

Area of Excellence Scheme – Highlights of Achievements

Molecular Neuroscience: Basic Research and Drug Discovery

In 2001, a cross-institutional research project led by the Hong Kong University of Science and Technology (HKUST) was allocated \$26.8 million from the University Grants Committee (UGC) Area of Excellence (AoE) Scheme. The five-year project, entitled “Molecular Neuroscience: Basic Research and Drug Discovery” aimed to advance the frontiers of neuroscience research, and establish new strategies and tools towards developing novel treatments for brain diseases. A highly-talented multi-disciplinary team with proven strengths in leading-edge research was amassed, cutting-edge research was undertaken, and a unique drug development approach based on Traditional Chinese Medicine (TCM) was established. Novel TCM-derived drug candidates as potential treatments for brain-related ailments were subsequently identified. Upon reassessment in 2007, UGC commended the project as “*an impressive programme with exceptional performance*” and provided the team with additional funding of \$27.5 million for another three years. With this sustained funding, the team examined the complex processes within the brain and explored the mechanisms underlying specific neuro-related diseases. The TCM-derived novel compounds underwent further pre-clinical investigations, while potential strategic partners for their downstream commercial development were identified.

Establishing Research Excellence

A unique knowledge-based drug-discovery strategy was undertaken whereby TCM herbs were used as the source for potential drug candidates. A world-class research infrastructure with best-in-class facilities for TCM herb fractionation and cell-based high throughput drug screening was developed. A large collection of herbs, correlated with specific neurological activities based on centuries of documentation, were amassed which facilitated herb selection, while the process of effectively isolating biologically active compounds from TCM herbs was developed and optimized. A variety of proprietary drug screening tools and novel methodologies as well as a variety of animal models were also established. All of these have major implications in brain research and the future development of therapeutics for brain diseases. Under the sustained funding, the team particularly focused on strengths in molecular and cellular mechanisms, resulting in numerous breakthroughs within the field. These include understanding the manner in which neural cells communicate with each other, unveiling previously unknown mechanisms that drive specific biological activities in normal and disease brains, identifying the key proteins and molecular targets that play major roles in neurodegenerative diseases, and developing drug leads for treating brain-related ailments. All of these have major implications in brain research and the future development of therapeutics for brain diseases. For instance, the AoE team has identified a novel role of a cell surface protein EphA4 in the regulation of brain plasticity, a phenomenon underlying our cognitive functions by allowing nerve cells to adjust their functional efficacy based on experience. Since many neurodegenerative diseases are associated with impaired neurotransmission, these findings highlight EphA4 as a potential target for developing novel treatments to alleviate cognitive deficits in afflicted patients.

Development of Therapeutic Drugs for Clinical Application

The project yielded a portfolio of novel and promising compounds with potential clinical applications in Alzheimer’s disease and insomnia. The team also identified TCM herbs as active drug leads against targets associated with Parkinson’s disease and depression. Due to the unique drug discovery strategy undertaken by the team, these have been explored by pharmaceutical companies for potential collaborations in their further development towards clinical trials.

Strategic Partnerships with Leading Global Pharmaceutical Companies

The AoE team forged strategic alliances with the biopharmaceutical industry to strengthen and enhance the project. For example, GlaxoSmithKline (GSK) R&D China, a China-based subsidiary of GSK, a leading pharmaceutical company, expressed their interest in the AoE deliverables and a strategic alliance between HKUST and GSK R&D China was established in 2009. The collaborative work between the two organizations is aimed at identifying drug leads for the treatment of neurodegenerative disorders and a joint “GSK R&D China - HKUST Neuroscience Laboratory” has been established at HKUST for this purpose. This has been an important strategic alliance as it has brought attention to the high level of research being undertaken at HKUST and placed Hong Kong prominently on the global R&D map.

Other Major Accomplishments

State Key Laboratory: In recognition of the achievements made under the AoE Scheme, in 2010, the Ministry of Science and Technology approved the establishment of the “State Key Laboratory (SKL) of Molecular Neuroscience” at HKUST, the first and only SKL at HKUST. This national standing represents the Chinese Government’s recognition of HKUST’s unremitting efforts and excellence in conducting neuroscience research and development. Armed with this distinction, the Laboratory aims to become one of the world’s leading research centers in this discipline - to advance basic research in molecular neuroscience, and to stimulate the formation of new biotechnology ventures in China.

Publications and Lectures: The breakthrough research undertaken under the AoE resulted in a vast output of publications in prestigious international journals such as *Cell*, *Science*, *Nature Cell Biology*, *Molecular Cell*, *Nature Neuroscience*, *Neuron*, *Nature Structural Biology*, *PLoS Biology*, *Journal of Cell Biology*, *PNAS*, *Journal of Neuroscience*, and *Journal of Biological Chemistry*. To date, the AoE team has published over 600 research papers. Team members have also been invited to deliver plenary or symposium lectures at over 300 international conferences and workshops, as well as write review articles on specific subjects in neuroscience-related research areas. The AoE team has actively promoted their breakthrough findings through international symposiums and conferences such as the prestigious Gordon Research Conference, a bi-annual event attended by leading neuroscientists and Nobel laureates, and by organizing the Molecular Neuroscience Seminar Series and the Croucher Advanced Study Institute.

Education and Training Opportunities for Young Local Scientists: The AoE project also significantly contributed to student training and skills development in the area of molecular neuroscience. More than 120 postgraduate students (PhD, MPhil and MSc) in participating departments were actively involved in the project, while over 40 undergraduate students were assigned to the project in each of the three years. Students thus acquired invaluable hands-on training in advanced technologies while sharpening their research proficiency.

**The above summary is written by the project team. The views expressed in the summary do not necessarily represent those of the University Grants Committee/ Research Grants Council.*