The screening of thousands of fluorescent molecules has revealed a specific label for neural stem cells

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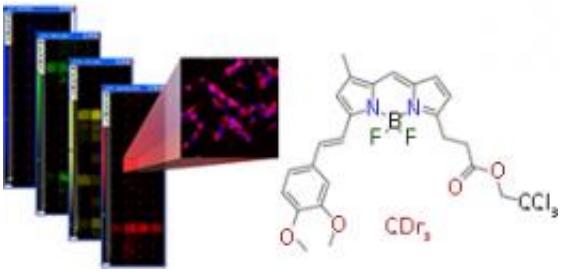

In a high-throughput screening of fluorescent molecules, the fluorescent compound CDr3 stained neural stem cells the most brightly and specifically. Credit: 2012 National Academy of Sciences, USA (inset, pink); © 2012 A*STAR Singapore Bioimaging Consortium (main image)

Neural stem cells are the precursors of cells in the nervous system. As well as being crucial for early development, they are present throughout life, contributing to flexibility and repair of the nervous system. As such, they can be used to study the brain, and may offer new ways of treating neurological disease.

Current techniques for identifying and labeling live neural stem cells use antibodies to detect specific cell-surface molecules. Small fluorescent molecules, which are commonly used to visualize the locations and movements of molecules and cells, may offer a more convenient and

safer alternative.

Young-Tae Chang at the A*STAR Singapore Bioimaging Consortium and co-workers have now identified a fluorescent compound that specifically labels neural stem cells by binding to an intracellular protein. The molecule, named CDr3, was singled out for its selective labeling of neural stem cells after testing thousands of fluorescent compounds from a 'Diversity Oriented Fluorescence Library', or DOFL.

"A DOFL is a collection of intrinsically fluorescent low molecular weight compounds which have been synthesized, purified and characterized in our lab," says co-author Seong-Wook Yun. "We have generated more than 10,000 DOFL compounds so far, each with different chemical and biological properties."

The researchers narrowed down the number of potentially useful molecules by assessing how strongly they labeled stem cells, and finally determined that CDr3 stained them the most selectively and brightly (see image). They confirmed the specificity of labeling by incubating CDr3 with different cell types and showing that it only stained neural stem cells. Growing stem cells in the presence of CDr3 also showed that it does not affect their survival or division.

A combination of molecular biology techniques revealed that CDr3 labeled the cells by binding to a neural stem cell-specific protein called FABP7. This is found inside the cell, unlike other labeling targets. "Conventionally, live neural stem cells have been identified by detecting cell surface molecules," explains Yun. "However, these molecules are also highly expressed in other types of cells. FABP7 is a specific intracellular marker of neural stem cells."

Labeling of neural stem cells with CDr3 not only allowed them to be identified, but also to be separated from other types of cells. According

to Yun, this is important for practical applications.

"Detection and isolation of live neural stem cells from heterogeneous cell populations is a key technology, not only for basic research but also for the development of cell-based therapeutics and drug development," he says.

More information: Yun, S.-W., Leong, C., Duanting, Z., Tan, Y. L., Lim, L. et al. Neural stem cell specific fluorescent chemical probe binding to FABP7. *Proceedings of the National Academy of Sciences* 109, 10214–10217 (2012). www.pnas.org/content/109/26/10214

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