, suggests the identity of the molecular mediators of metastatic competence within a heterogeneous primary tumour and the mechanism by which these cells then manipulate the switch between EMT and MET during the metastatic process. In primary tumours, early-response cells ($CD133^+/CD83^+$) acquired CSC properties upon mesenchymal stem cell (MSC) stimulation, migrating towards secondary sites, where MSCs secreted leukemia inhibitory factor (LIF) and activated LIF receptor (LIFR)/p-ERK/pS727-STAT3 signalling to promote proliferation associated with MET to support the formation of the premetastatic niche. Next, tumour-tropic MSCs circulated to the primary site, where the second subgroup of cells, which respond slowly to MSC stimulation, were located. These late-response cells ($CD151^+/CD38^+$) were directed by MSCs to acquire CSC properties associated with EMT through IL6R/pY705-STAT3 signalling and were then attracted by and migrated towards the premetastatic niche. In summary, STAT3 phosphorylation at Y705 and S727 differentially regulates the EMT-MET switch within the distinct molecular subtypes of CSCs to complete the metastatic process. Our findings in the present study suggest there are links among the tumor niche, STAT3, cell polarity, and CSCs, and indicate that targeting STAT3 may be an effective means of interfering with tumorigenesis and/or metastasis.



A model for STAT3 phosphorylation at Ser727 and Tyr705 differentially regulating the EMT–MET switch and cancer metastasis. Model proposing a pathway in which heterogeneous $CD151^+/CD38^+$ and $CD133^+/CD83^+$ CSC subtypes undergo STAT3/pY705-elicited EMT and STAT3/pS727-elicited MET, respectively, to achieve metastatic colonization in a manner regulated by MSCs.

Research Highlights

- Best Paper Award in 2019 Joint Conference of Taiwanese Society of Developmental Biology and Taiwan Society for Stem Cell Research
- Dr. Chien-Tien Hsu's Award in The Twenty-fourth Symposium on Recent Advances in Cellular and Molecular Biology, 2016
- Outstanding Research Award, Juei-Low Sung Foundation, Taiwan.

Research Output

- Lin W. H., Chang Y. W., Hong M. X., Hsu T. C., Lee K. C., Lin C., Lee J. L. * (2021). STAT3 phosphorylation at Ser727 and Tyr705 differentially regulates the EMT–MET switch and cancer metastasis. Oncogene 40:791-805.
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(from left) Professor J. L. Lee, Professor C. Lin, Dr. W. H. Lin, Dr. Y. W. Chang.

Material Science

Hierarchically targetable polysaccharide-coated solid lipid nanoparticles as an oral chemo/thermotherapy delivery system for local treatment of colon cancer

Professor Hsin-Cheng Chiu
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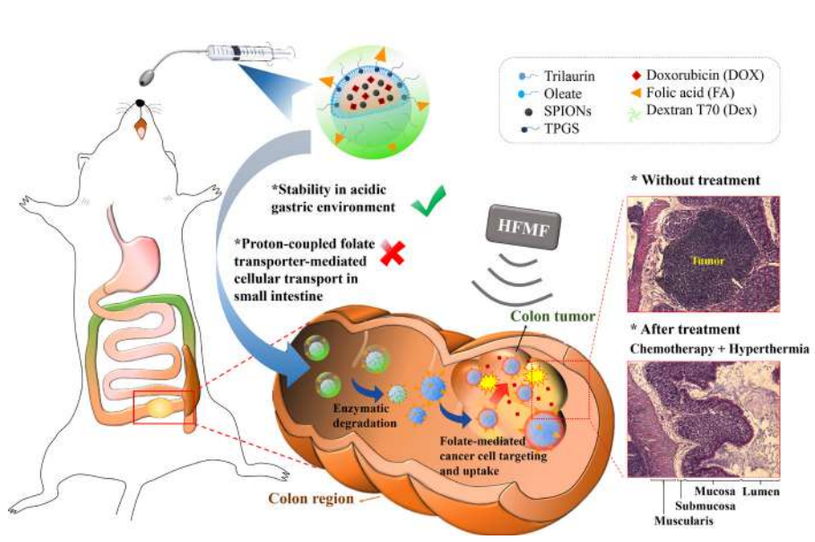
In this study, the solid lipid nanoparticle (SLN)-based chemo/magnetothermal combination therapy system for oral delivery and local treatment of colon cancer was developed. The SLNs loaded with doxorubicin (DOX) and superparamagnetic iron oxide nanoparticles (SPIONs) were surface modified with folic acid (FA)/D-α-tocopheryl polyethylene glycol 1000 succinate (FA-TPGS) adduct and octadecanol modified dextran (Oct-Dex) in a layer-by-layer architecture. SPIONs were adopted to generate hyperthermia therapy herein, yet not for MRI T2 imaging. The local combination treatment from both DOX chemotherapy and hyperthermia therapy upon the activation of SPIONs with high-frequency magnetic field (HFMF) were employed against orthotopic colon cancer for the synergistic antitumor effect while the tissue damage of major organs could be significantly reduced owing to the lack of systemic adsorption of the SLNs into blood circulation. Incorporating FA-TPGS onto particle surfaces enables the good dispersion of NPs in aqueous phase and the targeting of NPs to the FA receptor (FAR)-overexpressed cancer cells. Although it has been reported that proton-coupled folate transporters exist on brush border membranes of microvilli in small intestine, the issue can be fully addressed by the coating of the polysaccharide layers on the NP surfaces that prevents the biorecognization of FA residues on nanocarriers by FA transporters. The octadecanol-modified dextran coated on NP outer surfaces not only reduces the FAR-mediated transportation through brush border membranes in small intestine, but also provides the complementary association of dextran with dextranase, a bacteria-produced glucanohydrolase present exclusively in colon. Upon enzymatic degradation of dextran, the exposure of the FA residues on NP surfaces acting as the targeting ligands leads to the enhanced uptake of NPs by the FAR overexpressed cancer cells via receptor-mediated endocytosis and the pronounced antitumor performance of the chemo/magnetothermal combination therapy of the SLN formulations both in vitro and in vivo. In particular, the effective tumor growth inhibition of the orthotopic colon tumor and the substantial reduction of the nodule number and size of peritoneal carcinomatosis colorectal cancer for the tumor-bearing mice receiving this treatment clearly demonstrated the prominent therapeutic efficacy for local treatment by oral administration. Because of the restricted therapeutic action of the dual-targeted SLN therapy delivery system on the local tumor sites, no apparent systemic side effects were observed.



