

Whole-Cell Project of an extreme thermophile, *Thermus thermophilus* HB8

To create a medical environment in which each patient can choose the best medical treatment for him/herself, we should be able to predict the result of each medical treatment. However, the human genome encodes more than 20,000 proteins, and their functions are altered by many kinds of post-translational modifications, such as phosphorylation, glycosylation, and others. Since many molecular species cannot be quantitatively analyzed by the current technology, we presently cannot predict the results of medical treatments. Therefore, we intend to construct a new life science that can predict the response of an organism on the chemical basis.

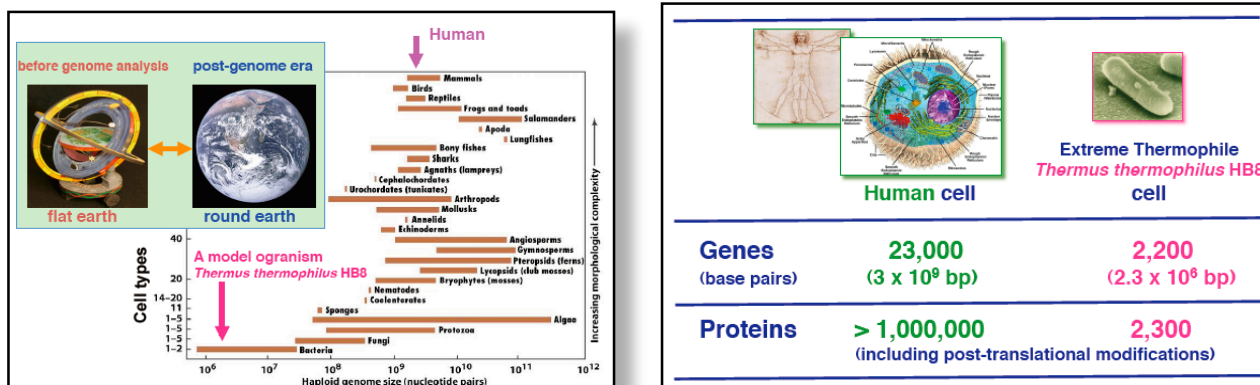


Fig. 1 Comparison of an extreme thermophile, *Thermus thermophilus* HB8 with human

The ultimate goal of the above basic life science is to understand the whole-cell phenomena in the cell at an atomic-resolution, on the basis of the structures and the functions of all of the molecules, and to predict all of the biological phenomena in the cell. To achieve this goal, we chose the extremely thermophilic organism, *Thermus thermophilus* HB8, as a model organism, because the essential 2,200 genes (proteins) encoded in its genome have been selected during evolution and are common to many organisms, including human (Fig. 2). Furthermore, as this strain is thermostable, this model organism is a good candidate for cell imaging analyses with the SPring-8 beamlines as well as X-ray structural analyses of its macromolecules.

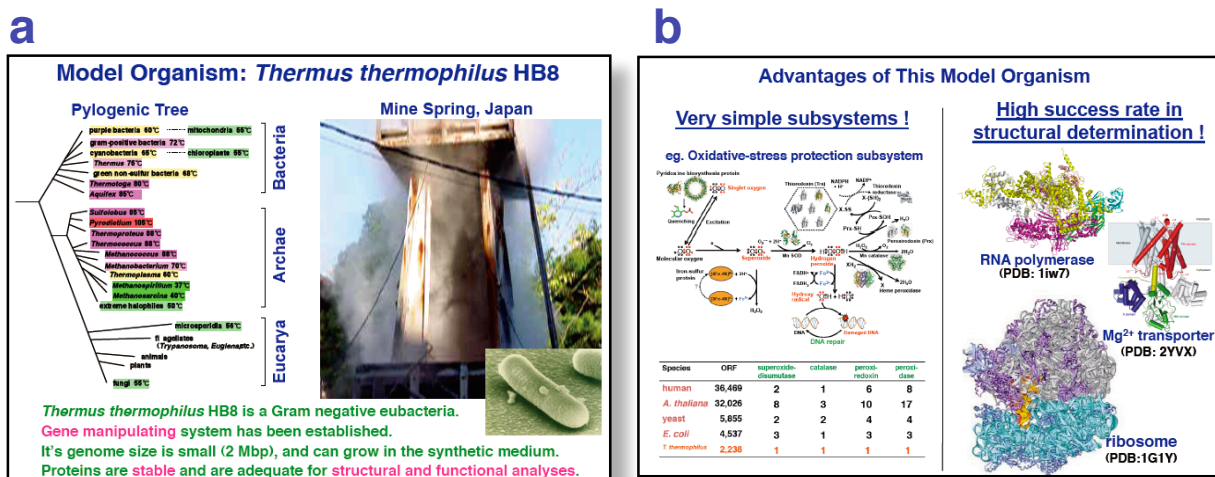


Fig. 2. Characteristic of an extremely thermophilic model organism, *Thermus thermophilus* HB8 (a), and Advantages of this model organism (b).

