Medicinal Bioconvergence Research Center:

Innovation of Drug Discovery through Novel Target Discovery and Convergence Technology

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The extension of life expectancy dramatically increases chronic diseases such as cancer, dementia, diabetes, and cardiovascular diseases. Besides, a pandemic is considered as one of the four major risks at global level based on the recent OECD reports. Nonetheless, new drug discovery stays stagnant during last decade and ironically, pharmaceutical industry suffers from low return of investment in R&D. In 2010, only 21 new drugs were approved by FDA, USA. (see Fig. 1).

Since 2009, the Korean Ministry of Education, Science and Technology (MEST) has initiated the new program named 'Global Frontier Project' that can provide solutions to the challenges in major R&D area. Medicinal Bioconvergence Research Center (Biocon) was selected as one of the three projects to solve current difficulties in new drug discovery. As medicine becomes more personal and stratified, Biocon foresees that the biggest bottleneck in drug discovery would be to secure novel therapeutic targets and biomarkers that can accurately address various human diseases. With this prediction, Biocon is initially focusing on novel therapeutic target discovery and validation that can be used by industry with high probability of success.

With the financial support of about 140 million dollars, this project will continue for a total 9-year period that is divided in three phases. By the end of the project, Biocon is aiming to establish '3D Atlas of Target-Drug Interactome' that shows the total map of the fully validated therapeutic targets with all the necessary attributes that are required for drug screening. (Fig. 2).

Fig. 1: Decreasing return of investment (ROI) in new drug discovery. Adapted from

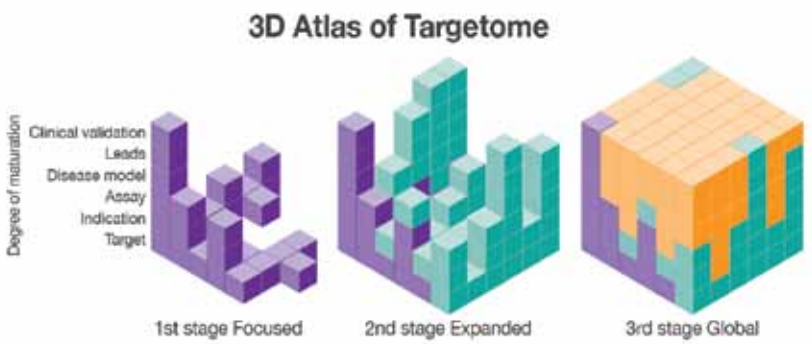

Fig. 2: Generation of fully validated target atlas that can be use for new drug discovery.

Biocon consists of intra- and extramural collaboration network. The inner core center is hosted by Seoul National University and the extramural research units consist of the teams for innovative target discovery, drug design, drug screening and disease modeling technologies (Fig. 3).

Biocon's projects are further strengthened by the experienced guidance of the international advisory board that covers global-level scientists such as Dr. Ada Yonath (a 2009 novel prize winner), Dr. Richard Lerner, Dr. Paul Schimmel (Scripps, USA), Dr. Nahum Sonenberg (McGill Univ, Canada) and Dr. Alex Matter (CEO, Experimental Therapeutic Center) etc.

Biocon's techonolgy code is S.A.F.E. that stands for smart, accurate, fast and economic. It believes that the current slump of drug discovery should be overcome by the combination of original science and innovative technology. For this, Biocon provides an open research platform and recruits global partners and colleagues with originality, creative mind and unique specialties. Biocon hopes to become an alternative collaborative model of drug discovery combining different sectors such as universities, institutes and industry as united team that can provide a more efficient, flexible and innovative platform for drug discovery (http://biocon.re.kr) (Fig. 4)

As the starting core target area, Biocon is looking into human aminoacyl-tRNA synthetases (ARSs) and their interacting target proteins. These enzymes emerged early in evolution and catalytically link their cognate amino acids to tRNAs for protein synthesis. For their roles as enzymes, ARSs have been considered as housekeeping proteins solely dedicated to protein synthesis. However, recent new findings on the novel functions of ARSs are rapidly changing the classical view of these enzymes and they are being emerged as central coordinators linking cell fate determination processes with protein synthesis (Fig. 5).