Schematic illustration of the hierarchically targetable SLN system for the local chemo/thermo combination therapy against colon cancer by oral administration.

Research Highlights

- MOST Outstanding Research Award
- Fellow of Biomaterials Science & Engineering (FBSE) of the International Union of Societies for Biomaterials Science and Engineering (IUSBSE)
- Professor Chau-Ren Lee Foundation Biomedical Engineering Award

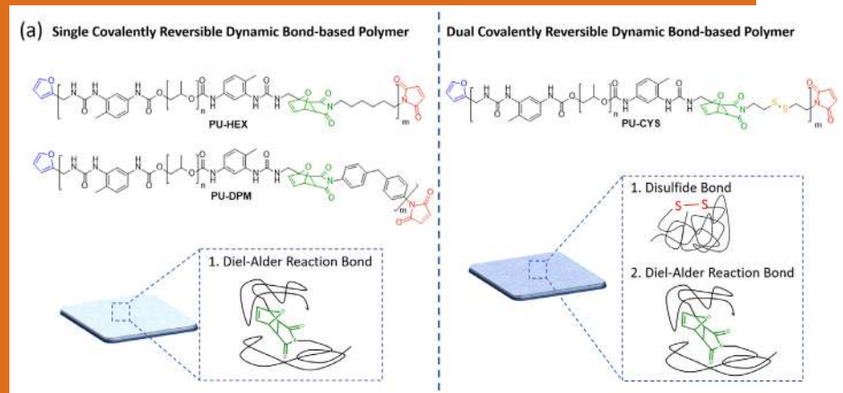
Research Output

- M. Y. Shen; T. I. Liu; T. W. Yu; R. Kv; W. H. Chiang; Y. C. Tsai; H. H. Chen; S. C. Lin; H. C. Chiu*, Hierarchically targetable polysaccharide-coated solid lipid nanoparticles as an oral chemo/thermotherapy delivery system for local treatment of colon cancer. Biomaterials 2019, 197, 86-100.
- T. I. Liu; T. Y. Lu; S. H. Chang; M. Y. Shen; H. C. Chiu*, Dual stimuli-guided lipid-based delivery system of cancer combination therapy. Journal of Controlled Release 2020, 318, 16-24.
- M. Y. Shen; S. H. Chang; T. I. Liu; T. Y. Liu; A. Sabu; H. H. Chen; H. C. Chiu*, Combo-targeted nanoassemblies as a chemotherapy delivery system against peritoneal carcinomatosis colorectal cancer. Biomaterials Science 2020, 8, 3885-3895.

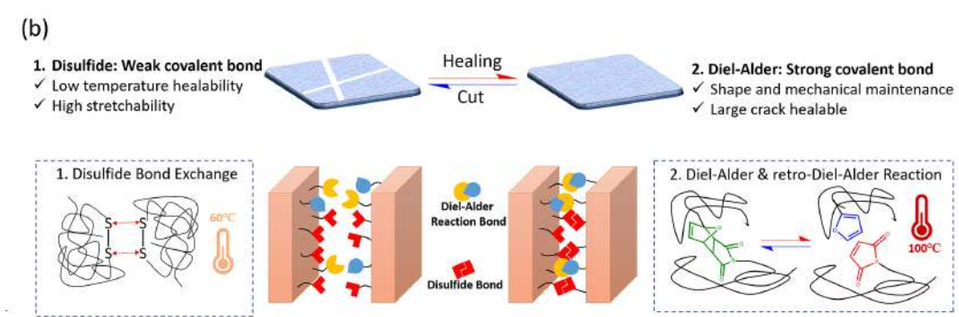
(from left) Professor Hsin-Cheng Chiu, Dr. Te-I Liu, Dr. Ming-Yin Shen, Ting-Wei Yu, Chi-Ya Wang

Professor Ho-Hsiu Chou
hhchou@mx.nthu.edu.tw

Disulfide bonds and Diel-Alder Reaction Bonds Hybrid Polymers with High Stretchability, Transparency, Recyclability, and Intrinsic Dual-Healability for Skin-like Tactile Sensing



(a) Illustration of the design concept and the chemical structure of PU-DPM, PU-HEX, and PU-CYS.



(b) Illustration of the healing concept of the dual covalent reversible dynamic bond

We successfully designed and synthesized a series of linear stretchable and healability polymers PU-DPM, PU-HEX, and PU-CYS. Compared to the DA reaction bonds polymer PU-DPM anad PU-HEX, the disulfide bonds and DA reaction bonds hybrid polymer PU-CYS presented not only the high strain values (up to 1,000%) and great transparency (>97%) because they contain soft linkers, but also the fast (60°C, 5 mins) and dual-mode healability that it can be healed by different covalently dynamic reversible bonds according to the scale of damage size. Furthermore, the resulting polymer can achieve excellent skin-adhesive capability during various free movement of human skin, and can be fabricated as the pyramidal microstructure for skin-like tactile sensor. This skin-inspired multifunctional material demonstrates great potential for applications in future wearables, soft electronics, smart robots, and electronic skins fields.

Research Highlights

- The back cover of J. Mater. Chem. A, 2021, 9

Research Output

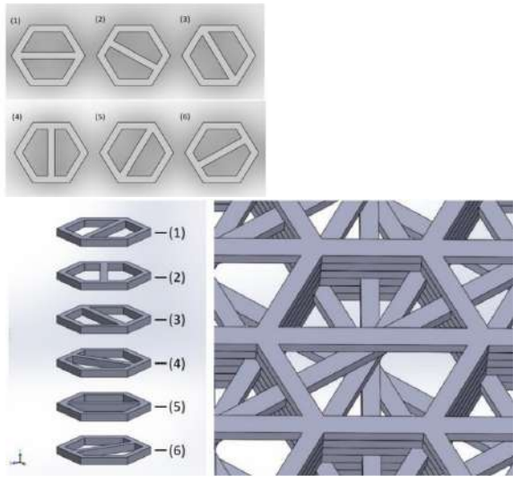
- J. Mater. Chem. A, 2021,9, 6109-6116

Professor Ho-Hsiu Chou (the middle, blue shirt), Dr. Chun Ming Yeh (rightmost).

