Make Invisible Visible: a Diversity Oriented Fluorescence Library Approach (DOFLA)

Young-Tae Chang

Department of Chemistry, National University of Singapore, Singapore

With the successful result of Human Genome Project, we are facing the problem of handling numerous target genes whose functions remain to be studied. In chemical genetics, instead of using gene knock-out or overexpression as in conventional genetics, a small molecule library is used to disclose a novel phenotype, eventually for the study of gene function. The currently popular affinity matrix technique is challenging because the transformation of the lead compound into an efficient affinity molecule without losing the biological activity is not easy, requiring intensive SAR studies. To surrogate the well known problem, our group has developed a linker tagged library and has successfully identified multiple target proteins so far. While successful, the affinity matrix technique requires a breakdown of the biological system to pool the proteins into one extract, which inherently introduce a lot of artifacts.

As the next generation of tagged library, we are currently developing fluorescence tagged libraries for in situ target identification and a visualization of the biological events using Diversity Oriented Fluorescence Library Approach (DOFLA). The basic hypothesis is DOFLA of the same fluorescence scaffold, but with various diversity elements directly attached around the core, may selectively respond to a broader range of target proteins in intact biological system and facilitate the mechanism elucidation and target identification. The high throughput strategy using colorful chemical genetics for stem cell study will be discussed.

Young-Tae Chang was born in Busan, Korea, in 1968. He studied chemistry in Pohang University of Science and Technology and received his B.S. in 1991. After one and half years of army service in Korea, he started his graduate study at POSTECH and received a Ph.D. in 1997 under the supervision of Prof. Sung-Kee Chung, working on the divergent synthesis of all possible regioisomers of myo-inositol phosphates. He did his postdoctoral work with Prof. Peter Schultz at UC Berkeley and The Scripps Research Institute. In 2000, he was appointed assistant professor at New York University and promoted to associated professor in 2005. He received the NSF Career award in 2005 and his research interests have been *chemical genetics, molecular evolution, and artificial tongues*. In September, 2007, he moved to National University of Singapore and Singapore Bioimaging Consortium. He is running Medicinal Chemistry Program of NUS as the leader, and Lab of bioimaging Probe Development at SBIC, Biopolis. He published more than 180 scientific papers/3 books and filed 30 patents so far; Tel : 65-6516-6774, E-mail: chmcyt@nus.edu.sg