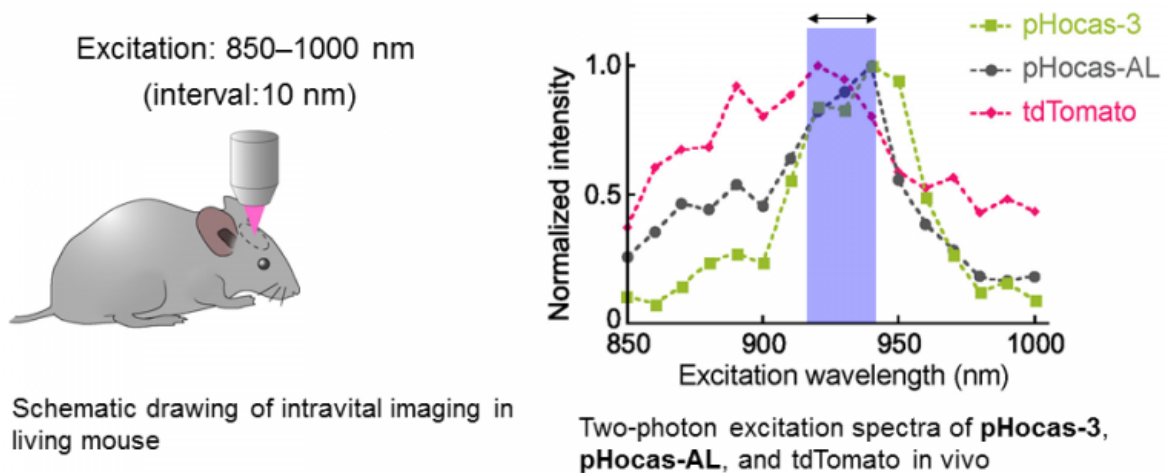


Real-time visualization of the function of bone-resorbing cells within animals

August 17 2016

In vivo excitation spectra of pHocas-3 and tdTomato



Excitation of multiple fluorophores with a **single laser source**



Time-lapse imaging with a short interval

Figure 1: In vivo excitation spectra of pHocas-3 and tdTomato

Researchers of Osaka University have discovered a way to visualize sites

where bone-resorbing cells (osteoclasts) were in the process of resorbing bone in living mice. This real-time visualization of changes in osteoclast localization and activity allowed the successful measurement of bone resorption intensity. Since this enables simple and quick access to information on the activity of osteoclasts, this discovery will contribute to the early diagnosis of affected areas and the development of new therapeutic drugs.

Osteoclasts are bone-resorbing cells that may cause osteoporosis and rheumatoid arthritis if there is an excess in bone resorption. So far, information on osteoclast localization could be gathered by using fluorescent proteins, but this method did not allow an examination of osteoclast activity. A group of researchers at the Immunology Frontier Research Center (IFReC), Osaka University, led by Kazuya Kikuchi, professor at the Graduate School of Engineering, and Masaru Ishii, professor at the Graduate School of Medicine, Osaka University, produced fluorescent probes that visualize those sites where osteoclasts are in the process of resorbing bone and developed their own imaging device. They thereby conducted a successful in vivo evaluation of osteoclast function.

The research team developed a mechanism by which small molecular probes (SMPs) are selectively delivered to the location of target cells. Up until then, application of SMPs to in vivo imaging was particularly challenging, as delivery to target tissues proved difficult. The researchers managed to optimize molecular delivery so that the molecular probes only had to be injected into the mice for imaging. The SMPs were equipped with a switch function that is only triggered at those areas where bone is being resorbed. This enabled the selective visualization of osteoclast activity. In combination with [fluorescent proteins](#) that label [target cells](#), the researchers succeeded in real time visualization of changes in cell localization and activity as well as the measurement of [bone resorption](#) intensity.