Professor Jane Wang
janewang@mx.nthu.edu.tw

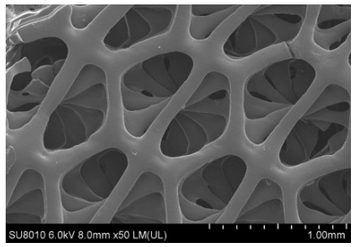
Design of photocurable, biodegradable scaffolds for liver lobule regeneration via digital light process-additive manufacturing

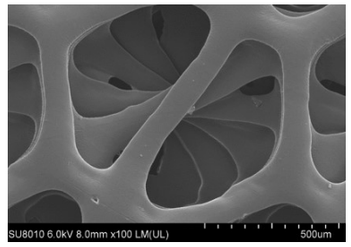
To enable the fabrication of scaffolds with a 3D structure for tissue engineering, the biodegradable, photocurable copolymers PGSA and PEGDA were applied in additive manufacturing in a DLP-AM system. In order to facilitate the regeneration of liver tissue, scaffolds with hexagonal shaped cavities were prepared via DLP-AM system to mimic liver lobules, one of the smallest functional units in livers. Since one liver lobule is roughly 1-2 mm in diameter, the designed hexagonal pores matches the size of natural liver lobules closely. Initial scaffold designs were calculated to be 12.36 mm^2 on a disc with diameter of 6.40 mm, occupying about 38.42% of the surface of the disc. However, initial seeding of hepatocytes were found either not adhered to the scaffolds or dead due to poor nutrient circulation in 5 days. In order to further facilitate the cell seeding effectiveness while maintaining medium circulation during cell culture, spiral staircase-shaped hexagons were designed with effective surface area was successfully increased to 23.72 mm^2, which is roughly 73.73% of the surface of the disc. As the hexagonal staircase (HS) structure aimed to increase the medium circulation vertically, it was observed during the cell culture, the designed through-holes were quickly filled up by the multiplying cells, and is likely to have subsequently reduced the efficiency of medium circulation as cell multiplies over longer culturing time. In order to maintain high medium circulation over a longer period of time, horizontal channels were also introduced to the staircase structures to help facilitate the horizontal exchange of culture medium, leading to the high diffusion staircase (HDS) scaffolds.

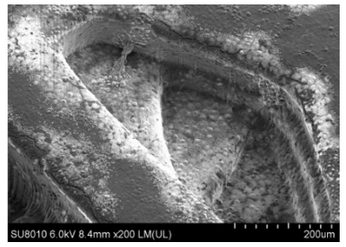


The design and 3D-printed hexagonal stair case scaffolds, seeded with FL83B cells, and cultured for 7 days.

Although the cell growth rate on HS structures was







higher on day 3, the multiplication of cells began to plateau on day 5. Cells seeded on HDS scaffolds showed a linear trend initially, but the cells on both of the 3D printed scaffolds had higher proliferation rates and the linear growth in metabolic activities for cells on the HDS scaffolds indicates their ability to sustain long-term cell culture and a good growth rate. In order to further improve the liver cell proliferation rate, the relationship between materials of scaffolds and the liver cell proliferation was investigated. It was found that The result demonstrates that the scaffolds made of 50% PGSA and 50% PEGDA are suitable for long-term cell culture of HepG2 both physically and biologically.

Overall, novel designs of HS and HDS scaffolds have been proposed for scaffold fabrication in the hope of developing a liver lobule model. It is expected that through 3D printing of HDS scaffolds with PGSA-co-PEGDA at a 1:1 weight ratio, liver lobule-shaped scaffolds can be produced for use in liver regeneration.

Research Highlights

- Ministry of Science and Technology Additive Manufacturing Integrated Grant
- National Health Research Institute Career Development Grant

Research Output

- Teng, C. L.; Chen, J. Y.; Chang, T. L.; Hsiao, S. K.; Hsieh, Y. K.; Villalobos Gorday, K.; Cheng, Y. L.; Wang, J., Design of photocurable, biodegradable scaffolds for liver lobule regeneration via digital light process-additive manufacturing. Biofabrication 2020, 12 (3), 035024.
- Chen, J.-Y.; V. Hwang, J.; Ao-Ieong, W.-S.; Lin, Y.-C.; Hsieh, Y.-K.; Cheng, Y.-L.; Wang, J., Study of physical and degradation properties of 3D-printed biodegradable, photocurable copolymers, PGSA-co-PEGDA and PGSA-co-PCLDA. 2018; Vol. 10, p 1263.
- Wang, J.; Cheng, Y.-L.; Chen, Y.-W.; Shie, M.-Y. (2018), 3D Printable biodegradable polymer composite. US Patent# 10,377,865.

(from top left) Jeffrey Huang, Grant Chen, Visiting Scholar, Sarah Huang, Chia-Ling Teng, Dr. Wai-Sam Ao-Ieong, Dr. Terence Chang (from bottom left) Kaiser A. Villalobos Gorday, Prof. Jane Wang, June-Yo Chen, Tim Hsiao, Wen Huang, Hung-Ruei Lin

Microstructure and Tensile Property of a precipitation strengthened High Entropy Alloy Processed by Selective Laser Melting and Post Heat Treatment

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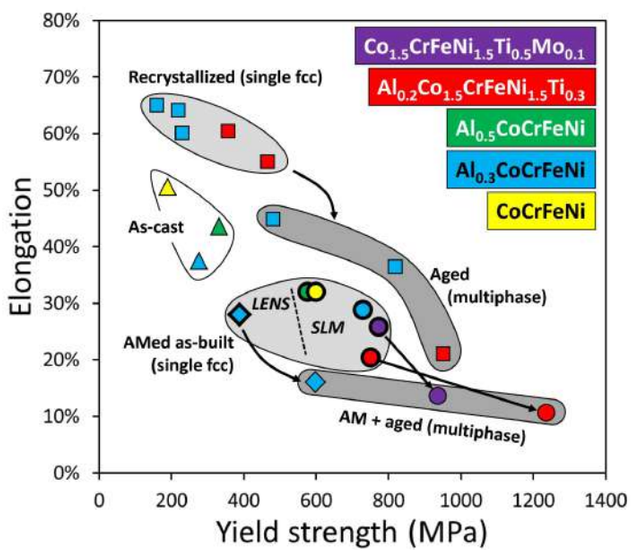


The yield strength (1235 MPa) and ultimate tensile strength (1550 MPa) achieved in this work are the highest to-date for HEAs subjected to laser additive manufacturing processes.

