Chemoenzymatic Synthesis of β-lactones and β-hydroxy acids

**Background:**
β-Lactones are a class of biologically active molecules containing a reactive ester that have the potential to treat obesity, diabetes, infections, and cancer. β-Lactones are difficult to synthesize because high instability due to ring strain. Current synthetic methodologies for preparing enantiomerically pure β-lactones and precursor β-hydroxy acids are limited by multiple steps, low yields, non-catalytic reactions, and lack of stereochemical control.

**Technology Description:**
Researchers at Washington University have developed a novel enzymatic process to synthesize structurally diverse peptide β-lactones and β-hydroxy acids including active pharmaceutical ingredients and natural products. The process enables the enantio- and diastereoselective synthesis of peptide β-lactones and β-hydroxy acids from simple aldehydes. The starting aldehydes are first converted to chiral β-hydroxy acids using a robust and highly stereoselective L-threonine aldolase that outperforms most industrially utilized aldolases in terms of stability, robustness, catalytic efficiency, enantioselectivity, diastereoselectivity, and substrate scope. The resulting α-amino-β-hydroxy acids can be converted into peptides and cyclized to the C-terminal β-lactone derivatives using an efficient non-ribosomal peptide synthetase catalyst. The simplicity, selectivity, and scope of this chemoenzymatic approach to high value β-lactones and β-hydroxy acids is unmatched by existing synthetic and enzymatic techniques.

**Key Advantages:**
- High stereoselectivity, catalytic efficiency, and scalability
- Broad substrate scope and robust performance in batch and flow applications
- Enzymatic process is easier, higher yielding, more stereoselective, and more cost effective than the current chemical syntheses

**Patent/Patent Application:** Pending

**Publication:** Schaffer et al., Nature Chemical Biology online May 15, 2017

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