Medical Xpress

New System Boosts Yield of Isoflavonoids That Bind Estrogen Receptors

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(PhysOrg.com) -- The promise of new pharmaceutical treatments from a class of powerful plant compounds called isoflavonoids has remained unfulfilled because of problems biosynthesizing sufficient quantities of the compound in pure forms or well-defined mixtures.

Now, funded by a Phase 1 Small Business Innovation Research grant, University at Buffalo engineers report in Chemistry & Biology that they have developed a versatile microbial system to produce quantities of some of these compounds up to seven times more than what was previously attained.

"This is an important, initial step in the construction of a system that can potentially synthesize thousands of natural and non-natural isoflavonoids," says Mattheos A. G. Koffas, PhD, associate professor in the UB Department of Chemical and Biological Engineering in the School of Engineering and Applied Sciences and lead author.

Although additional hurdles remain before this new process will be commercially viable, the new compounds produced by UB researchers demonstrated altered estrogen receptor binding activity, a property that makes them good candidates for potential breast cancer treatments and other important pharmaceutical agents.

"We have shown that a couple of compounds are good estrogen receptor binders in vitro, meaning they could inhibit estrogen from binding to its receptor," says Koffas, "so if further testing in animals is promising, they

may become suitable drug candidates for breast cancer."

Because estrogen receptor binders can prevent cancer-causing compounds from binding to estrogen, they may be able to thwart the growth of cancerous tumors.

Koffas says that they were able to achieve the higher yields of the compound because their method optimizes in yeast the combined action of three enzymes that produce isoflavones.

A key obstacle the UB researchers overcame was finding an efficient way to express an important enzyme, isoflavone synthase, which reacts with two additional enzymes in order to complete the synthesis of the isoflavonoids.

The UB researchers also were able to create a small library of non-natural (synthetic) isoflavonoid derivatives.

Provided by University at Buffalo

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