Besides, recent reports show that the mutations of these enzymes and their interacting factors are associated with human cancers and neurodegenerative diseases. More interestingly, several different human ARSs are secreted as novel cytokines with distinct activities. Based on the recent progress on the novel functions and pathologic implications

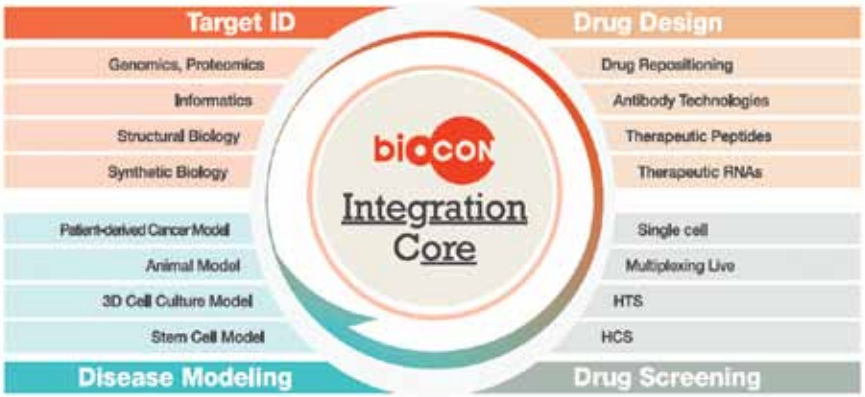

Fig. 3: Functional architecture of Medicinal Bioconvergence Research Center (Biocon). The center consists of 4+1 functional units. The four units are for the innovation of target identification, drug design, drug screening and disease modeling, and the results produced by these four units are integrated in integration core.

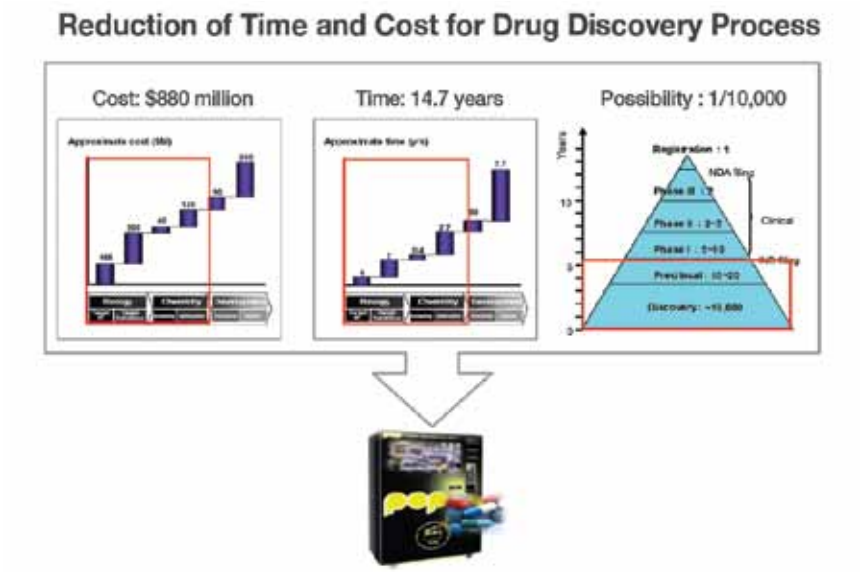

Fig. 4: Biocon is designed to innovate the upstream process in drug discovery through the integrated research and convergence technologies.

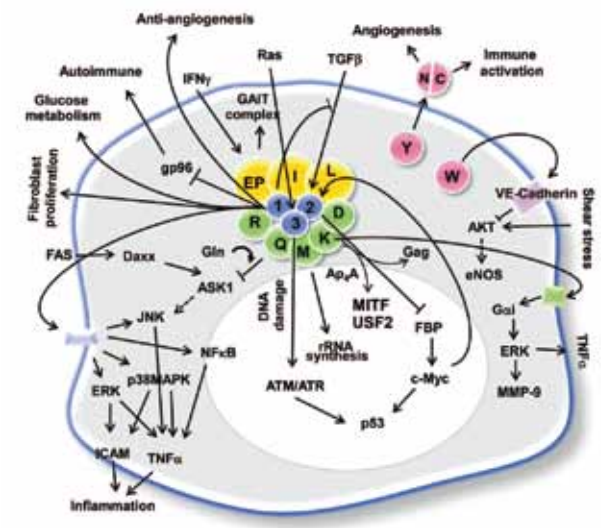

Fig. 5: Cell signaling pathways that are controlled by non-canonical activities of human ARSs. Alphabets such as K, M, Y, W etc stand for the corresponding aminoacyl-tRNA synthetases such as lysyl-, methionyl, tyrosyl- and tryptophanyl-tRNA synthetases, respectively, and the numbers, 1, 2, 3 represent ARS-interacting multifunctional proteins (AIMPs 1, 2 and 3). Adapted from PNAS 105, 11043, 2008 with slight modification.

of these ancient enzymes and their associated factors, Biocon considers that this enzyme family has enormous potential and novelty to explore as a new drug target space as well as therapeutic materials with distinct applications (Fig. 6).

