(Form4-2)

JOINT RESEARCH PROJECT

FINAL REPORT
For Japan-Korea Joint Research Project

AREA	1. Mathematics & Physics 2. Chemistry & Material Science (3. Biology) 4. Informatics & Mechatronics 5. Geo-Science & Space Science 6. Medical Science 7. Humanities & Social Sciences

1. Research Title:

Target Identification of biologically active small molecules with chemical genomics

2. Term of Research: From July 1, 2009 To June 30, 2011

3. Total Budget

a. Financial Support by JSPS: Total amount: 2 Mil. and 4 hundred thousand yen

1st Year 900 thousand yen 2nd Year 1 Mil. and 2 hundred thousand yen

3rd Year 300 thousand yen

b. Other Financial Support : Total amount: thousand yen

4. Project Organization

a. Japanese Principal Researcher	
Name	**Dr. Yoshida, Minoru**
Institution / Department	**RIKEN ASI** **Chemical Genomics Research Group**
Position	**Group Director**
b. Korean Principal Researcher	
Name	**Dr. Kwon, Ho Jeong**
Institution / Department	**Yonsei Universrity,** **Departement of Biotechnology**
Position	**Professor**

c. List of Japanese-side Participants (Except for Principal Researcher)

Name	Institution/Department	Position
Yashiroda, Yoko	RIKEN ASI, Chemical Genetics Laboratory	Senior Research Scientist
Matsuyama, Akihisa	RIKEN ASI, Chemical Genetics Laboratory	Senior Research Scientist
Takemoto, Yasushi	RIKEN ASI, Chemical Genomics Research Group	Visiting Researcher
Arita, Yuko	RIKEN ASI Chemical Genomics Research Group	Visiting Scientist

d. List of Korean-side Participants (Except for Principal Researcher)

Name	Institution/Department	Position
Cho, Yoon Sun	Yonsei University, College of Life Science and Biotechnology, Department of Biotechnology	Ph.D. Student
Kim, Ki Hyun	Yonsei University, College of Life Science and Biotechnology, Department of Biotechnology	Ph.D. Student
Kim, Nam Hee	Yonsei University, College of Life Science and Biotechnology, Department of Biotechnology	Ph.D. Student
Jung, Hye Jin	Yonsei University, College of Life Science and Biotechnology, Department of Biotechnology	Research Professor

5. Number of Exchanges during the Final Fiscal Year*

*Japanese fiscal year begins April 1.

a. from Japan to Korea

Name	Home Institution	Duration	Host Institution
None	None	None	None
For Final Fiscal Year(FY2011) Total: 0 persons		For Final Fiscal Year(FY2011) Total: 0 man-days	
Numbers of Exchanges during the past fiscal years			
FY2009: Total 4 persons FY2010: Total 5 persons			

b. from Korea to Japan

Name	Home Institution	Duration	Host Institution
None	None	None	None
For Final Fiscal Year(FY2011) Total: 0 persons		For Final Fiscal Year(FY2011) Total: 0 man-days	
Numbers of Exchanges during the past fiscal years			
FY2009: Total 4 persons FY2010: Total 4 persons			

6. Objective of Research

Chemical genomics is a new integrated discipline utilizing biologically active small molecules toward functional analysis of genome and drug discovery. With chemical genomics, a number of small molecules such as angiogenesis inhibitors and histone deacetylase (HDAC) inhibitors have been identified by Yoshida and Kwon's group. For the systemic analysis of mode of actions of these small molecules, high throughput target identification of small molecules is necessary. In this joint project, Yoshida group of Japan Chemical Genomics Laboratory in RIKEN will develop the ORFeome system based target identification technology using fission yeast open reading frames (ORFs). The ORFeome technology will be applied to the discovery of direct target proteins of biologically active small molecules that have been discovered by Kwon's group of Korea Chemical Genomics Laboratory in Yonsei University. With close collaboration between these two well-known specialists in the field, effective target identification of biologically active small molecules and validation will be possible and this information will provide new insight on mode of actions of small molecules of interests and basis for drug discovery.

7. Methodology

Small molecules from natural and synthetic origins have played critical roles to explore novel biological functions of gene or genome and provide new targets and chemical entries for drug discovery. As diverse chemical libraries become available, high throughput technology is crucial in obtaining fast and accurate results. Breakthrough in new technologies both screening of new biologically active small molecules and identification of targets for small molecules are essential to get better understanding of mechanisms of small molecules in complex biological systems. Technologies such as phage display biopanning, protein microarray, and surface plasmon resonance have been developed and confirmed in finding the direct target for bioactive small molecules (Shim *et al, Chem. & Biol,* 2004). Recently, a new technology was developed by Yoshida group in Japan that uses fission yeast open reading frames (ORFs) to screen the direct target protein of a small molecule (Matsuyama *et al, Nat. Biotech.,* 2006). This ORFeome technology is an effective method that can be used to discover the target binding protein for already known small molecules as well as novel small molecule identities. With the Japan-Korea Basic Scientific Cooperation Program, novel targets of biologically active small molecules can be identified and validated using newly developed ORFeome technology. ORFeome technology overcomes the limitations of previously developed chemical genomics methods for target identification of small molecules. Indeed, the entire genome of fission yeast is sequenced, which outnumbers the limited number of genomes that could be previously detected through phage display biopanning or protein microarray. High throughput screening of biologically active small molecules will result in identification of novel target proteins responsible for phenotype changes. After identification of the target proteins, validation with a number of biological experiments will be effectively carried out. Accordingly, the new ORFeome technology along with new small molecules with interesting biological activities will be used to expand the basis of new small molecules and targets that will be utilized as new drug candidates.