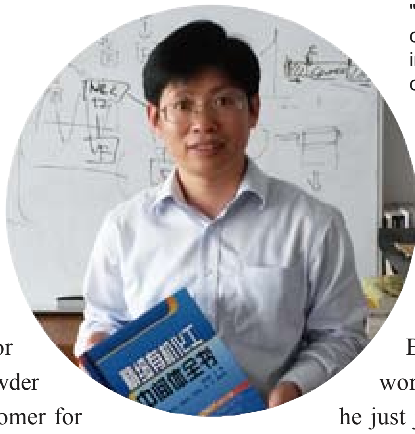
Green and Aromatic Future

By SONG Jianlan (Staff Reporter)



"Described in this manual over 2,800 organic chemicals are of crucial importance for industries in China. Our dream is, one day we can produce all of them through green biotech methods rather than chemical synthesis, in economically feasible ways," says Prof. WANG Qinhong, principal investigator at TIB. (Photo by ZHANG Guoqiang)

"This is what we are trying to produce from fermentation via synthetic microbial cell factories," Prof. WANG Qinhong shows the author a vial, in which some salt-like white powder can be seen. "It is adipic acid, the monomer for nylon, a staple artificial fiber – you might know that," he smiles and continues to explain: "After amination, adipic acid will turn into hexanediamine; and nylon is exactly the product of the polymerization reaction between this derivative and adipic acid itself. Both our clothes and shoes can be made from it."

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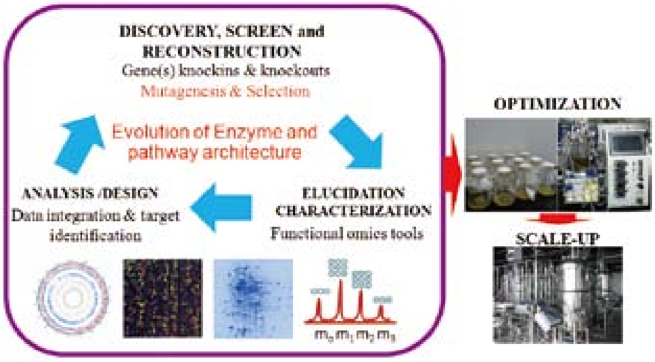
Scientists at the Tianjin Institute of Industrial Biotechnology (TIB), CAS endeavor to blaze a way out for producing adipic acid, the monomer for nylon, through fermentation of synthetic microbial cell factories. (Photo by SONG J.)

WANG, principal investigator at the Tianjin Institute of Industrial Biotechnology (TIB), CAS, has been working in this direction since 2009, when he just joined this young entity then still taking form. "Actually it is also the core mission of our institute: to substitute the current chemical method for industrial manufacture with biotech methods, using renewable resources rather than fossil resources as raw materials. In this way we will be able to avoid over exploitation of fossil resources, and save our natural environment from deterioration," he further remarks.

At present, adipic acid is still produced from splitting decomposition of petroleum. "But we all know that this is not sustainable. Fossil resources are non-renewable, and they are depleting fast," WANG says. "For the time being however, it is very hard to invent a green biotech method to produce adipic acid at costs low enough to substitute chemical methods based on fossil resources. It has to reach a very high conversion rate to meet that standard, especially when the price of crude oil is at such a low; and that is why for now no biotech method has been thrown into industrial application yet," he continues with some regret: "But we are working towards that end and maybe one day we will get there. It takes time, but it is worth doing to get ready before the advent of the fate."

Truly natural fibers are getting more and more popular on the market, but still they are generally much more expensive than artificial fibers. "It would be a luxury to use a rug made of natural fibers," WANG remarks. "More importantly, even if we all could afford this, still we would need artificial fibers to make other products. For example, we need them to synthesize industrial plastic, which is



A schematic map illustrates the overall idea of the design and construction of optimal biological tools (synthetic microbial cell factories) for biomanufacture of bulk chemicals widely used in industry. (Image by courtesy of Prof. WANG Q.)

widely used in automobiles and shoes. We might also need nylon to synthesize some materials of special properties, say of very good plasticity. Moreover, adipic acid is also a raw material for the synthesis of some bulk chemicals widely used in industrial manufacture like polyurethane (PU), just to give an example," he introduces.

