MEDIA RELEASE

Synthetic Macromolecules Proven to Kill Multidrug-resistant Cancer Cells, Prevent the Spread of Cancer, and Avert Drug Resistance Development

Singapore, April 12, 2018 – A multidisciplinary research team from A*STAR's Institute of Molecular and Cell Biology (IMCB), Institute of Bioengineering and Nanotechnology (IBN), and Genome Institute of Singapore (GIS), together with IBM Research, has developed synthetic macromolecules that have been proven to kill multidrug-resistant cancer cells and cancer stem cells, prevent the spread of cancer cells (metastasis), and avert the development of drug resistance. These novel macromolecules have the potential to be developed into an anti-cancer drug to treat cancer patients and prevent cancer relapse.

The team focused its studies heavily on the use of macromolecules – large molecules or polymeric assemblies – which exhibit unique properties to attack diseases by mechanisms different from traditional therapies. This emerging discipline of study, pioneered by researchers such as Dr Yi Yan Yang from A*STAR's IBN and Dr James Hedrick from IBM Research, is known as Macromolecular Therapeutics. Its use in destroying cancer cells was demonstrated in collaboration with Dr Qingfeng Chen from A*STAR's IMCB, and Dr Paola Florez de Sessions from A*STAR's GIS, and was recently published in the peer-reviewed journal, *Journal of the American Chemical Society*.

Cancer affects many people, and is a leading cause of death worldwide. Multiple treatments with conventional chemotherapeutic drugs have led to the development of drug resistance, therefore cancer metastasis and relapse also occur in many patients. The US government has established the Cancer Moonshot initiative with the intent of vastly accelerating cancer research and delivering improved treatment regimens. A critical aim of this programme, outlined in the 2016 Blue Ribbon Panel Report, is to overcome drug resistance of cancer. There is an urgent need to develop new therapeutics that can kill multidrug-resistant cancer cells without inducing drug resistance development after multiple treatments.

To tackle such a complex challenge, a multidisciplinary research team that involved researchers from diverse fields including chemistry (IBM Research), cancer biology (IMCB), bioengineering (IBN), and genomics (GIS), was required. In this study, the researchers demonstrated that a macromolecule containing positively charged components could bind to the negatively charged surfaces of cancer cells. They also proved that another portion of the macromolecule assimilated into the cell membrane, poked holes in the cancer cell and destroyed it. In early tests, the macromolecule proved successful in 1) combating multidrug-resistant cancer cells and cancer stem cells, 2) preventing cancer cell migration (metastasis) and 3) defying drug resistance after multiple treatment applications.

The new study was built on a May 2016 study about the discovery of a macromolecule to treat viruses, and a more recent study published in March 2018 which showed that macromolecules may help fight superbugs such as MRSA in the future. The study of macromolecular therapeutics spans several years and multiple diseases, affording numerous applications including consumer product additives, treating systemic viral and bacterial infections, addressing agricultural disease, and cancer treatment. Fundamental

advancements in synthetic polymer chemistry form the foundation for these therapeutic platforms, enabling the preparation of biocompatible and degradable macromolecules with precisely defined properties.

“Our hypothesis was that with macromolecular compounds, we could limit the growth of tumours by inducing membrane lysis and necrosis inside tumours without significant adverse effects in patients,” said Dr Qingfeng Chen, Principal Investigator at A*STAR’s IMCB.

Dr Yi Yan Yang, Group Leader at A*STAR’s IBN, said, “The macromolecules were designed to self-assemble into core-shell structured nanoparticles, which accumulate in tumour tissues. The shell prevents the anti-cancer core from interacting with healthy cells before reaching the tumour. Upon arrival at the tumour site, the shell will crack open to expose the cancer-killing component that interacts with negative charges on the cancer cell membrane to disrupt the membrane and kill the cell.”

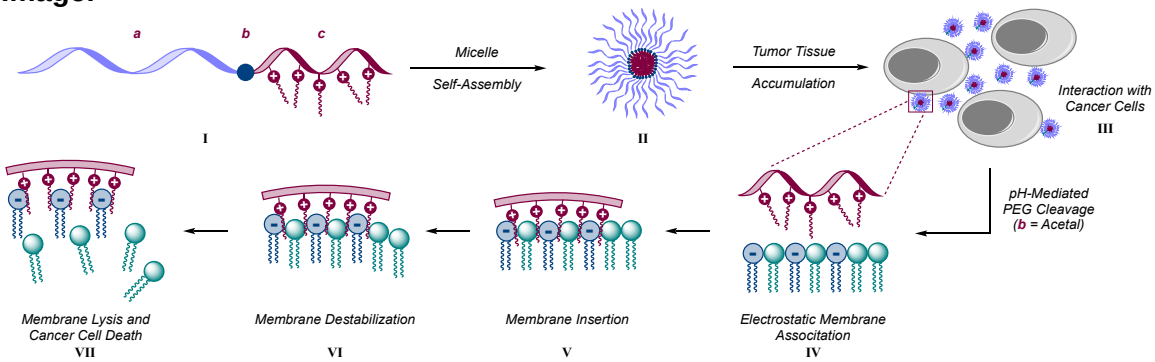
The team collaborated with Dr Paola Florez de Sessions from A*STAR’s GIS to perform the transcriptomic analysis. They found that the macromolecular compounds were relatively inert compared to conventional anti-cancer drugs.

