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Researchers found that they can make large mixtures of biologically active compounds from a few chemical ingredients in just a few hours. They made 6,000 peptides from just 23 building blocks and identified a novel molecule that blocks a key enzyme used by the hepatitis C virus (schematic above).

Future antibiotic-making kits for amateurs?

Researchers in Switzerland and Japan have developed a rapid, simple and safe method for generating large libraries of novel organic molecules in a fraction of the time required for traditional organic synthesis.

Led by Professor Jeffrey Bode of the Institute of Transformative Bio-Molecules at Nagoya University in Japan, the research team is now applying its “synthetic fermentation” strategy to make molecular kits that can be used simply and safely to discover novel antibiotics.

Microorganisms can synthesise mixtures of complex organic molecules, such as antibiotics, from simple organic building blocks by fermentation. Inspired by this approach, Professor Bode and his colleagues found that they could make large mixtures of biologically active compounds from a few chemical ingredients in just a few hours, rather than the months it would normally take trained chemists. To do so, the team applied a powerful bond-making reaction, called KAHA (alpha-ketoacid-hydroxylamine) ligation, which enables the rapid formation of “amide” chemical bonds, found in peptides and proteins. The KAHA ligation uses special types of organic molecules to form new bonds without the usual need for toxic chemical reagents.

Using synthetic fermentation, the researchers have shown that about 6,000 novel peptides can be made from only 23 building blocks. What’s more, they have demonstrated the practicality of this approach by

identifying a novel molecule that blocks a key enzyme used by the hepatitis C virus.

“Our dream is to provide a do-it-yourself method – one that can be applied by anyone, anywhere to make and assess millions of organic molecules, without using dangerous reagents,” says Professor Bode. “For example, we envision that synthetic fermentation could be used by farmers to generate and identify new anti-bacterial or anti-fungal molecules to treat plant diseases.” By combining a handful of molecules in a variety of ways, a farmer could identify a novel combination that treats plant infections.

He adds that the next step is to determine the most efficient way to screen the thousands or even millions of chemical compounds that can be generated using synthetic fermentation.

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