TOOLBOX

New databases decode gene expression in brain cells

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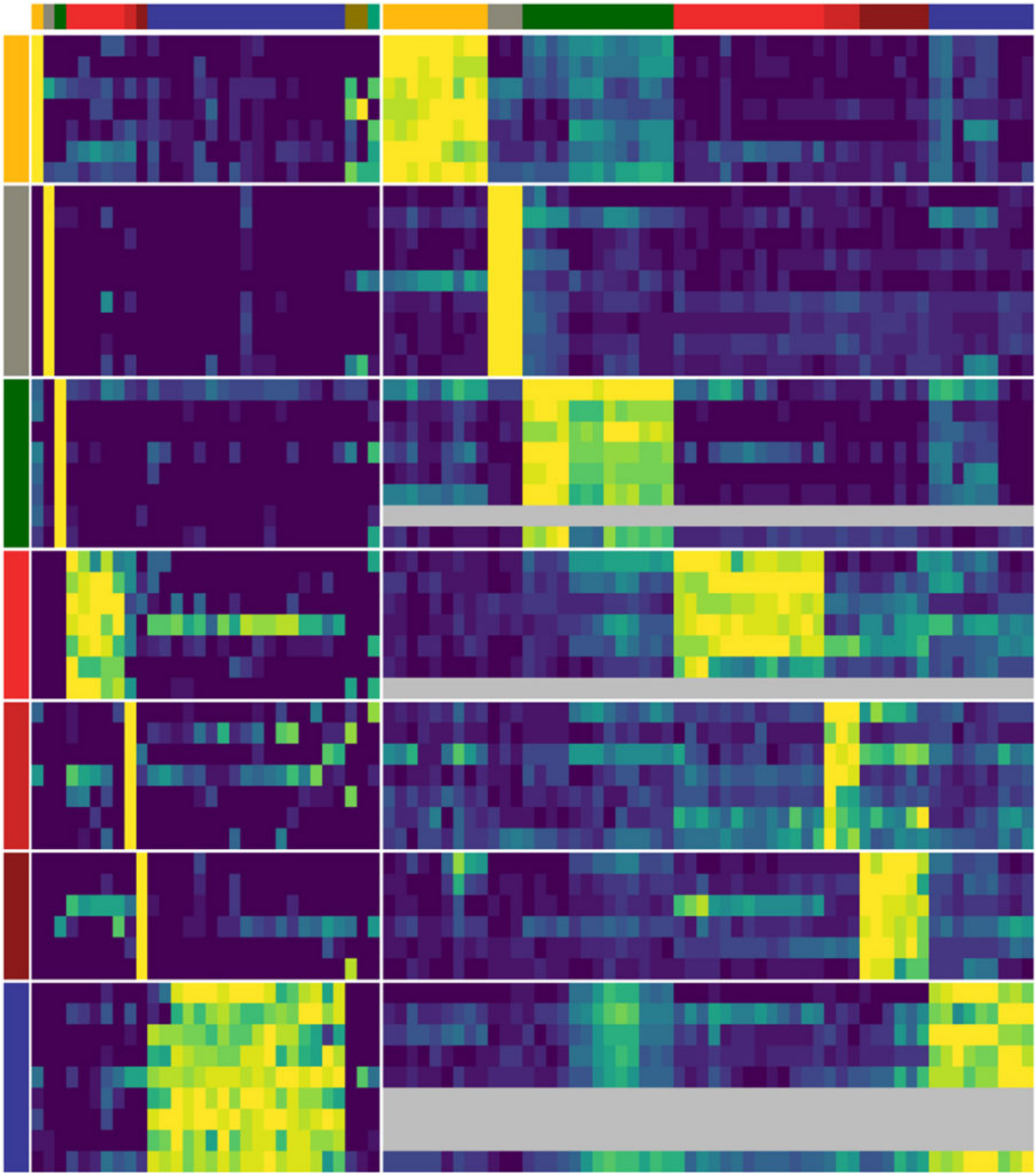

Two new databases that catalog the genes expressed in specific brain cells could help researchers interpret data on gene expression in postmortem brains[1,2].

Scientists could use the resources to say, for example, whether changes in gene expression seen in autism brains stem from a loss or gain of a particular type of neuron.

For one of the resources, scientists modified a relatively new strategy for teasing out gene expression in individual cells. The technique involves tagging and channeling individual cells into tiny water droplets. It allows researchers to sequence the messenger RNA — the molecular templates for proteins — from one cell at a time.

But this method requires first separating individual cells into the droplets, which is difficult to do because neurons and support cells tend to stick together in postmortem tissue.

To solve this problem, the researchers broke down cell walls and isolated only the cells' nuclei — which contain all of the cells' genetic information. They encapsulated the nuclei into the water droplets for sequencing.

They also used a technique that sequences genomic regions that are loosely wrapped around support proteins called histones. This 'open' conformation allows the cells' regulatory machinery to access these regions, and so denotes the regions that were in play in that cell type.

The researchers assessed gene expression in postmortem tissue from the cerebral cortex (the brain's outer rind) and cerebellum of six adults. They developed an algorithm that combines the RNA and histone data and assigns it to particular types of cells.

The resulting database denotes the genes expressed in 35 types of brain cells. It also pinpoints regulators of gene expression, or transcription factors, that are active in individual cells.

On the mark:

The researchers used the method to determine whether genetic variants associated with various conditions are likely to affect certain cell types.

Their results suggest that autism has a bigger impact on neurons than it does on glia, the brain's support cells. The researchers note that the finding should be interpreted with caution, however, because it stems from adult brains, and autism emerges in early childhood.

The second resource, **NeuroExpresso**, includes gene expression profiles for 36 types of mouse brain cells in 12 brain regions. This database makes use of published sequences of single cells from mouse brains. In most of the studies, scientists purified a specific cell type from brain tissue before sequencing.

NeuroExpresso's creators used their compilation to identify sets of 'marker' genes that are expressed at higher rates in specific cell types.

Expression of these marker genes can reveal the relative abundance of certain cell types in postmortem brain tissue. The markers also can show whether a set of genes that are mutated in people with a condition such as autism are likely to affect certain cell types. The work appeared in November in *eNeuro*.

The researchers are continually updating NeuroExpresso as other teams publish more expression data from single cells, including those from human brains.

REFERENCES:

1. Lake B.B. *et al. Nat. Biotechnol.* **36**, 70-80 (2018) **PubMed**
2. Mancarci B.O. *et al. eNeuro* **4**, ENEURO.0212-17.2017 (2017) **PubMed**