

Tokyo Institute of Technology
The University of Electro-Communications

Illuminating detection of deep cancers

Tokyo Tech and UEC researchers develop a new bioluminescence imaging system to improve detection sensitivity of targets in deep tissues

To see right through something is to know its true intent—the same could be said to apply to biological tissues, especially tumors.

Bioluminescence imaging with a firefly enzyme, called luciferase, and its substrate D-luciferin, is widely used to monitor biological processes. However, the emission wavelength of bioluminescence produced by D-luciferin limits the sensitivity of this technique. At 562 nm, this light does not effectively penetrate biological tissues.

To overcome this limitation, a team of Tokyo Tech and the University of Electro-Communications (UEC) researchers developed a luciferin analog (a compound that resembles another in structure) that can produce bioluminescence with near-infrared wavelength and is applicable in animal experiments. This allows markedly higher target-detection sensitivity, even at very low concentrations.

A novel soluble luciferin analog

The UEC researchers had previously synthesized a novel luciferin analog, AkaLumine, by altering the chemical structure of D-luciferin. While the emission wavelength of bioluminescence produced by AkaLumine yielded high penetration, its insolubility hindered its use. The team moved beyond this to screen for water-soluble derivatives of AkaLumine, and discovered that one of them, AkaLumine hydrochloride (AkaLumine-HCl), was in fact soluble. The Tokyo Tech researchers evaluated these substrates and had provided proper information for directing it to be practical use in animal experiments, making AkaLumine-HCL applicable for bioluminescence imaging of deep tissues.

AkaLumine-HCl emitted near-infrared bioluminescence at 677 nm when reacted with firefly luciferase (Figure 1), and had greatly improved tissue-penetration efficiency. In 4-mm or 8-mm slice of beef, AkaLumine-HCl bioluminescence showed penetration 5-fold and 8.3-fold higher than bioluminescence produced by D-Luciferin (Figure 2). Notably, achieving such a high sensitivity using D-luciferin would require a 60-fold higher concentration.

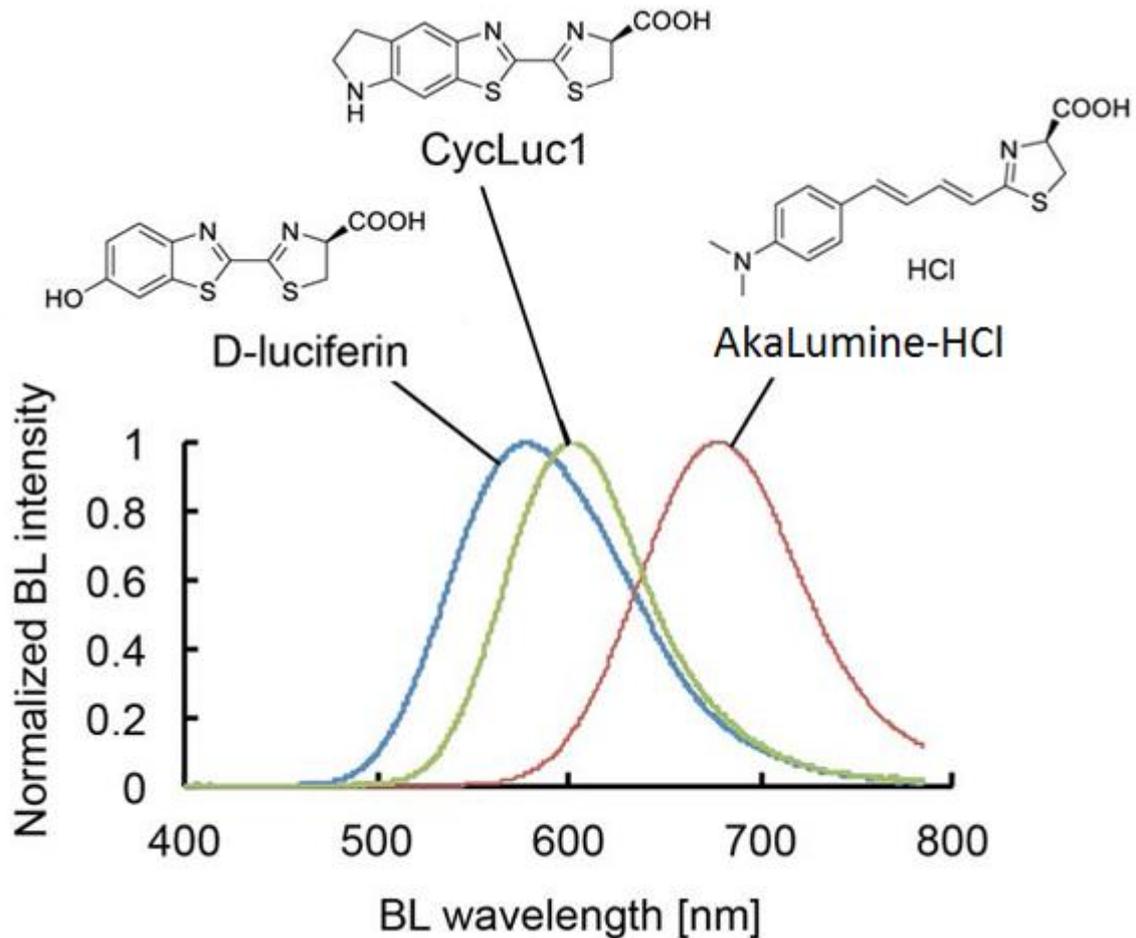


Figure 1. Bioluminescence emission spectra of D-luciferin, CycLuc1 or AkaLumine-HCl.