“While we are excited about the promise of this study, we note that it is still in its early stages of research. We are seeking pharmaceutical industry partners to help accelerate making this macromolecular treatment available to cancer patients,” said Dr James Hedrick, Distinguished Research Staff Member at IBM Research – Almaden, San Jose, California.

Reference:

1. Nathaniel H. Park, Wei Cheng, Fritz Lai, Chuan Yang, Paola Florez de Sessions, Balamurugan Periaswamy, Collins Wenhan Chu, Simone Bianco, Shaoqiong Liu, Shrinivas Venkataraman, Qingfeng Chen, Yi Yan Yang, James L. Hedrick, “Addressing Drug Resistance in Cancer with Macromolecular Chemotherapeutic Agents”. *Journal of the American Chemical Society*.

Image:



Macromolecule self-assembles into core/shell structured nanoparticle that accumulates in tumour tissue, cleaves the shell to expose the anti-cancer component that interacts with negative charges on cell membrane, disrupts the membrane, killing the cell.

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About the Institute of Molecular and Cell Biology

The Institute of Molecular and Cell Biology (IMCB) was launched on 23 January 1985, with its official opening ceremony held on 2 October 1987 at the National University of Singapore (NUS). It subsequently became an autonomous research institute (RI) of A*STAR, moving to Biopolis in 2004. IMCB's vision is to be a premier cell and molecular biology institute which addresses the mechanistic basis of human diseases and its mission is to conduct cutting-edge discovery research in disease pathways; to groom early career researchers to be future leaders in research; and to collaborate with medical and industry communities for research impact. IMCB plays an important role training and recruiting scientific talents, and has contributed to the development of other research entities in Singapore. Its success in fostering a biomedical research culture in Singapore has catalysed Singapore's transformation into an international hub for biomedical research, development and innovation.

Funded primarily by the Biomedical Research Council (BMRC) of A*STAR, IMCB's Discovery research comprises 5 major programmes: Cancer Cell Signalling, Multi-Modal Molecular (M3) Biology, Epigenetics and Diseases, Stem Cell, Regenerative Medicine and Ageing, and Technology and Translation. IMCB's technologies and platforms focus on Genome-wide RNAi, Humanised Mouse Models, Proteomics and Protein Engineering, Gene Therapy and Gene Editing, and Molecular Histopathology.

IMCB strives to maintain the scientific excellence of PI-driven research and at the same time aims to promote collaborative team-based projects of medical and industrial relevance.

For more information about IMCB, please visit www.imcb.a-star.edu.sg.

About the Genome Institute of Singapore
The Genome Institute of Singapore (GIS) is an institute of the Agency for Science, Technology and Research (A*STAR). It has a global vision that seeks to use genomic sciences to achieve extraordinary improvements in human health and public prosperity. Established in 2000 as a centre for genomic discovery, the GIS will pursue the integration of technology, genetics and biology towards academic, economic and societal impact.

The key research areas at the GIS include Human Genetics, Infectious Diseases, Cancer Therapeutics and Stratified Oncology, Stem Cell and Regenerative Biology, Cancer Stem Cell Biology, Computational and Systems Biology, and Translational Research.

The genomics infrastructure at the GIS is utilised to train new scientific talent, to function as a bridge for academic and industrial research, and to explore scientific questions of high impact.

For more information about GIS, please visit www.gis.a-star.edu.sg.

About the Institute of Bioengineering and Nanotechnology
The Institute of Bioengineering and Nanotechnology (IBN) is the world's first bioengineering and nanotechnology research institute. Established in 2003, IBN's mission is to conduct multidisciplinary research across science, engineering, and medicine for breakthroughs to improve healthcare and quality of life. IBN's research activities are focused on Nanomedicine, Synthetic Biosystems, Biodevices and Diagnostics, and Green Chemistry and Energy. The Institute has published over 1,330 papers in leading scientific journals, filed over 660 active patents and patent applications on its inventions, and established 13 spin-off companies. To nurture young research talents, IBN runs a Youth Research Program that offers students research attachment opportunities and exposure to biomedical research. For more information on IBN, please visit www.ibn.a-star.edu.sg.

About the Agency for Science, Technology and Research (A*STAR)
The Agency for Science, Technology and Research (A*STAR) is Singapore's lead public sector agency that spearheads economic oriented research to advance scientific discovery and develop innovative technology. Through open innovation, we collaborate with our partners in both the public and private sectors to benefit society.

As a Science and Technology Organisation, A*STAR bridges the gap between academia and industry. Our research creates economic growth and jobs for Singapore, and enhances lives by contributing to societal benefits such as improving outcomes in healthcare, urban living, and sustainability.

We play a key role in nurturing and developing a diversity of talent and leaders in our Agency and Research Institutes, the wider research community and industry. A*STAR oversees 18 biomedical sciences and physical sciences and engineering research entities primarily located in Biopolis and Fusionopolis.

For more information on A*STAR, please visit www.a-star.edu.sg.