Starting the research of ARSs in human pathology, Biocon will expand its investigation to other target area as the project is progressed. For the rapid expansion of the target discovery and validation, Biocon will incorporate diverse cutting-edge technologies not only from bioscience area such as bioinformatics, genomics, proteomics, cellomics and animal models, but also from other disciplines such as chemical, nano, microfluidic and biochip technologies (Fig. 7). With these research contents and innovative technologies, Biocon aims to become "the World Best Target Factory" that fills up the upstream gap for global drug discovery community.

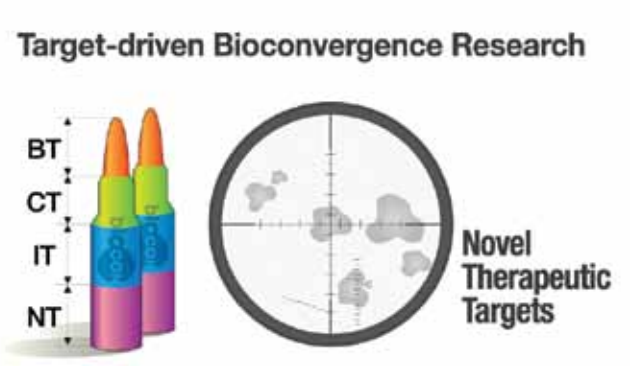

Fig. 6: Interaction network between human ARSs and known cancer-associated factors. Adapted from Nat Rev Cancer in press 2011 with slight modification

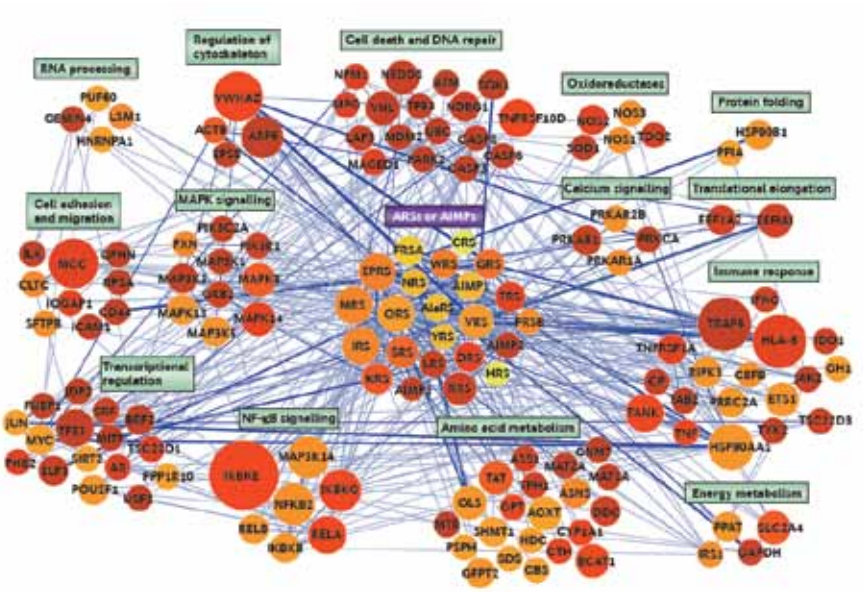

Fig. 7: Biocon pursues target-driven convergence research for the rapid discovery and validation of effective therapeutic targets that can be used for novel drug discovery.

About the Author

Sunghoon Kim received his Bachelor's degree at Seoul National University College of Pharmacy, Master's degree at Korea Advanced Institute of Science and Technology Department of Biological Sciences, Korea and PhD degree at Division of Biology and Medicine, Brown University, USA. He then worked as post-doctoral fellow at MIT. He is currently a Professor at College of Pharmacy and also at Graduate School of Convergence Technology of Seoul National University. He also serves as Adjunct Professor for the graduate program of Bioinformatics, Genetic Engineering and Cancer Biology. He received several prestigious awards provided by various scientific communities as well as by Korean government such as the Korea scientist award (2003) and the scientist of the year (2006). He has led a National Creative Research Initiative of Korea as a Director during 1998-2007. Through this project under the name of "Center for ARS Network", he has discovered many new functions and factors associated with human aminoacyl-tRNA synthetases (ARSs) and unveiled many pathological connections of these enzymes with various human diseases. From this contribution, he is globally recognized as a frontier to open the field of "cell signaling and biomedical applications mediated by tRNA synthetases" that is rapidly emerging. Since 2010, he is leading "Medicinal Bioconvergence Research Center" that is one of the biggest top-down research projects launched by the Ministry of Education, Science and Technology in Korea (MEST). In this project, he is paving a rapid and efficient target identification and validation system through integrated biology with convergence technologies and is linking this system to facilitate novel drug discovery.