05/22/2017

Collaboration with A*STAR's p53 Laboratory to establish the novel drug screening technology facilitating the "undruggable" PPI targets to "druggable".

Nagoya, Japan – May, 22, 2017 - MEDICAL & BIOLOGICAL LABORATORIES Co., Ltd. (MBL) announced today that it has entered into a collaboration agreement with the p53 Laboratory, Agency for Science, Technology and Research (A*STAR) in Singapore to establish the novel screening technology which accelerates the drug discovery targeting Protein-Protein Interactions (PPIs). MBL provides an innovative real-time PPI visualization technology called Fluoppi™ to simultaneously visualize the cell permeability and intracellular activity of the PPI-targeted peptide therapeutic candidate developed by p53 Laboratory.

Fluoppi™ enables the real-time "visualization" of intracellular PPIs in living cells

MBL has developed a technology called Fluoppi™, which visualizes modulations of PPIs in living cells. This novel technology is marketed globally and utilized by users such as pharmaceutical companies as a unique drug screening tool.

Inhibition of PPI requires compounds with relatively large molecular weight. However, these compounds have low cell membrane permeability and are often unable to enter cells. Therefore, there are many cases that compounds showing PPI inhibition in biochemical assays fail to show activity in cell-based assay. Phenotypic assays are performed to check the effect of drug candidates inside the cells especially in the case of drug discovery targeting tumorigeneses, but this fails to discriminate whether the cell death is due to an on-target effect or an off-target effect. For such cases, Fluoppi™ allows researchers to "visualize" the drug candidates that penetrate the living cells and modulate intracellular PPIs. This provides evidence that the drug candidate actually has the intended mechanism of action.
For further information of Fluoppi™, please see the URL below:
http://ruo.mbl.co.jp/bio/g/product/flprotein/fluoppi.html

By enhancing the practical utility of Fluoppi™ technology through this collaboration, MBL aims to contribute to the drug discovery of novel peptide drugs and PPI modulators which could lead to the new treatment for currently untreatable diseases.

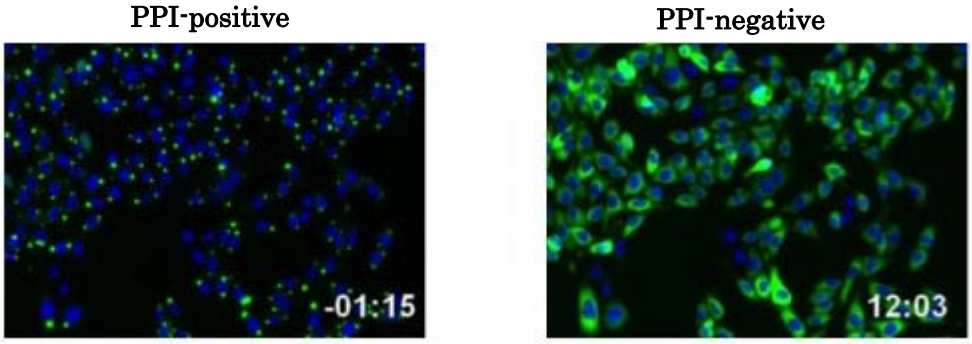

Fig. Visualization of PPI using Fluoppi™

Intracellular PPI as a novel drug target

Because of the shortage of new drug candidates, growing interest has been paid to PPIs as drug discovery targets. Conventional drug targets such as kinase, GPCR, ion channel, extracellular protein comprise only 20 % of all the proteins in our body. To reach the remaining 80 % traditionally "undruggable" targets, many pharmaceutical companies start drug discovery targeting PPIs.

This change is supported by recent technology innovation. It has been difficult to develop PPI modulators because PPI composite surface has few pockets that are deep enough for small molecule compounds to bind comparing to ATP binding pocket of kinase or ligand binding site of GPCR. This results in difficulty to develop high potent compounds. However, progress of structure chemistry, computer chemistry, strategies to create low molecular weight of compounds, and diversification of drug modality enable successful modulations of PPIs by drugs and now many candidates are being studied in clinical trials.

Peptide therapeutics enable targeting intracellular PPI

Intensive R&D competition occurs globally to develop peptide drugs, because of its high specificity which is comparable to antibody medicine and its ability to target intracellular molecules which could not targeted by antibody. The global peptide therapeutics market was valued at $17.5 billion in 2015[*1]. To use peptides as drugs targeting intracellular PPIs, there are problems such as low stability in blood and low cellular membrane permeability. Researchers are now trying to resolve these problems by chemical modification to the peptides. Specifically, p53 Laboratory has a technology by which linear peptides are cyclized to create stapled peptides with high stability and membrane permeability. By using this technology, they produce peptide therapeutic candidates targeting intracellular PPI.

[References]

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[*1] SABYASACHI GHOSH, (2016) Peptide therapeutics market: forecast and analysis 2015-2025. Oligos & Peptides - Chimica Oggi - Chemistry Today - vol. 34(2), 5-7

About p53 Laboratory

The A*STAR p53 Laboratory, is headed by Professor Sir David Lane. Widely known as the founder of the p53 molecule, Professor Sir David Lane is a globally famous and award-winning researcher who has published more than 350 research papers. The p53 Laboratory engages in comprehensive R&D activity ranging from basic research to the development of new therapeutics and diagnostics focusing on p53 pathway.

About MBL
MEDICAL & BIOLOGICAL LABORATORIES, Co., Ltd. was founded in 1969 as the first antibody manufacturer in Japan. MBL then expanded its business beyond immunology into other areas of research, such as gene diagnoses and topics related to intercellular signaling. MBL now conducts research, development, production, and sale of clinical diagnostic and basic laboratory reagents.

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