A high entropy alloy $Al_{0.2}Co_{1.5}CrFeNi_{1.5}Ti_{0.3}$ was fabricated by SLM and then subjected to direct ageing heat treatment at 750°C for 50 h. Its microstructure was distinctively different from that of cast & wrought and heat-treated sample, which possessed FCC matrix with a dispersion of $L1_2$ particles. The sub-micron segregation and internal stress associated with SLM process affected the microstructure evolution after direct ageing; a complex microstructure, containing not only $L1_2$ precipitates, but also nano oxide dispersions, and $L2_1$ structured particles with subgrain boundaries, was obtained. The microstructure produced by the SLM plus post heat treatment significantly improved the tensile properties at both room temperature and 500°C. The yield strengths at room temperature and 500°C were 284 MPa and 229 MPa higher than those of cast & wrought counterparts. Detailed analysis on the strengthening contributions has indicated that $L1_2$ phase precipitation strengthening could contribute around 500 MPa, which was similar for both processing routes after the same ageing treatment, however, the complex microstructure of DA-SLM sample provided additional strengthenings from finer grain size, nano oxides, internal stress, and the $L2_1$ phase with a subgrain structure that accounts for 4%, 7%, 44%, and 45%, respectively at room temperature. The yield strength and ultimate tensile strength of $Al_{0.2}Co_{1.5}CrFeNi_{1.5}Ti_{0.3}$ HEA processed by SLM plus direct ageing are 1235 MPa and 1550 MPa, respectively, and they are among the highest to-date for HEAs subjected to laser additive manufacturing processes.

(from left) Professor Tadashi Furuhara, Professor An-Chou Yeh, Assistant Professor Fei Sun.

Research Awards

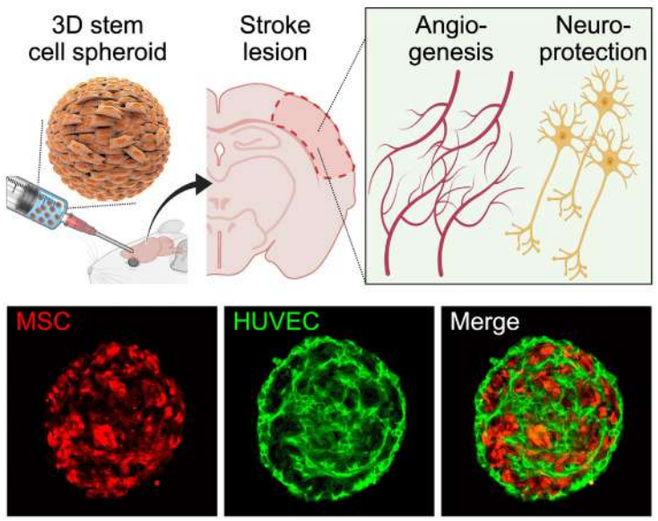
- 2020 Mercator Fellow Award - Awarded by German DFG
- 2018 Excellent Young Academic Award - Awarded by Taiwan Materials Research Society
- 2017 Mercator Fellow Award - Awarded by German DFG

Research Output

- Wei-Chih Lin, Yao-Jen Chang, Tzu-Hou Hsu, Stéphane Gorsse, Fei Sun, Tadashi Furuhara, An-Chou Yeh*, "Microstructure and Tensile Property of a precipitation strengthened High Entropy Alloy Processed by Selective Laser Melting and Post Heat Treatment", Additive Manufacturing, (36) 101601. (2020)
- Yung-Ta Chen, Yao-Jen Chang, Hideyuki Murakami, Stéphane Gorsse, An-Chou Yeh*, "Designing high entropy superalloys for elevated temperature application", Scripta Materialia, (187), Pages 177-182. (2020)
- Stéphane Gorsse, Yung-Ta Chen, Wei-Che Hsu, Hideyuki Murakami, An-Chou Yeh*, "Modeling the precipitation processes and the formation of hierarchical microstructures in a single crystal high entropy superalloy", Scripta Materialia, (193) Pages 147-152. (2021)
- Pant title: HIGH ENTROPY SUPERALLOYS, Issue No.: US10,472,702, B2 (US Patent), Issue Date: 2019/11/12, Inventors: YEH, AN-CHOU、TSAO, TE-KANG
- Patent Title: POWDER MATERIAL AND MANUFACTURING METHOD THEREOF, Issue No: I671336 (Taiwan (R.O.C.) Patent), Issue Date: 2019/09/11, Inventors: CHANG, KAI-CHUN、CHANG, YA-LING、YEH, AN-CHOU、YEH, JIEN-WEI、LIN, SU-JIEN、TSAI, TSE-WEI
- Patent Title: SUPERALLOY DESIGNED SPECIFICALLY FOR ADDITIVE MANUFACTURING, Issue No: I668310 (Taiwan (R.O.C.) Patent), Issue Date: 2019/08/11, Inventors: HO, I TING、YEH, AN-CHOU

Professor Chieh-Cheng Huang
chiehcheng@mx.nthu.edu.tw

Transplantation of 3D stem cell spheroids ameliorates ischemic stroke brain injury



By assembling into a 3D spherical configuration before intracranial transplantation, the postengrafted retention and survival of mesenchymal stem cells (MSCs) and human umbilical vein endothelial cells (HUVECs) and their therapeutic potential for treating ischemic stroke can be enhanced significantly, eventually leading to superior brain structural and motor functional restoration.

