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Bleomycin Potency Boost

Combinatorial biosynthesis produces analog with uniquely high activity

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Bleomycins are approved drugs used in cocktails with other medicines for conditions such as testicular cancer, but they have serious side effects, including lung inflammation. Now, a team has used combinatorial biosynthesis (genetic engineering of biosynthetic pathways) to create a designed bleomycin with uniquely high potency, which could lead to anticancer agents with improved side-effect profiles. The work was carried out by Yanwen Duan of Hunan Engineering Research Center of Combinatorial Biosynthesis & Natural Product Drug Discovery, in China; Ben Shen of Scripps Research Institute; and coworkers (*J. Am. Chem. Soc.*, DOI: 10.1021/ja3056535). The researchers previously cloned and characterized the biosynthetic gene clusters that bacteria use to produce bleomycins. By analyzing the clusters, they were able to devise a plan for engineering analogs with potentially higher activity, and they succeeded by creating 6′-deoxybleomycin Z, the most potent bleomycin analog to date. The analog could lead to "new bleomycin chemotherapy regimens with reduced dosage, thereby lessening dose-limiting side effects and the incidence of lung toxicity," Shen says.

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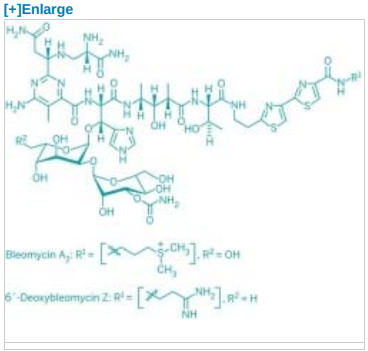

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