"That might explain why the global demand for adipic acid can mount to 3 millon tons a year. It is impossible to fulfill all this demand with natural fibers," WANG asserts. "Therefore we are trying to design and construct optimal tools ranging from enzymes, metabolic pathways to cell factories to turn this dream into reality, integrating state-of-the-art technologies from new biology and engineering," he further introduces.

On the other hand, WANG's team has endeavored to investigate the functions, properties and involved mechanisms of these newly designed and synthesized biomolecules. "Such investigations draw on the know-how obtained from the above-mentioned design and construction of biological tools, and in turn their results feed the design, construction and optimization of such tools with renewed ideas," he introduces.

Once a desirable property emerges in the newly constructed cell, it can be enhanced via genetic modification and metabolic evolution, a technology to artificially select the cells of the best performance every time they reproduce themselves. Only on condition that cells hosting such promising properties can be differentiated and separated correctly, however.

"It would be very slow to screen such promising candidates manually from a large library of varied cells," WANG advances: "It would be wonderful to have a smart machine here to do this automatically, right?"

Therefore WANG initiated a project to develop a machine for high-throughput screening of microbial cells. "Now such integral system for high-throughput screening of microbial cells is not available on the market at all," WANG explains: "Why not build one myself?! I need it!"

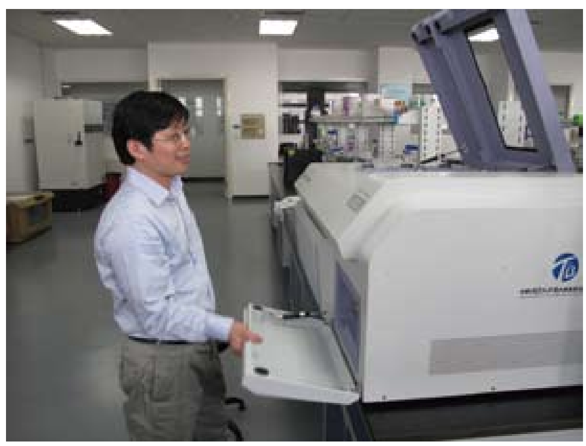
A difficulty in developing such an instrument is how to differentiate the products secreted from each cell. "This is easy if the adipic acid remains in the host cells; but it is 'secreted' out by the cells – therefore the molecules of adipic acid mix up all together despite their sources. Therefore we adopt a smart trick – in the first instance we cover each cell with a thin membrane of oil via droplet microfluidic chip, to isolate them from each other. Subsequently the adipic acid produced by a certain cell will be sealed in a capsule independent from others, making it possible for the machine to correctly detect the right targets," WANG recalls.

Now WANG has built a prototype system and put it into a test run. "It is handy, easy to use, and affordable," he describes.

WANG hopes that this machine will gear up their development of an idealistic cell factory for adipic acid. "We would like it to process 1.0×10^5~10^7 cells a day, differentiating and separating those cells excellent at producing adipic acid from their neighborhood. That will greatly improve our efficiency."

WANG's efforts in constructing a desirable cell factory for adipic acid production are already seeing some encouraging results, including some not so acid – something fragrant instead.

"From the upper reaches of the designed pathways we can get some interesting derivative products, for example aromatic compounds including tea polyphenol (TP), which was first discovered and extracted from tea," WANG introduces: "It is relatively easier to reach a conversion rate acceptable for the industry, as prices for TP are very high on the market. We might succeed in that direction first."



WANG and the prototype machine of his integral system for droplet microfluidic high-throughput screening of microbial cells. (Photo by SONG J.)