While a number of clinical trials employing stem cells to treat ischemic stroke are ongoing, several key challenges remain to be addressed. To maximize the efficacy of stem cell-based therapy, approaches that can effectively retain the administered cells at the desired site and maintain their survival are required. However, cell transplantation employing a conventional trypsin-based approach for cell harvesting is limited by the inefficiency of the current cell delivery approach and the vulnerability of detached anchorage-dependent cells in the hostile microenvironment of target tissues, including the infarcted brain.

Herein, the preassembly of MSCs and ECs into a 3D spherical configuration could efficiently (i) maintain the cell-matrix interaction during the entire procedure of cell harvesting and transplantation, (ii) reduce cell leakage from the site of injection, and (iii) protect the engrafted cells from the harsh environment in ischemic brain tissue, thereby addressing the major challenges in cell therapy. Compared with conventional two-dimensional monolayered culture, the 3D spheroid configuration is characterized by enhanced cell-cell and cell-extracellular matrix interactions that effectively recapitulate the microenvironment of native tissue, thus encouraging the secretion of soluble factors and the release of extracellular vesicles and thereby contributing to increased survival and therapeutic capability. Additionally, although MSCs are already known for their ability to modulate the local microenvironment through paracrine signaling, our results indicated that the incorporation of ECs could further enhance the ultimate therapeutic potential of 3D MSC/EC spheroids by further boosting their capacity to secrete therapeutic agents.

In summary, by assembling cells into a 3D spheroid configuration, the critical underlying causes of cell loss during transplantation could be effectively addressed. Compared with the MSC/EC suspension, the 3D MSC/EC spheroids displayed increased postengrafted cell retention, survival, and therapeutic function. As a result of their therapeutic versatility, the transplantation of 3D MSC/EC spheroids significantly ameliorated poststroke glial scarring and promoted neurogenesis, angiogenesis, and functional recovery in a mouse model of ischemic stroke.

Despite several limitations, these results establish an important proof-of-concept for future clinical translation of 3D spheroid-based cell therapy for the treatment of ischemic stroke.

Research Highlights

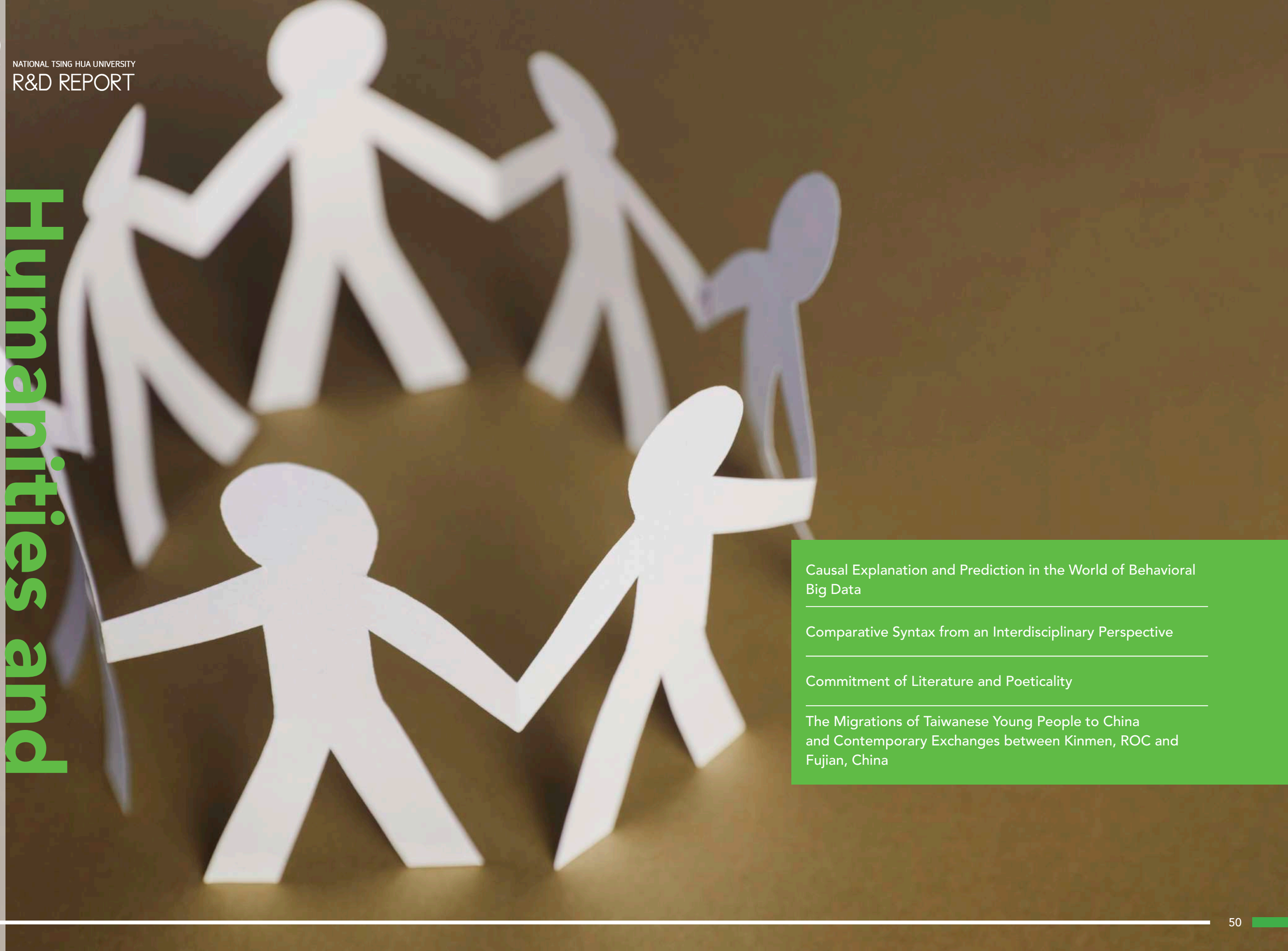
- Young Scholar Fellowship (Einstein Program), Ministry of Science and Technology

Research Output

- Transplantation of 3D MSC/HUVEC spheroids with neuroprotective and proangiogenic potentials ameliorates ischemic stroke brain injury. Biomaterials, 272, 120765 (2021).
- Injection of hybrid 3D spheroids composed of podocytes, mesenchymal stem cells, and vascular endothelial cells into the renal cortex improves kidney function and replenishes glomerular podocytes. Bioengineering & Translational Medicine, 2, e10212 (2021).
- Bioactive decellularized extracellular matrix derived from 3D stem cell spheroids under macromolecular crowding serves as a scaffold for tissue engineering. Advanced Healthcare Materials, 20, 202100024 (2021).
- 3D Spheroids of umbilical cord blood MSC-derived Schwann cells promote peripheral nerve regeneration. Frontiers in Cell and Developmental Biology, 8, 604946 (2020).