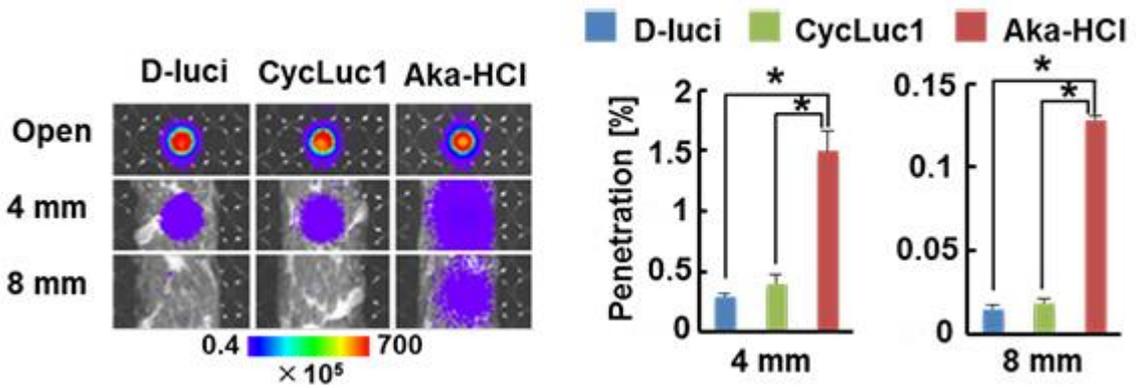


Figure 2. Biological tissue penetration efficiency of bioluminescence
Optical imaging of the biological tissue (4-mm/8mm-thick sliced beef) were placed on the wells with each substrate (left). Penetration efficiency of bioluminescence through the tissue (right).

To further evaluate the performance of AkaLumine-HCl in a lung cancer mouse model, the researchers compared the bioluminescence signals from mouse lung cancer treated with AkaLumine-HCl, D-luciferin, and its superior counterpart, cyclic alkylaminoluciferin (CycLuc1). Remarkably, AkaLumine-HCl significantly increased detection sensitivity of lung tumors as compared with D-luciferin and CycLuc1 (Figure 3).

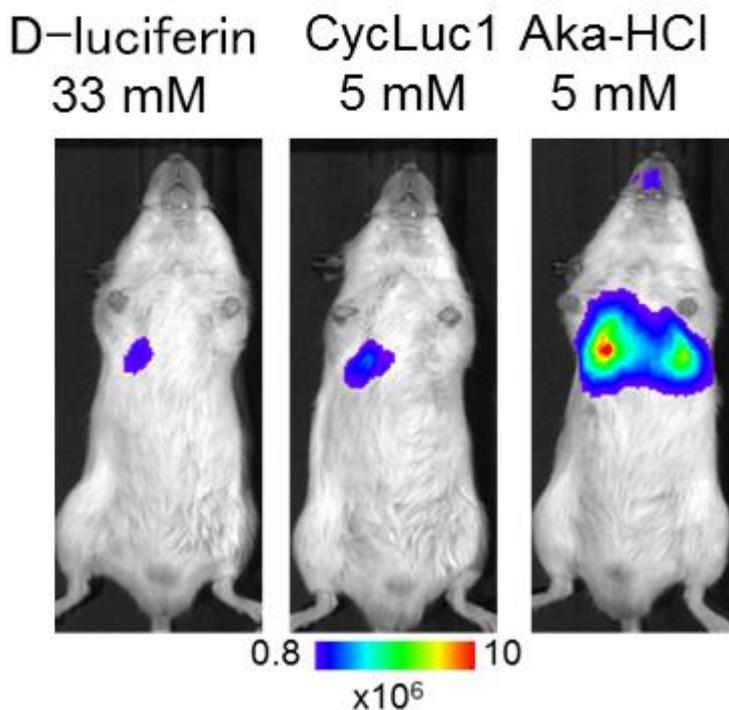


Figure 3. Bioluminescence imaging of lung tumor

Immediate applicability

Owing to its superior properties that enable higher sensitivity and accuracy, AkaLumine-HCl has potential to become the preferred choice for bioluminescence imaging. Nonetheless, for now, the benefits that its discovery brings can already be reaped in bioluminescence imaging studies in small animal models.

Reference

Authors: Takahiro Kuchimaru¹, Satoshi Iwano², Masahiro Kiyama², Shun Mitsumata¹, Tetsuya Kadonosono¹, Haruki Niwa², Shojiro Maki², Shinae Kizaka-Kondoh^{1*}

Title of original paper: A luciferin analog generating near-infrared bioluminescence achieves highly sensitive deep-tissue imaging

Journal: *Nature Communications*

DOI : [10.1038/ncomms11856](https://doi.org/10.1038/ncomms11856)

Affiliations: ¹School of Life Science and Technology, Tokyo Institute of Technology
²Graduate School of Informatics and Engineering, The University of Electro-Communications

Contact

Emiko Kawaguchi

Center for Public Affairs and Communications,

Tokyo Institute of Technology

E-mail: media@jim.titech.ac.jp

Tel: +81-3-5734-2975

Public Relations Center

The University of Electro-Communications

E-mail: kouhou-k@office.uec.ac.jp

Tel: +81-42-443-5019