



## Dual-Enzyme Responsive Peptides

Tech ID: 29379 / UC Case 2017-446-0

### SUMMARY

UCLA researchers in the Department of Chemistry & Biochemistry have developed a dual-enzyme responsive peptide system that requires sequential digestion by two separate enzymes for cleavage at the C-terminal position of lysine.

### BACKGROUND

Due to their high selectivity and specificity, enzyme responsive systems are commonly used for diagnostic and drug delivery applications. Currently, most enzyme responsive technologies are sensitive to a single enzyme, or a single enzyme in combination with an environmental stimulus. For example, caspase-sensitive reporters, which respond to peroxide production or to cancer-related matrix metalloproteinases, have been designated to detect cell injury as well as to monitor reactivation of the apoptotic pathway after anti-cancer therapy delivery. Trypsin responsive sequences have been incorporated into abuse-deterrent opioid formulations, which allow drug release only at specific locations in vivo. Although many single-enzyme responsive systems show promise in specific targeting, response to more than one enzyme would allow for greater target selectivity and indirect enzyme detection, and provide information about cellular environments.

### INNOVATION

Researchers at UCLA have designed a dual-enzyme responsive peptide system that requires sequential digestion by two enzymes for cargo release from the C-terminus. In this system, the peptide is first cleaved by an enzyme that unmaskes the recognition site for a second enzyme, allowing for digestion and release of the final product. These peptides can be used in polymeric formulations, either as cross-linkers or incorporated into the backbone, installing dual-enzyme sensitivity. This method may also be useful for delayed release formulations/prodrugs, allowing degradation of abuse-deterrent opioid formulations to be better controlled when sequences that require digestions by multiple enzymes are installed.

### APPLICATIONS

- ▶ Enzyme-responsive systems for diagnostic and drug delivery applications
- ▶ Selective biodegradation of materials for biomedical applications (i.e. location-specific degradation and drug release for abuse-deterrent opioid formulations)

### ADVANTAGES

- ▶ Allows much greater selectivity and specificity
- ▶ Better-controlled degradation of opioid formulations

### STATE OF DEVELOPMENT

Have demonstrated sequences that are responsive to trypsin/chymotrypsin, trypsin/papain, and trypsin/caspase 3.

### PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	11,879,019	01/23/2024	2017-446
European Patent Office	Published Application	3555280	10/23/2019	2017-446

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### INVENTORS

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### OTHER INFORMATION

#### KEYWORDS

Opioid, abuse-deterrent formulation, drug delivery, enzyme responsive system, biodegradation, trypsin, chymotrypsin, papain, caspase

#### CATEGORIZED AS

- ▶ Medical
  - ▶ Delivery Systems
  - ▶ Disease: Substance Abuse

#### RELATED CASES

2017-446-0

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- ▶ PolyProtek: Platform for Delivering and Stabilizing Therapeutic Biologics, Vaccines, and Industrial Enzymes
- ▶ A Novel Basic Fibroblast Growth Factor Conjugate for Broad Therapeutic Application
- ▶ Update To Degradable Trehalose Glycopolymers
- ▶ Noncrushable/Nonabusable Pill Formulations
- ▶ Trehalose Hydrogels For Stabilization And Delivery Of Proteins
- ▶ A Novel Glycopolymer to Enhance Protein Stability

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