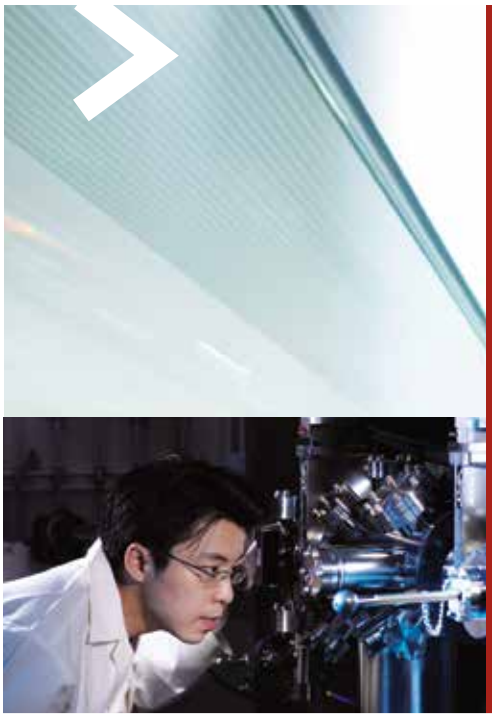
ISSUE 4 · 2013

PUSHING

Frontiers

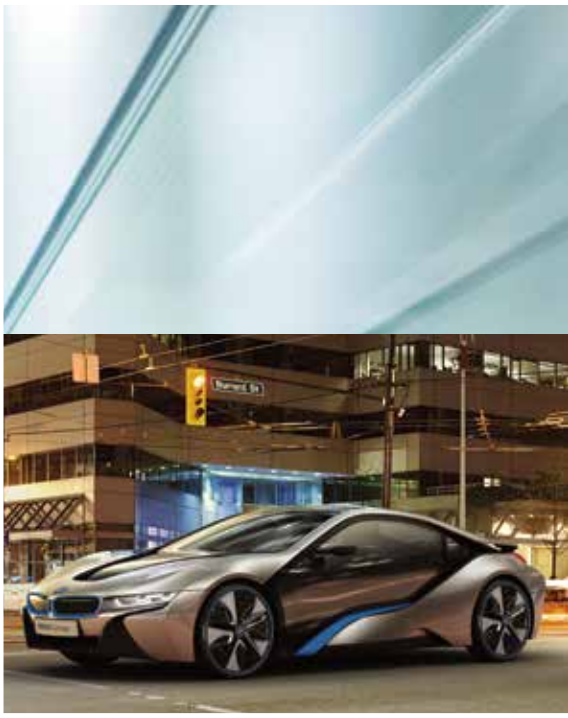
SINGAPORE



In Good Company

Big Businesses On NTU Campus

- Rolls-Royce
- BMW
- Lockheed Martin



RESEARCH & INNOVATION

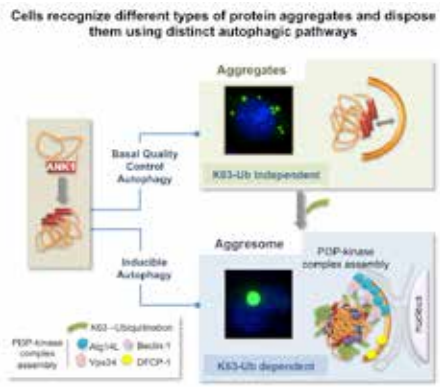
Coming To NTU In Singapore

World Cultural Council 30th Award Ceremony

Inaugural World Academic Summit

NANYANG TECHNOLOGICAL UNIVERSITY

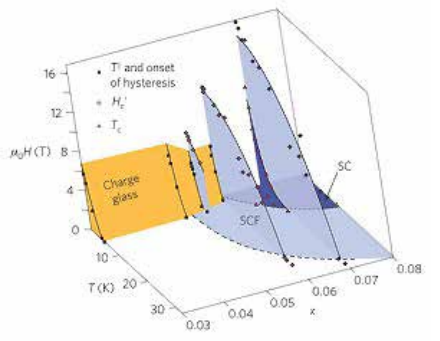
New Insights Into Key Cellular Mechanisms Pave The Way For Novel Treatments For Neurodegenerative Diseases



Neurodegenerative diseases such as Parkinson's disease and Alzheimer's disease are associated with aggregates of proteins that fail to be cleared from brain cells by the cells' proteolytic systems. A study led by Asst Prof Esther Wong from NTU's School of Biological Sciences, in collaboration with US scientists from the New York Albert Einstein College of Medicine, Mount Sinai School of Medicine and Boston University Medical School, finds that inclusion of the protein synphilin-1 (Sph1) in protein aggregates promotes autophagy, a degradative mechanism that sequesters and discharges protein aggregates and other dysfunctional cellular components. The researchers further show that small protein aggregates are mainly removed through basal quality-control autophagy while disposal of large protein aggresomes is achieved through inducible autophagy. In addition, the study demonstrates that the ANK1 peptide domain of Sph1 is both necessary and sufficient for basal as well as inducible autophagic clearance. The study has implications on the development of therapeutics for cellular disorders that are associated with dysfunctional protein aggregates.

