

Recombinant bacterium boosts production of compound that can relieve menopause symptoms

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A soy isoflavone derivative that goes by the scientific moniker, (S)-equol, has proven potent for mitigating menopausal symptoms. However, it has been impossible to produce in quantities sufficient for widespread commercial nutraceutical production. But now, a team of Korean researchers reports having constructed a recombinant bacterium which they say can boost production. The research is published January 22nd in *Applied and Environmental Microbiology*, a journal of the American Society for Microbiology.

Equol is produced naturally in small quantities by the human intestine-abiding bacterium, Slackia isoflavoniconvertens. Clinical studies have shown that this compound reduces hot flashes, night sweats, bone loss, and other menopausal symptoms, with no harmful side effects, and studies in several human cell lines suggest that it might eventually prove to prevent prostate cancer. But the anaerobic S. isoflavoniconvertens' productivity was too low for large-scale production, and that bacterium doesn't work well with industrial fermenters, said lead investigator Byung-Gee Kim, PhD, a professor in the Department of Chemical and Biological Engineering, Seoul National University, Seoul, Korea.

To increase production of (S)-equol, the investigators cloned the enzymes of the compound's biosynthetic pathway into a strain of the laboratory bacterium, Escherichia coli, which is commonly used, among other things, for industrial purposes. But although this bacterium enabled



easier control of production, and although the investigators assembled optimum environmental conditions for the <u>bacterium</u>, including its preferred acidity level and temperature, the yield still remained too low for commercial production, said Kim.

The researchers then tried another way to raise production. They identified the rate-determining enzyme in the biosynthetic pathway. "We replaced the slower, naturally-occurring enzyme with a mutant version of that enzyme, which is faster," said Kim.

The mutant enzyme has substantially increased production of (S)-equol. However, the process has yet to achieve sufficient productivity for industrial production, said Kim. "We showed a partial success, and we are working to improve it."

More information: Pyung-Gang Lee et al. P212A mutant of dihydrodaidzein reductase enhances ()-equol productivity and enantioselectivity in recombinant whole cell reaction system, *Applied and Environmental Microbiology* (2016). DOI: 10.1128/AEM.03584-15

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