Professor Chieh-Cheng Huang's group.

Humanities and Social Sciences



Causal Explanation and Prediction in the World of Behavioral Big Data

Comparative Syntax from an Interdisciplinary Perspective

Commitment of Literature and Poeticality

The Migrations of Taiwanese Young People to China and Contemporary Exchanges between Kinmen, ROC and Fujian, China

Professor Galit Shmueli
galit.shmueli@iss.nthu.edu.tw

Causal Explanation and Prediction in the World of Behavioral Big Data

My work on **Behavioral Big Data** focused on two areas: (1) the use of large-scale behavioral randomized experiments in social science, and (2) methodological, technical, and ethical issues related to conducting research with behavioral big data (BBD).

Contribution #1: Large-scale behavioral randomized experiments

Large-scale behavioral randomized experiments (RCTs) have become popular in research and in industry. With my colleagues Ravi Bapna and Ahmed Umyarov (University of Minnesota) and Jui Ramprasad (McGill University), we collaborated with a large dating website in N. America and ran an RCT to investigate the effect of anonymous browsing on matching outcomes. We discovered important effects related to weak signaling and specifically, how they affect women differently from men (Bapna et al. 2016). From this work, I've noticed the richness of RCT data, realizing its potential to provide more valuable theoretical and practical information than simply measuring the average treatment effect (ATE), as they often contain information beyond just the treatment assignment and outcome of interest. Researchers using RCTs often subgroup or condition on variables other than the treatment variables, for many good reasons. In particular, designing and conducting RCTs is costly to researchers and subjects, and therefore it is important to derive greater value from RCT data - measuring not just the ATE but also finding more nuanced insights about underlying theoretical mechanisms and generalizing the inferences. Unfortunately, there are many confusing and even contradictory guidelines on the use of subgroups or auxiliary variables in RCTs. Collaborating with Ali Tafti (U Illinois at Chicago) we embarked on a project "Leveraging covariates in randomized experiments guided by causal structure" that introduces Pearl's causal diagrams (DAGs) into the RCT context (Tafti & Shmueli, 2020).

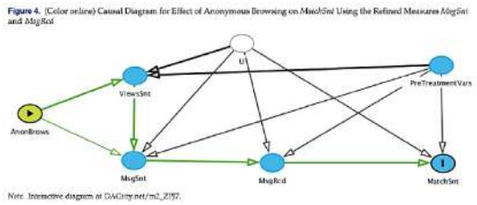


Figure 4. (Color online) Causal Diagram for Effect of Anonymous Browsing on MatchSnt Using the Refined Measures MsgSnt and MsgRcd

Note. Interactive diagram at DAGitty.net/m2_2197.

Using subgroups and auxiliary variables in randomized controlled experiments (RCTs), based on Pearl's causal diagramming framework (from Tafti & Shmueli, 2020)

Contribution #2: Research Using Behavioral Big Data

Given my experience working with BBD, collaborating with academics and industry, I've decided to raise awareness to the critical issues. My papers and keynote speeches on "Research Dilemmas with Behavioral Big Data" (Shmueli, 2017) and "Analyzing Behavioral Big Data: Methodological, Practical, Ethical, and Moral Issues" (Shmueli, 2017a) are aimed to expose data scientists and behavioral researchers to the new challenges and opportunities with large behavioral datasets. "Adjusting to the GDPR: The Impact on Data Scientists and Behavioral Researchers" (Greene et al., 2019) we extend this work to the new legal landscape.

Contribution #3: Models for Time Series BBD

A type of BBD less studied is time series. IoT and other user-level technologies result in large collections of user-level time series. In collaboration with Rob Hyndman (Monash University, Australia), CY Sin (NTHU) and PhD student Mahsa Ashouri, we've developed methods for modeling such data. In "Tree-based Methods for Clustering Time Series Using Domain-Relevant Attributes" (Ashouri et al., 2019) we proposed methods based on model-based partitioning (MOB) trees for time-series clustering that capture temporal information (trend, seasonality, autocorrelation) and domain-relevant cross-sectional attributes. The methods produce forecasts on par with classic forecasting methods, yet are significantly faster, thereby suitable for large collections of time-series. The simple parametric forecasting models allow for interpretable time-series clusters. This interpretability is crucial in many decision-making applications.

Research Highlights

- 2020: Elected Fellow, Institute of Mathematical Statistics (IMS)
- 2020: Inaugural Teaching Innovation Award, INFORMS Information Systems Society
- 2020: Outstanding Teaching Award, National Tsing Hua University
- 2016: Outstanding Research Award, Ministry of Science and Technology (MOST)
- 2016: E.SUN Bank Academic Award

Research Output

- Bapna, R., Ramprasad, J., Shmueli, G. and Umyarov, A. (2016), One-Way Mirrors and Weak-Signaling in Online Dating: A Randomized Field Experiment, Management Science, vol 62, no 11 (Nov 2016), pp. 3100-3122.
- Shmueli, G. and Yahav, I. (2018), The Forest or the Trees? Tackling Simpson's Paradox with Classification Trees, Production and Operations Management (POM), vol 27, no 4, pp. 696-716.
- Sharma, P., Sarstedt, M., Shmueli, G., and Thiele, K. O. (2019), PLS-Based Model Selec- tion: The Role of Alternative Explanations in MIS Research, Journal of the Association for Information Systems, vol 20, no 4, Article 4.
- Tafti, A. R. and Shmueli, G. (2020), Beyond overall treatment effects: Leveraging covariates in randomized experiments guided by causal structure, Information Systems Research, vol 31 issue 4, pp. 1183-1199.
- Sharma, P., Shmueli, G., Sarstedt, M., Danks, N., and Ray, S. (2021), Prediction-oriented model selection in partial least squares path modeling, Decision Sciences Journal, vol 52 issue 3, pp. 567-607. (Top 10% most downloaded DSJ papers in 2018-2019).

