Active Structure of FR901451, a Potent Macrocyclic Elastase Inhibitor

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Bacteria produce a lot of bioactive and structurally unimaginable compounds. Among them, FR901451 from *Flexibaccter sp.* No.758 is known to have large tri-macrocyclic structure and to inhibit porcine pancreatic elastase, which in turn resembles the attractive drug target leukocyte elastase [1]. The crystal structure of FR901451 as bound to pancreatic elastase was solved at 2.5 Å resolution. The inhibitor occupies the most prominent subsites S1' to S3 of the elastase and prevents a hydrolytic attack by covering the active center with its rigid ring structure. The observed binding structure may help to design potent elastase inhibitors.

[1] Fujita T., Hatanaka H., Hayashi K., Shigematsu N., Takase S., Okamoto M., OkuharaM., *J. Antibiotics*, 1993, **47**, 1359.

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