Photostable pH-activatable Probe

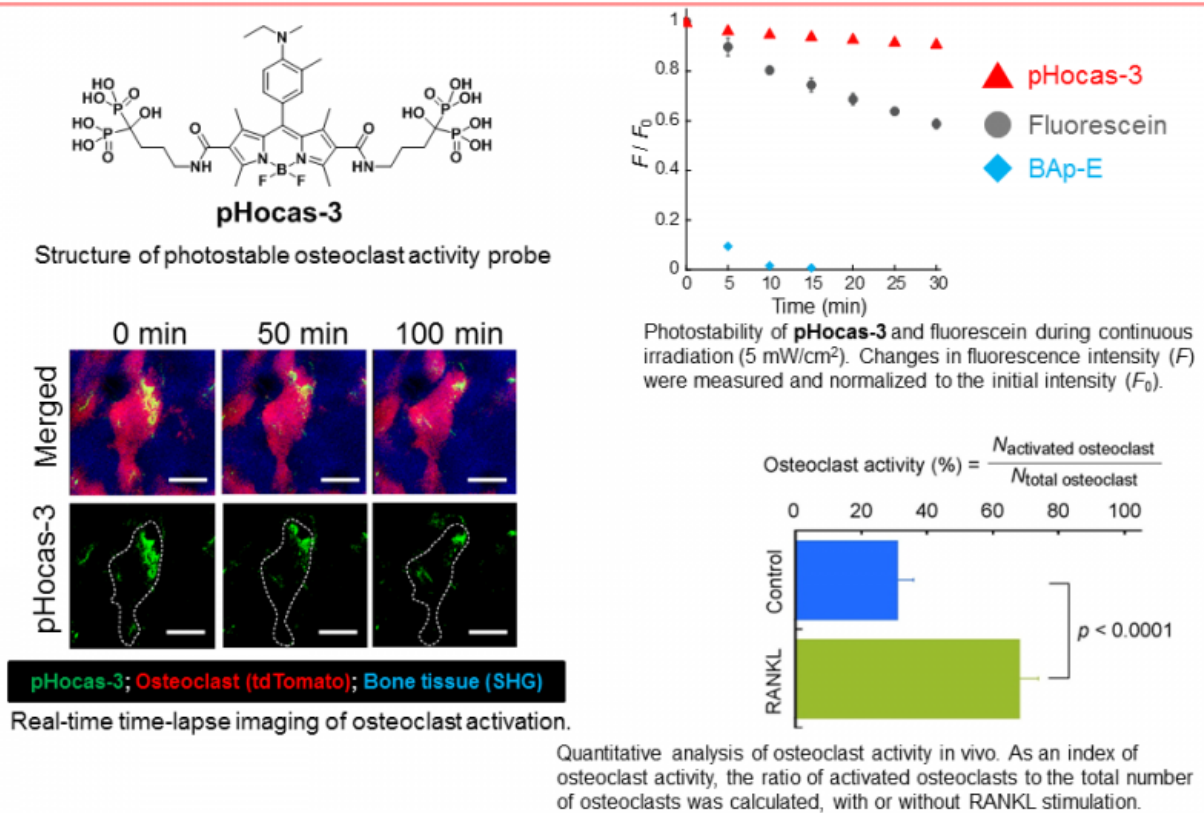


Figure 2: Photostable pH-activatable Probe

This research will have great impact in the field of in vivo imaging as it established an in vivo imaging method that allows simple and quick measurement in detecting osteoclasts that are in the process of resorbing bone. This will also benefit early diagnosis and the screening of new therapeutic drugs. The study carries broader social and academic relevance as it was conducted as interdisciplinary research, spanning such areas as molecular design based on physical chemistry principles, the creation of functional [fluorescent probes](#) by synthetic organic

chemistry, and the clarification of intravital mechanisms using immunological knowledge and technology. It therefore serves as an example of research that achieved positive results starting from basic research that led to application in medical research.

This research was featured in the electronic version of *Nature Chemical Biology* on June 7, 2016.

More information: Hiroki Maeda et al. Real-time intravital imaging of pH variation associated with osteoclast activity, *Nature Chemical Biology* (2016). [DOI: 10.1038/nchembio.2096](https://doi.org/10.1038/nchembio.2096)

Provided by Osaka University

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