(from left) Prof. Galit Shmueli, Prof. Ravi Bapna, Prof. Jui Ramaprasad

(from left) Prof. Inbal Yahav, Dr. Mahsa Ashouri, Prof. Chor-Yiu Sin, Prof. Ali R. Tafti, Prof. Pratyush Nidhi Sharma, Prof. Marko Sarstedt, Prof. Nicholas Patrick Danks, Prof. Soumya Ray, Prof. Akhmed Umyarov

Comparative Syntax from an Interdisciplinary Perspective

Professor Wei-Tien Dylan Tsai
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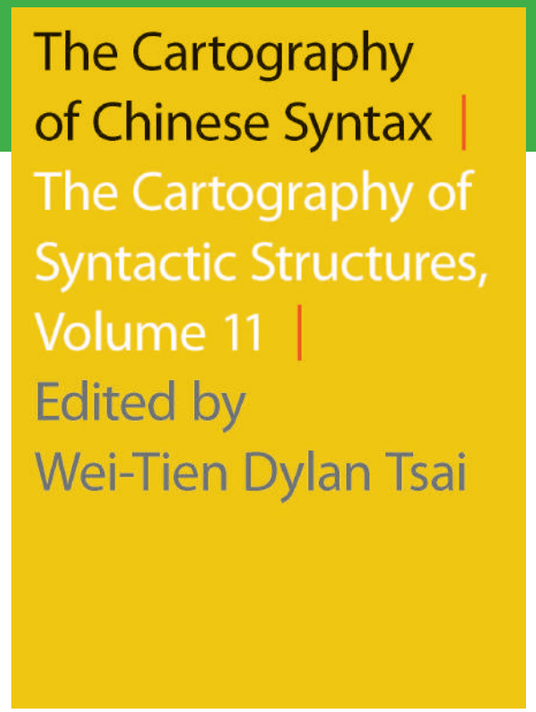


book cover of The Cartography of Chinese Syntax

First and foremost, I investigated the nature of silent mood/force categories within the principles-and-parameters framework, and showed how particular morpho-syntax factors may interact with the setting of a macro-parameter such as analyticity. On the empirical front, I extended my research on the quantificational/predicational properties of reflexive and wh-expressions across languages: These expressions may be construed either as operators or variables, depending on the type of architecture employed to construct an operator-variable pair. The particular settings of individual languages in turn motivate the choice between the two most important operations of syntax, i.e., Merge and Move.

In recent years, I also got interested in the experimental aspects of grammaticality judgments and disambiguation strategies. I have learnt from years' experience of fieldwork and questionnaire studies that text examples are both misleading and inefficient. Though lacking the relevant expertise, I took the initiative to work with people in the experimental science, producing some very interesting results on non-canonical question construals, which are shown to be triggered by certain silent categories in the syntactic structure. Finally, as a fresh move to broaden the landscape of Chinese linguistics and to create a more healthy and friendly job market for our younger generations, I reached out and proposed a joint venture with Prof. Jason Chang from the department of computer science at NTHU. We have received a 4-year excellence grant from the Ministry of Science and Technology of Taiwan, and have carried out a series of data-scientific studies on Modern Chinese grammar (including Chinese Linggle and a big data analysis of so-called "transitivization" phenomena).

Research Highlights

- President of Linguistic Society of Taiwan, 2017~2019
- Editor of International Journal of Chinese Linguistics, 2013~
- Associate Editorial Board of Linguistic Inquiry, 2012~

Research Output

- Tsai, Wei-Tien Dylan (2018) "High Applicatives are not High Enough: A Cartographic Solution," Lingua Sinica 4.1: 1-12.
- Tsai, Wei-Tien Dylan, ed., (2015) The Cartography of Chinese Syntax, New York: Oxford University Press.
- Tsai, Wei-Tien Dylan (2015) "On the Topography of Chinese Modals," in Ur Shlonsky (ed.), Beyond Functional Sequence, 275-294. New York: Oxford University Press.

Professor Tsai, project assistants, and seminar students

Commitment of Literature and Poeticality

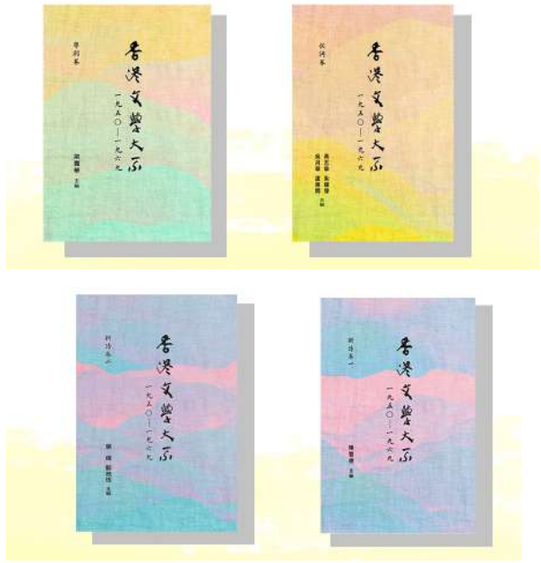
Professor CHAN, Kwok Kou Leonard
ckkleonard@mx.nthu.edu.tw

Discourses on Chinese Lyrical Tradition and Literary Historiography (Taipei, China Times Publishing Company, 2021).

My research focuses not only on the internal structure of literature, but also the synchronic and diachronic interrelation and interaction of various series of structures including those of different art forms, and cultural, social, and political environments which were often regarded as contexts extrinsic to literature. My achievements are as follows:

1. Compilation of *The Compendium of Hong Kong Literature 1950-1969*:
Refusing to consign to oblivion Hong Kong literature, I have been working with colleagues to compile the *Compendium of Hong Kong Literature 1950-1969* since 2017. The output will be a set of 16 volumes in print form, and 5 of which are published. Each of these volumes consists of a selection of the major texts of a particular genre, such as poetry, essay, novel, drama, literary critiques, etc., and a long introduction addressing the production of these selected texts and their aesthetic and historical values. With the completion of this project, we are able to demonstrate that literature of a particular place is also the embodiment of its physical and spiritual characters.

