

26G-ISMS03 **Combinatorial Solid-Phase Synthesis and Biological Evaluation of Cyclodepsipeptide Destruxin B as a Negative Regulator for Osteoclast Morphology**

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Cyclodepsipeptide destruxins were firstly isolated from *Metarhizium anisopliae*, and consist of five amino acids ( $\beta$ -Ala, L-MeAla, L-MeVal, L-Ile, and L-Pro) and an  $\alpha$ -hydroxy acid derivative.<sup>1</sup> In particular, destruxin B (**1**) that possesses an isobutyl moiety as a side-chain on an  $\alpha$ -hydroxy acid derivative, reversibly inhibits bone-resorbing activity of osteoclasts without affecting cell viability.<sup>2</sup> Therefore, destruxins can be a promising candidate for developing novel anti-resorptive agents. Because of structural and biological properties of **1**, combinatorial synthesis and biological evaluation of cyclodepsipeptide destruxin B (**1**) were demonstrated.<sup>3</sup> We designed 64-member analogues toward elucidation of structure-activity relationships, and the cyclization precursors were readily prepared by solid-phase peptide synthesis using a split and pool method. After cleavage from the polymer-support, macrolactonization utilizing MNBA-DMAPO in the solution phase was successfully performed in parallel to afford desired destruxin analogues in moderate to good yields. In this presentation, details of combinatorial synthesis and biological evaluation of the synthesized analogues will be discussed.

#### References

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