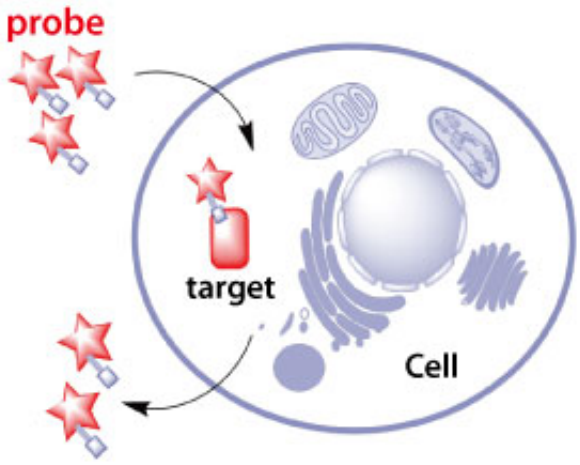
Probes that can easily enter cells to label target molecules only can be readily made thanks to a new model

November 2 2016



A new model developed by A*STAR researchers allow probes to be designed that can enter cells easily and label target molecules only. This will enable improved imaging of cellular processes. Credit: A*STAR Singapore Bioimaging Consortium

A new model developed by A*STAR researchers will assist the production of tailor-made probes for imaging specific molecules inside cells. This method promises to improve the imaging of living cells and hence uncover more secrets about how they operate.

Small chemicals that latch onto specific biomolecules inside living cells

and emit light when irradiated by laser light—known as fluorescent probes—are widely used to explore the roles and functions of biomolecules in cells.

However, this highly popular imaging technique suffers from two significant problems. First, probes often attach to other biomolecules besides the target ones, which gives rise to a background signal that can obscure the signal from the target biomolecule. Second, some probes struggle to cross cell membranes, making them hard to smuggle into live cells.

Now, Young-Tae Chang of the A*STAR Singapore Bioimaging Consortium and his co-workers have developed a predictive model that can overcome both problems. This model can be used to develop designer probes that are highly specific to single biomolecules and can cross cell membranes with ease.

The team investigated more than a thousand probes and statistically analyzed the results. They discovered that the behavior of probes inside cells is mainly determined by just three properties: their solubilities in water and fatty substances (known as lipids) and also a parameter that indicates the charged surface area of a molecule.

Furthermore, the researchers identified the optimal values of these parameters for specific situations. Chang explains: "For example, if we know that probes with high hydrophilicity may not be able to cross a cell membrane, we can adjust the hydrophilicity to the ideal value given by the model."

The team demonstrated this approach by using probes to specifically label various organelles, such as mitochondria, lysosome and the Golgi apparatus. They also used probes to label proteins in cells.

Chang is excited about this potential of the method. "Using cell-permeable, background-free probes will allow a far better imaging for exploring dynamic processes of intracellular biomolecules in their native environment, especially in the fields of chemistry, biology and medicine."

The team plans to extend their technique in various ways. "A long journey has just started," says Chang. "We aim to expand the system for performing multicolor intracellular labeling to examine subcellular structures with precise detail in a complex biological environment. We also dream of developing a toolbox of probes with various functional groups for extensive applications."

More information: Samira Husen Alamudi et al. Development of background-free tame fluorescent probes for intracellular live cell imaging, *Nature Communications* (2016). DOI: 10.1038/ncomms11964

Provided by Agency for Science, Technology and Research (A*STAR), Singapore