

An Osteoadsorbptive Fluorogenic Substrate of Cathepsin K for Imaging Osteoclast Activity and Migration

Tech ID: 29052 / UC Case 2017-723-0

SUMMARY

UCLA researchers in the Department of Dentistry have developed a novel fluorescent probe for studying the role of osteoclasts in bone diseases and for detecting the early onset of bone resorption by targeting an important protein Cathepsin K. This probe can also deliver drug molecules to bone resorption sites with high specificity.

BACKGROUND

Osteoporosis, rheumatoid arthritis, multiple myeloma and other bone ailments are debilitating diseases that involve abnormal breakdown of bones (bone resorption), leading to devastating skeletal defects and poor quality of life. Cathepsin K is produced by osteoclast cells to aid in breaking down collagen in bones, and its activity plays an important role in the development and progression of the aforementioned diseases. Molecular probes for cathepsin K have been developed to study the effects of this protein and osteoclast cells in many disease models. However, these probes do not specifically target bone tissues in animal models and have a short half-life for imaging.

INNOVATION

A molecular probe called OFS-1 has been developed to detect cathepsin K activity in vitro and in vivo. This novel probe is linked to a compound called bisphosphonate that binds strongly to bones, making the OFS-1 probe highly specific for targeting bones. OFS-1 contains a cleavable fluorophore-quencher pair, which is activated when cathepsin K cleaves OFS-1. Therefore OFS-1 can be used for sensitive and early detection of bone resorption in diseases. Activated OFS-1 remains bound to osteoclast cells after interaction with cathepsin K, making it easy to track fluorescent osteoclasts over time. Additionally, OFS-1 can be linked to a near infrared dye instead of a fluorescent dye to increase tissue penetration in live animal models. The probe can also be attached to drug molecules for targeted drug delivery at specific cathepsin K active sites for bone disease and cancer treatments.

APPLICATIONS

Research studies on the effects of cathepsin K and osteoclasts for:

- ▶ Osteoporosis
- ▶ Osteoarthritis
- ▶ Rheumatoid arthritis
- ▶ Multiple myeloma

Targeted drug delivery for:

- ▶ Bone resorption abnormalities in the diseases mentioned above
- ▶ Bone metastasis of cancer

ADVANTAGES

- ▶ Highly specific for bone tissues
- ▶ Flexible attachment of different types of fluorophores/probes
- ▶ Can be used in vivo and in vitro
- ▶ Can be used for drug delivery
- ▶ Long half-life

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OTHER INFORMATION

KEYWORDS

FRET-quencher, Cathepsin K, Osteoclast, Bone Resorption, Molecular Probe, Fluorescent Probe, Targeted Drug Delivery

CATEGORIZED AS

- ▶ **Biotechnology**
 - ▶ Health
- ▶ **Imaging**
 - ▶ Medical
 - ▶ Molecular
- ▶ **Medical**
 - ▶ Delivery Systems
 - ▶ Disease: Autoimmune and Inflammation
 - ▶ Disease: Cancer
 - ▶ Disease: Musculoskeletal Disorders
 - ▶ Imaging
 - ▶ Research Tools

RELATED CASES

2017-723-0

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	11,219,697	01/11/2022	2017-723

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