Cellular communications visualized with a vibrant color palette

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A University of Alberta-led research team has dramatically expanded the palette of fluorescent highlighters that can be used to track the movement of messengers inside of single cells.

Until now, cellular imaging of the calcium ion, the key messenger for intracellular communication, required the use of a green fluorescent indicator. Accordingly, imaging of calcium ions produced monochromatic images and movies in shades of green. The addition of new red and blue fluorescent indicators now provides researchers with a vivid full colour view of calcium ions moving about in their role as the intracellular signaling messenger.

Imaging of the calcium ion is commonly used by researchers to monitor cellular activity such as the firing of neurons. However, since calcium ions are themselves colourless, it is necessary to introduce a coloured indicator protein into the cell. When these coloured indicator proteins bind to calcium ions they can either increase in fluorescent brightness or change the colour of their fluorescence. These changes in brightness or colour can be easily visualized by researchers using appropriate microscopy equipment.

The ability to examine the dynamics of calcium ions inside a single cell in more detail could help pharmaceutical researchers determine if a drug designed to affect a specific cell is hitting its target. They could also help researchers to better visualize neuronal activity in model organisms such as transgenic worms or mice.

The University of Alberta research team, led by chemistry PhD candidate Yongxin Zhao, engineered the new genetically encoded indicator proteins using bacterial cells.

The use of bacterial cells to engineer the new indicators was key to achieving this breakthrough. The indicator genes were programmed to be sent to the outside of the bacterial cytoplasmic membrane. Once outside, the calcium ion concentration could be experimentally altered to find the indicator variants that had the desired colour and largest changes in brightness. Using this approach, the researchers performed directed laboratory evolution to ultimately provide the optimized indicator proteins.

More information: The research is published in the Sept. 8 issue of *Science Express* : www.sciencemag.org/content/early/recent

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