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In This Issue

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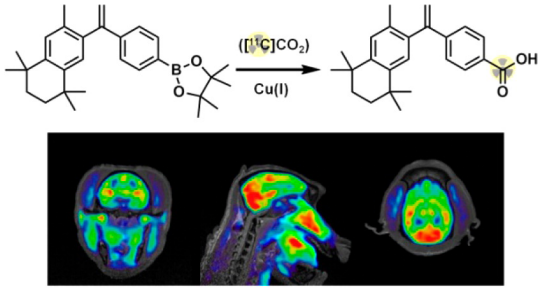
RADIOLABELED BEXAROTENE IN PET IMAGING

Bexarotene is an anticancer drug and FDA-approved synthetic retinoid for the treatment of cutaneous T cell lymphoma. It is also currently being considered as a potential treatment for Alzheimer's disease. The specific mechanism of action remains to be determined, but appears to involve the upregulation of Apolipoprotein E. With the apparent usefulness of bexarotene as an anti-Alzheimer drug, a better understanding of its mechanism at the molecular and cellular level is of primary importance.

Positron emission technology (PET) imaging can be used to quantify the biodistribution of bexarotene, target engagement, and receptor occupancy. Rotstein et al. (DOI: 10.1021/ml500065q) reports the synthesis of [^{11}C]bexarotene and the optimized radiolabeling conditions for complex carboxylic acids and their derivatives. PET imaging in a nonhuman primate has demonstrated brain uptake of [^{11}C] bexarotene. Thus, [^{11}C]bexarotene and other carbon-11 labeled retinoids could be instrumental in deciphering the mechanism of action and, subsequently, in Alzheimer's disease drug development.

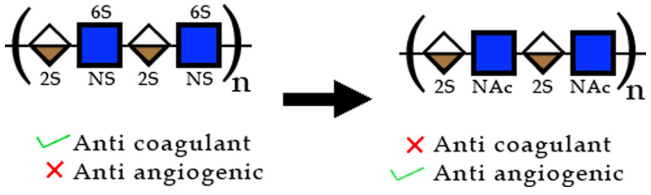


[^{11}C]Bexarotene penetrates non-human primate blood-brain barrier

CHEMOGENESIS OF AN ANTIANGIOGENIC GLYCOSAMINOGLYCAN

Acharan sulfate is a glycosaminoglycan from the giant African snail, *Achatina fulica*, and was shown to have antitumor activity, which may be related to the inhibition of angiogenesis. However, it is very difficult to synthesize de novo. On the other hand, heparin is a commercially available, known anticoagulant, but has minimal antiangiogenic properties.

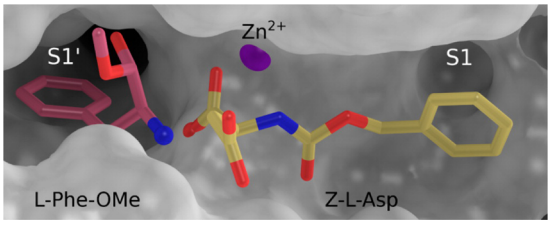
In this issue, Raman et al. (DOI: 10.1021/ml400498d) investigated whether commercially available heparin, an anticoagulant that has a minimal antiangiogenic effect, can be used as a precursor to produce a glycosaminoglycan with inverse properties. Given the widespread biological roles of glycosaminoglycan chains in diseases and physiology, this study addresses the need and provides an option for novel antiangiogenic therapies that are less expensive and easy to produce.



SYNTHESIS OF ASPARTAME BY THERMOLYSIN: AN X-RAY STRUCTURAL STUDY

Aspartame is a widely used low-calorie sweetener that has been used for 30 years. It is a protected dipeptide (L-aspartyl-L-phenylalanine methyl ester), which is enzymatically synthesized in large scale using protease-mediated synthesis of the dipetidyl precursor. However, this reaction is inefficient.

Here, Birrane et al. (DOI: 10.1021/ml500101z) describe the atomic resolution crystal structures of thermolysin complexed with the protected amino acid precursors of the artificial sweetener aspartame. The authors show how inhibition of thermolysin affects the aspartame precursor synthesis. The reported structures may be useful tools in improving the synthesis of the aspartame precursor, provide understanding of their mechanisms, and facilitate their broader adoption in commercial-scale processes.



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