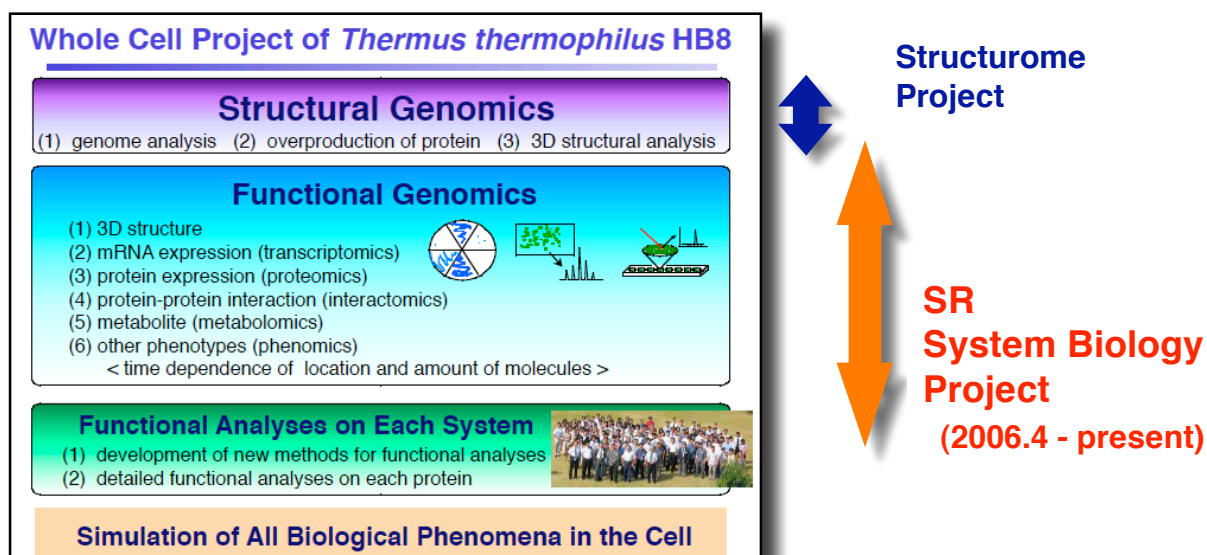


Fig. 3. Four steps for understanding the whole-cell system, and its relation with projects.

In order to understand the whole-cell phenomena, the research will proceed in the following four steps (Fig. 3).

1. Structural genomics step

After the genome analysis, almost all of the proteins (about 2,000) of *T. thermophilus* HB8 have been overproduced by using an *Escherichia coli* protein-production system. After purification and crystallization, the three-dimensional structures of the expressed proteins have been determined.

2. Functional genomics (Funcionics) step

Genome-wide funcionics studies include the studies of transcriptomics (mRNA expression analysis), proteomics (protein expression analysis), and metabolomics (low molecular weight metabolite analysis). In order to understand the global biological phenomena, it is essential to discover the functions of the approximately 500 kinds of functionally-unknown proteins remaining in the cell.

3. Detailed analytical step of each subsystem

Before the rise of structural and functional genomics, almost all the biochemists were primarily working on this step. Improvements of new analytical methods, including various imaging methods, and new concepts for each subsystem and its constituent molecules, including “molecular crowding”, are essential for this step. Data collection for each enzymatic reaction step under fixed conditions (for example, 20 mM phosphate, 100 mM KCl, pH 7.0, 70°C (or 25°C)) will be essential for the simulation step. Information on the time dependence of the position and concentration of each molecule is also necessary for system biological study.

4. Final step of this system biology process (Prediction of whole-cell phenomena)

By integrating all of the data obtained from the first to third steps, we will try to interpret the

global biological phenomena in the cell at an atomic level. The final goal of this step is “prediction”, not explanation. In order to achieve this goal, progress in new scientific fields, such as “imaging”, “computation”, and others is essential, and interdisciplinary collaborations will be very fruitful.

The research targets are the whole-cell biological phenomena consisting of only about 2,000 genes (proteins), which are condensed during evolution. These genes (proteins) are essential and common to many organisms, including human, animals, plants, and bacteria. The research output from the whole-cell project will form the basis of a wide range of systems biology.

Resources and their related information

The plasmids for protein expression (1,900 clones) and the plasmids for gene disruption (1,000 clones) are available to the public through the RIKEN BioResource Center (see <http://www.thermus.org>). Some of the information about protein production (protein expression and purification), crystallization, structure, and functomics (transcriptomics, proteomics, and metabolomics) is also available from our database (<http://www.thermus.org>) (Fig. 4) and public databases.

Structural-Biological Whole Cell Project

What's New

- May. 18, 2009 Top page was updated.
- May. 16, 2009 Seminar Page was updated.
- Jan. 26, 2008 Renewed member lists.
- Change of encoding: from Shift_JIS to UTF-8.
- Top Page was updated. (Added "Recent 10 articles of *T. thermophilus*" and "Database")
- Sep. 10, 2007 Top Page was updated.
- May. 01, 2007 Renewed member lists.
- Dec. 19, 2006 New Page : Electron microscope of *Thermus thermophilus* HB8

Recent 10 articles of *T. thermophilus*

- Kitamura, Y. et al., (2009) Structure of D-alanine-D-alanine ligase from *Thermus thermophilus* HB8: cumulative conformational change and enzyme-ligand interactions *Acta Crystallogr D Biol Crystallogr* **65** : 1090-106
- Niyou, Y. K. et al., (2009) Role of galE on Biofilm Formation by *Thermus* spp. *Biochem Biophys Res Commun* :

Protein expression vectors are now available from BRC

1695 Clones of *Thermus thermophilus* HB8 are available from RIKEN BioResource Center (BRC).

http://www.brc.riken.jp/lab/khalent/thermus_en.html

All clones are constructed in pET expression system without tag residues.
Clone set: Clones are shipped as frozen recombinant *E. coli*/DH5a in 96-well plates with dry-ice.
Single clone: Clone(s) is shipped as DNA solution in TE buffer in individual tube.

THB8 Genomic DNA is available for purchase at TaKaRa.

Product Name	Takara Code
<i>Thermus thermophilus</i> HB8 Genomic DNA Solution	3071

Fig. 3. Web page of Whole-Cell Project ([http:// www.thermus.org](http://www.thermus.org)).