Virus-based approach for measuring variations in gene regulatory elements

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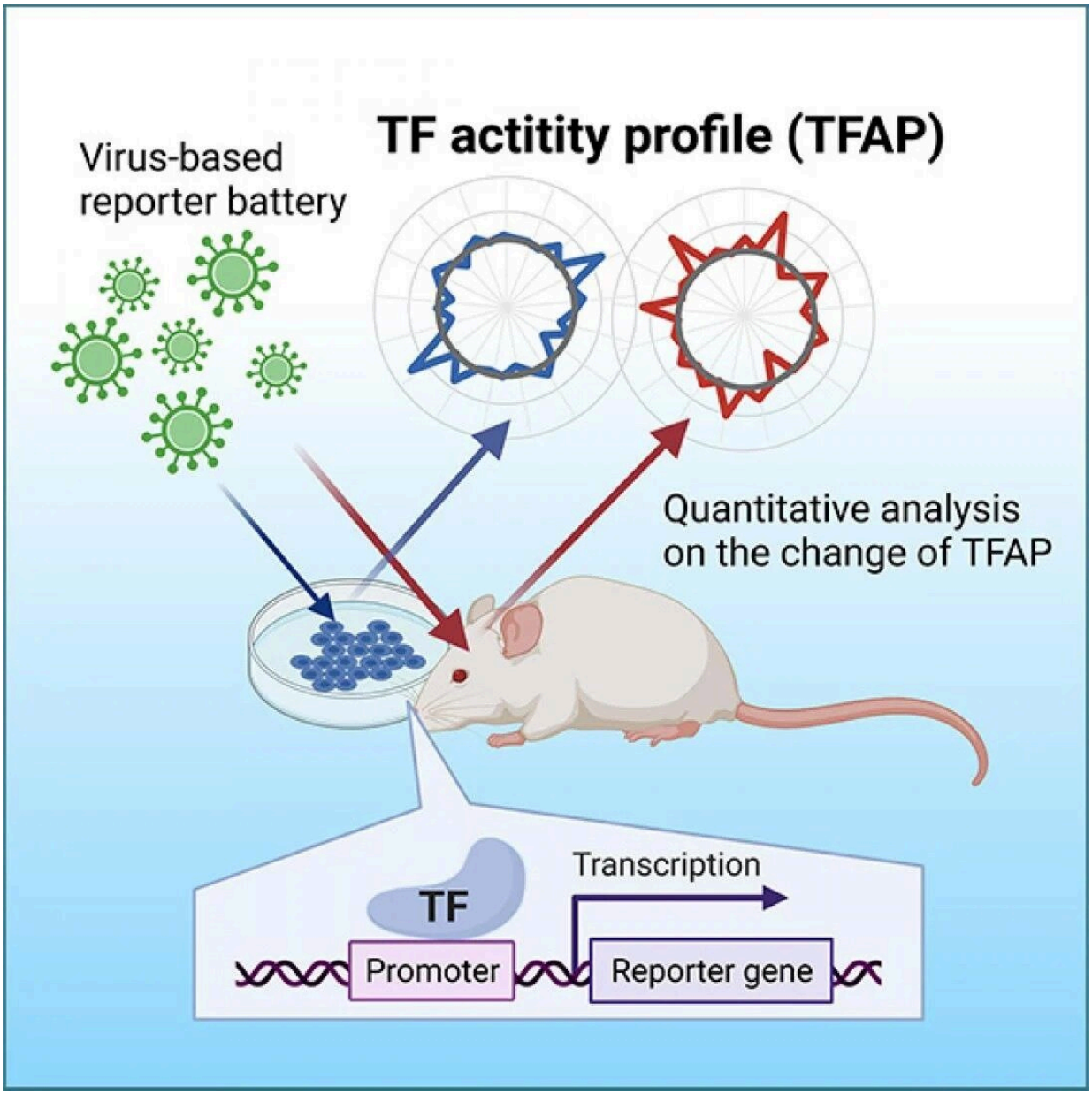

The approach involves infecting cells and living organisms with viruses carrying gene sequences that, when activated, lead to a measurable change. Credit: H. Abe and K. Abe

Tohoku University scientists in Japan have developed a virus-based approach for measuring variations in gene regulatory elements, called transcription factors, as conditions change in live organisms. The research, published in the journal *iScience,* will help scientists develop a clearer understanding of gene regulation, with implications for understanding how diseases develop and what can be done to treat them.

"Transcription factors directly regulate the copying of DNA code into RNA, the process that leads to protein formation," says Kentaro Abe, a developmental biologist and neuroscientist at Tohoku University. "They also play a core role in establishing the function and identities of cells. But, until now, there has not been a way to measure their activity in live organisms. Our study reports a novel method for quantifying the activity of multiple transcription factors 'in vivo,'" he says.

The approach involves infecting cells with viruses, each carrying a DNA sequence, called a transcription factor binding sequence (TFBS), that is activated when it binds to its complementary transcription factor. The researchers chose TFBSs that bind to one of 56 different transcription factors. The binding process turns on another gene carried by the virus, which signals the cell to manufacture fluorescent proteins, indicating that a specific transcription factor is active within the cell. The fluorescent proteins are then measured with a PCR test.

The scientists first tested their approach by infecting different types of cells in petri dishes with the viruses, each carrying a different TFBS. They found that different transcription factors were active in each cell

type. They also found they could change the transcription factor profile of each cell type by treating them with different drugs.

The researchers then injected their viruses into the brain of 15-day-old mouse embryos and left to develop and be born. The mice were divided at 8–12 months of age into three groups. The first group was moved to larger, more comfortable cages with toys shortly before being euthanized. The second group was placed in water for 12 minutes two days in a row, where they were forced to swim. The third group was left untouched in their home cage. The scientists analyzed the brain, finding a significant difference in the transcription factor profile between the three groups of mice.

"Building on our approach, we are now trying to quantitatively analyze how the activity of transcription factors changes with various physiological conditions, including development, learning, lifestyle changes, stress and disease progression," says Abe. "These analyses will help pinpoint the transcription factors responsible for the plastic change of organisms and pave the way towards understanding its molecular mechanisms."

More information: Hitomi Abe et al, PCR-based profiling of transcription factor activity in vivo by a virus-based reporter battery, *iScience* (2022). DOI: 10.1016/j.isci.2022.103927

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