KYUSHU UNIVERSITY

Public Relations Office, Kyushu University
744 Motooka Nishi-ku Fukuoka, 819-0395
TEL: +81-92-802-2443 FAX: +81-92-802-2139
E-MAIL: koho@jimu.kyushu-u.ac.jp
URL: https://www.kyushu-u.ac.jp

PRESS RELEASE (2025/08/04)

Visualizing the Mechanics of Hormone-Driven Gene Activation: Insights into Breast Cancer

Kanazawa, Japan—Scientists at Kanazawa University's Nano Life Science Institute (WPI-NanoLSI), including Professor Masaharu Hazawa of Kyushu University's Faculty of Science, have captured real-time footage showing how a key hormone receptor activates genes, offering a clearer view into one of the most fundamental processes in biology.

Using high-speed atomic force microscopy (HS-AFM), researchers directly visualized how the estrogen receptor alpha (ERα) binds to DNA and switches on genes in response to the hormone estrogen. Their findings, published in *ACS Nano*, reveal new molecular details of hormone signaling, with important implications for diseases like breast cancer.

Estrogen receptors play a critical role in controlling gene activity in many tissues. When estrogen binds to ERα, the protein changes shape, forms a dimer (a molecular pair), and attaches to specific regions of DNA called estrogen response elements (EREs). Although the importance of this process has been known for decades, it had never before been observed unfolding at the single-molecule level in real time.

To capture this, the researchers used HS-AFM to scan individual ERα molecules interacting with DNA. They compared the behavior of ERα with and without estrogen present. Their experiments showed that ERα could bind to DNA without estrogen but did so less precisely and less stably. When estrogen was present, ERα molecules dimerized more efficiently and exhibited targeted, stable binding to ERE sequences.

"Our study shows that estrogen acts like a molecular matchmaker," says Richard Wong of Kanazawa University. "It not only triggers ERα to find the right DNA sequence but also stabilizes its grip, ensuring accurate gene activation."

Based on these observations, the team proposed a new 'Ligand-Induced Dimerization' (LID) model explaining how hormones fine-tune the dynamic behavior of receptors at the DNA level. This work provides direct visual evidence of how molecular signals from hormones lead to precise gene control—a fundamental advance that could guide new strategies for treating hormone-driven diseases.

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For more information about this research, see "Zooming into Gene Activation: Estrogen Receptor α Dimerization and DNA Binding Visualized by High-Speed Atomic Force Microscopy," Goro Nishide, Tomoka Ishibashi, Keesiang Lim, Yujia Qiu, Masaharu Hazawa, Ayami Matsushima and Richard W. Wong *ACS Nano*, https://doi.org/10.1021/acsnano.4c14943

About Kyushu University
Founded in 1911, Kyushu University is one of Japan's leading research-oriented institutes of higher education, consistently ranking as one of the top ten Japanese universities in the Times Higher Education World University Rankings and the QS World Rankings. The university is one of the seven national universities in Japan, located in Fukuoka, on the island

of Kyushu—the most southwestern of Japan's four main islands with a population and land size slightly larger than Belgium. Kyushu U's multiple campuses—home to around 19,000 students and 8000 faculty and staff—are located around Fukuoka City, a coastal metropolis that is frequently ranked among the world's most livable cities and historically known as Japan's gateway to Asia. Through its VISION 2030, Kyushu U will "drive social change with integrative knowledge." By fusing the spectrum of knowledge, from the humanities and arts to engineering and medical sciences, Kyushu U will strengthen its research in the key areas of decarbonization, medicine and health, and environment and food, to tackle society's most pressing issues.

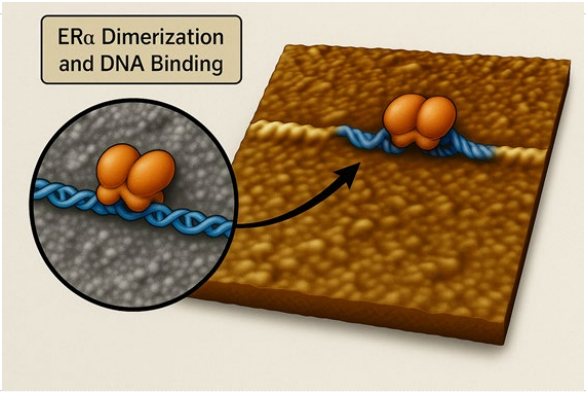

Fig. 1. How Estrogen Receptor Binds DNA.
This illustration shows the estrogen receptor alpha (ERα, in orange) attaching to DNA (in blue) as a pair, or dimer. The image is based on real-time, high-speed atomic force microscopy (HS-AFM) data, showing how ERα recognizes and binds specific DNA sequences to activate genes. The close-up highlights the dimer sitting on the DNA strand — a key step in hormone-driven gene regulation.

[Contact]
Ayami Matsushima, Professor
Department of Chemistry Faculty of Science
Tel: +81-92-802-4159
E-mail: ayami@chem.kyushu-univ.jp