The article "Molecular determinants of selective clearance of protein inclusions by autophagy" was published in Nature Communications *(2012) Vol. 3: 1240; DOI:10.1038/ncomms2244.*

Unravelling The Electronic Structure Of High Temperature Superconductors

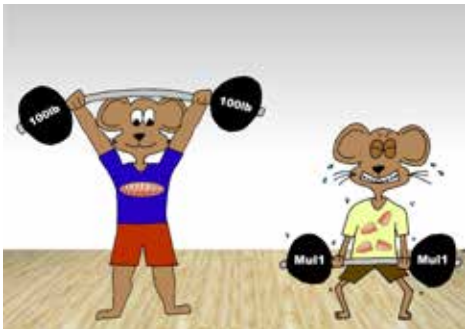


Phase diagram of the glassy region and of the onset of superconducting fluctuations in $La_{2-x}Sr_xCuO_4$.

The complex electronic structure of high temperature superconductors poses immense challenges in determining how these materials lose their electrical resistance and how to modify them to make this transition occur above room temperature. Assoc Prof Christos Panagopoulos from NTU's School of Physical and Mathematical Sciences, together with an international research team, elucidated the processes that are involved in the transition from plain insulators such as La_2CuO_4 to unconventional superconductors through doping with strontium ($La_{2-x}Sr_xCuO_4$). Their study indicates a charge ordering instability due to a disproportionation of electrons – an intrinsic property of these superconductors – that is linked to the emergence of high temperature superconductivity, and demonstrates that the superconductor insulator transition is not an abrupt transition. Understanding the electronic properties of these materials is essential for innovations such as power lines using superconducting wires that do not lose electricity in transit. In addition, superconductors exhibit special magnetic properties that could allow for levitated, frictionless trains and stronger, more durable permanent magnets like those used in wind turbines.

The article "Emergence of superconductivity from the dynamically heterogeneous insulating state in $La_{2-x}Sr_xCuO_4$" was published in Nature Materials *(2012) Vol. 12: 47; DOI:10.1038/NMAT3487.*

Molecular Insights Into Mitochondria Loss In Muscle Cells Could Open Up New Therapies Against Skeletal Muscle Wasting



Skeletal muscle wasting is a consequence of myopathies (muscular diseases, e.g. muscular dystrophy) or conditions like cancer, AIDS, sepsis, obesity, diabetes and ageing. Also starvation, muscle disuse and motor neuron diseases such as multiple sclerosis frequently lead to muscle loss. Assoc Prof Ravi Kambadur from NTU's School of Biological Sciences, in collaboration with researchers from the National University of Singapore and the Agency for Science, Technology and Research, recently unravelled the molecular basis for the extensive dysfunction and loss of muscle cell mitochondria during skeletal muscle wasting. Studies in muscle cell cultures and mouse models showed that starvation or denervation (interruption of the nerve-muscle connection) enhanced the activity of a novel mitochondrial protein, Mul1, through a cellular signalling cascade involving Myostatin. The increased expression of Mul1 through Myostatin was responsible for the mitochondrial dysfunction and loss observed in *in vitro* and *in vivo* models of muscle wasting.

Future joint clinical research with Singaporean hospitals aims to evaluate pharmacological inhibition of Myostatin and Mul1 as a tool to control skeletal muscle wasting and other conditions such as obesity and diabetes.

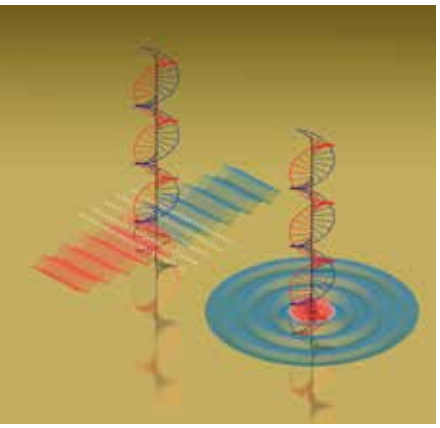
The study "The ubiquitin ligase Mul1 induces mitophagy in skeletal muscle in response to muscle-wasting stimuli" was published in Cell Metabolism *(2012) Vol. 16: 613, DOI:10.1016/j.cmet.2012.10.005.*

SynPhNe: A Platform For Recovery From Paralysis After Stroke

Dr John Heng (right) and Banerji Subhasis (left), wearing the arm gloves.