2. Monograph Published: *Discourses on Chinese Lyrical Tradition and Literary Historiography*:
Corresponding to the "Hong Kong project" but with a broader horizon, I conducted an extensive research to delve into the "Chinese lyrical tradition". I expound the theses and discourses of prominent scholars such as Chen Shih-hsiang (1912-1971), Kao Yu-kung (1929-2016), Lin Geng (1910-2006), Hu Langcheng (1906-1981), Sima Chengfeg (1920-1980), as well as that of Jaroslav Průšek (1906-1980), the greatest Czech sinologist in the twentieth century. Their views on the formation and development of the Chinese literary tradition are salient for our understanding of the history of Chinese literature and culture, and also the interweaving relationship between literature and the society. The output is a recently published monograph entitled *Discourses on Chinese Lyrical Tradition and Literary Historiography*.



The Compendium of Hong Kong Literature 1950-1969. (Hong Kong, The Commercial Press, 2020).

3. Integrated Research Project reviewed and supported by the Ministry of Science and Technology:
In the course of the investigation mentioned above, I found that the conception of "poeticality" is an issue needed to be addressed, both historically and theoretically. Hence I invited four colleagues from the Department of Chinese Literature, National Tsing Hua University, to form a team to conduct the research. We submit a project proposal entitled "A Study of the 'Poeticality' of Chinese Literature" for the application of funding from the Ministry of Science and Technology. This is a multi-year Integrated Research Project aiming to throw lights on the genesis of poeticality in different periods of the historical past, and examine the various factors contributing to its continuity, interruption, and deviation. The project has been reviewed and approved with very encouraging comments.

Research Highlights

- 2019-2021. Yushan Scholar Program, Ministry of Education
- 2019-2021. Arts Development Grant, from Hong Kong Arts Development Council (Project title: "The Compendium of Hong Kong Literature 1950-1969")
- 2021-2024. Integrated Research Project, supported by the Ministry of Science and Technology (Project title: "A Study of the 'Poeticality' of Chinese Literature.")

Research Output

- *Discourses on Chinese Lyrical Tradition and Literary Historiography* (Taipei, China Times Publishing Company, 2021).
- "In and Out of 'Lyric Aesthetics'—Kao Yu-kung's Academic Journey Revisited," *Journal of Chinese Literature* (Beijing and Hong Kong), 7 (Dec 2019): 131-151.
- "Ruptures and Continuities in Literature and Literary History: General Preface to the *Compendium of Hong Kong Literature 1950-1969*," *NTU Studies in Taiwan Literature* (Taipei), 23 (Feb 2020): 1-20.

Professor. CHAN, Kwok Kou Leonard

The Migrations of Taiwanese Young People to China and Contemporary Exchanges between Kinmen, ROC and Fujian, China

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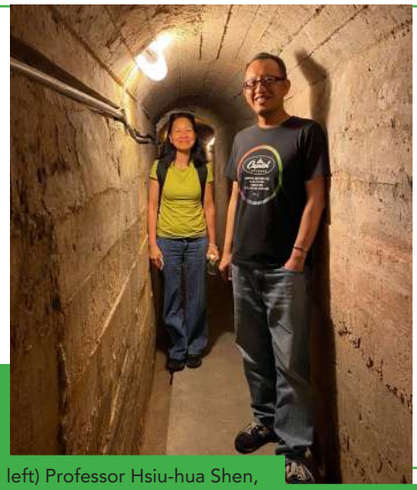
The photo was taken during a fieldtrip in Kinmen, ROC. It was a large painted wall advert at a popular tourist site for historical western-style buildings in Kinmen. The ad is about selling "Mao Zedong bubble tea "mixed with Kinmen Kaoliang Liquor, milk, and tea. The photo shows how Kinmen's special positions between Taiwan and China and how cross-Strait politics have ironically translated into daily life.

The number of Taiwanese students to China for study has increased significantly in the last two decades. This phenomenon has much to do with Chinese government's political agenda to claim Taiwan's sovereignty by releasing educational resources and privileges to and by promoting a nationalistic discourse of "Chinese Dream" upon Taiwanese. Our research project explores the social and political processes in which Taiwanese travel to China for educational purposes. In our analyses, we adopt the concept of "rent" from economic sociology to conceptualize Chinese government's educational privileges to Taiwanese as "educational rent." We also take the concept of "migration infrastructure" as the analyzing framework to investigate how Chinese government's educational rents mobilize various Taiwanese and Chinese to establish migration infrastructures to make it possible for educational movements from Taiwan to China. Our research project is a timing study to understand the significances of "China Factor" in the field of international education. We have coauthored a journal article, "Rent-Seeking" and Migration Infrastructure: Educational Movements from Taiwan to China" which is under reviewed. Through our field works, we have found that Kinmen, a frontier of Taiwan to China an important and interesting place for various cross-border exchanges between Taiwan and China. Thus, we have developed a research project to explore contemporary exchanges between Kinmen and Fujian, China and how such exchanges have shaped local imaginations of economic developments and political identities. We have also developed another collaborative research project, "Taiwanese Young Talents' Migrations to China and the Social and Political Implications of Such Crossings" funded by the Ministry of Science and Technology, Taiwan to expand our previous project on Taiwanese students to China to include other groups of Taiwanese youth who have gone to China to start a business or to work. We hope through our research projects to understand the contemporary processes and mechanisms of making Taiwanese people migrating to China for economic and other opportunities, the significance of China Factor in shaping Taiwan and China relations, and China's strategies of attracting foreign talents to China.

Research Output

- Hsiu-hua Shen & Chih-peng Cheng. "Rent-Seeking" and "Migration Infrastructure: Educational Movements from Taiwan to China," under review.
- Hsiu-hua Shen, 2021. "Kinmen: As a Borderland of Frontier and Margin." Presented at the annual meeting Taiwanese Anthropological Meeting, September 26, 2021.



(from left) Professor Hsiu-hua Shen, Professor Chih-peng Cheng during a fieldtrip in Quemoy, 2019.