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# Anticancer Prospect Made From Scratch

Total Synthesis: Chemists map route to natural product (+)-fusarisetin A

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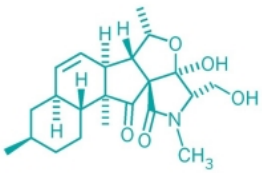

(+)-Fusarisetin A

**The natural product** (+)-fusarisetin A, which has promising anticancer properties and an unusually complex structure, has succumbed to total synthesis.

(+)-Fusarisetin A has intrigued drug designers because experiments show that it inhibits migration and metastasis of cancer cells, seemingly without exhibiting cell-killing proclivities that might point to toxic tendencies. The compound's complicated architecture, including a fused five-ring system and 10 stereocenters, has made it challenging to synthesize.

Last year, Korean and Japanese scientists first isolated the natural product from a soil fungus and proposed its structure (*J. Am. Chem. Soc.*, DOI: 10.1021/ja1110688). This year, two independent teams—Ang Li and coworkers at Shanghai Institute of Organic Chemistry and Emmanuel A. Theodorakis and colleagues at the University of California, San Diego—synthesized the proposed structure from the starting material (*S*)-(–)-citronellal (*J. Am. Chem. Soc.*, DOI: 10.1021/ja211444m and 10.1021/ja300807e). But the optical rotation of the compound they made didn't match that of the natural product, revealing that the proposed structure had been misassigned.

Shuanhu Gao and coworkers at East China Normal University, Shanghai, have now used (*R*)-(+)-citronellal as a starting material to achieve the first total synthesis of the bona fide natural product (*Angew. Chem. Int. Ed.*, DOI: 10.1002/anie.201202455). Li's and Theodorakis' groups have also completed the synthesis of (+)-fusarisetin A, but Gao's team is first out of the publication gate.

"Fusarisetin is an architecturally fascinating structure, rich with stereochemical and synthetic challenges enhanced further by the density of its functionality," comments synthetic organic chemist Paul A. Wender of Stanford University. "Its biological activity is equally intriguing and hopefully will draw more attention in future work, now made possible by the impressive synthetic studies reported independently."

The three groups' strategies "have some thematic similarities and are capable of step-economically delivering the natural product or its enantiomer, depending on the selection of starting-material chirality," Wender adds. "Each approach offers flexibility and brevity that together will enable future mode-of-action studies."

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