Rehabilitation after stroke is a long and cumbersome process with often limited success and high patient dropout rates. The Synergistic Physio-Neuro Stroke Rehabilitation Device (SynPhNe), developed by a team of researchers led by Dr John Heng and PhD student Banerji Subhasis from the Robotics Research Centre at NTU's School of Mechanical and Aerospace Engineering, has shown impressive results in improving patients' physical abilities beyond the levels reached by conventional rehabilitation therapy. SynPhNe consists of patented computer software connected to a specifically designed neural sensor headset and a sensor arm glove, and allows the coordinated training of the patient's brain and body abilities. Conveniently usable at home, the multi-modal associative learning system requires the patient to follow instructional videos for limb movements while the sensors provide feedback on the stress, attention, activation and relaxation levels of both brain and muscles. Immediate feedback enables the patients to learn, adjust and control the brain-body coordination of the affected muscles. Patients who had reached a progress plateau after several months of conventional treatment achieved significant progress in their ability to carry out everyday tasks after using SynPhNe for a 4-week trial period. A start-up company is being planned to commercialise a portable version of the SynPhNe stroke therapy kit for rent or at-home rehabilitation.

Precise Directing Of Optical Data Signals to Electronic Devices

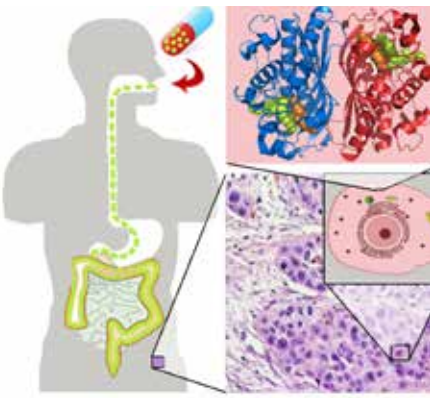


Picture Credit: Samuel Twist.

A new generation of on-chip optical interconnects can convert data information directional and efficiently from optical to electronic devices. An innovative study, led by NTU graduate Dr Jiao Lin and the Microoptics group from NTU's School of Electrical and Electronic Engineering together with researchers from Harvard School of Engineering and Applied Sciences, USA, discovered a way to precisely control the directivity of data signals. Using a nanoscale coupler made up of a thin sheet of gold, incoming light is converted into surface plasmon polaritons (SPPs) – the oscillations or 'waves' formed by the electrons at the surface of a metal. Tiny slit perforations in the gold sheet device – featuring a distinct herringbone structure – direct the incoming light depending on its polarisation. Left- and right-handed circular light will be routed to the left or right, respectively, while linear polarised light will be routed equally in both directions. Thus, manipulating the polarisation of the light signal allows precise directing of the data signal. In addition, the new plasmonic device can be applied to circular structures that create radially convergent and divergent SPPs. The innovation has important applications in optical information technology and optoelectronics.

The study "Polarization-controlled tunable directional coupling of surface plasmon polaritons" was published in Science *(2013) Vol. 340: 331; DOI:10.1126/science.1233746.*

Direct Monitoring Of Drug Efficacy In Cells And Tissues



The path of a drug from pill to drug target.

The efficiency with which a drug reaches and interacts with its target proteins in cells is critical for the outcome of drug therapies. Drug-target engagement can vary significantly during therapy and in individual patients, bearing risks of inherent or acquired drug resistance. In addition, the adverse effects of drug therapies are often caused by excessive or off-target drug binding. Due to the lack of suitable methods to monitor drug-target engagement directly in cells and tissues, drug efficacy is measured indirectly in downstream cellular responses. A new method discovered by a research team led by Prof Pär Nordlund from NTU's School of Biological Sciences allows measuring drug-target engagement directly in cell lysates of mammalian cell cultures. The novel cellular thermal shift assay (CETSA) measures changes in the thermal melting curves and thus stabilisation patterns of target proteins exposed to different temperatures and varying drug concentrations. The isothermal dose-response procedure applied in the CETSA yields characteristic fingerprints of drug-target engagement and allows validating drug binding in cancer cell lines and monitoring of drug transport and activation processes, off-target effects, drug resistance and drug distribution in tissues. Since the new method will likely be a valuable tool at many steps of drug development, several pharmaceutical companies have already expressed interest in research collaborations.

The study " Monitoring drug target engagement in cells and tissues using the cellular thermal shift assay" was published in Science *(2013) Vol. 341: 84; DOI:10.1126/science.1233606.*