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# Novel genetic engineering approaches for lineage analysis and exploration of Akt function in cortical development

## Results in Brief

# Combinatorial labelling of nervous system cells

Mammalian brain development involves the coordinated interaction of cells of different origins. An EU-funded project studied cerebral cortex development using a multicolour multi-clonal labelling strategy.

HEALTH

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The cerebral cortex, or the outer layer of neural tissue of the mammalian brain, has numerous functions, including memory, attention and language. Cortical mini-columns are the basic functional units of the cortex, each comprising about a hundred neurons. Mini-columns develop from the progenitor cells within the embryo.

Until now, it was difficult to simultaneously mark multiple neural progenitors with distinct labels and track their descendants over long periods of time. The EU-funded BRAINBOWAKT (Novel genetic engineering approaches for lineage analysis and exploration of Akt function in cortical development) project applied a revolutionary method to track individual neural cells. In the developed Brainbow process, the individual cells in the brain could be distinguished from neighbouring neurons using fluorescent proteins.

Scientists developed novel genetic engineering techniques to mark multiple neighbouring progenitors and their descendants in vivo with unambiguous labels. Brainbow constructs expressing an expanded palette of trichromatic markers (red, yellow and cyan fluorescent proteins) were addressed to specific subcellular compartments. These transgenes were introduced into the embryonic mouse forebrain by electroporation. It was possible to label progenitor cells over several rounds of cell division, and to track their descendants to adult stages.

Generating transgenic mice with the new Brainbow constructs permitted labelling of neural progenitors in stages and at locations where electroporation cannot be performed.

Brainbow was further developed to modulate the function of candidate proteins in vivo. The end result was a genetic mosaic where the status of gene expression in the cells was colour coded. This approach allows for tracking neighbouring cells with different gene expression levels within the same sample.

The established strategy finally made possible the investigation of cellular architecture in the process of mini-column formation. BRAINBOWAKT activities have resulted in the development of a useful animal model and strategies that are applicable for studying intact tissues in numerous biological contexts.

## Keywords

Combinatorial labelling, cerebral cortex, neural progenitors, BRAINBOWAKT, lineage analysis

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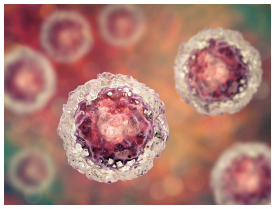

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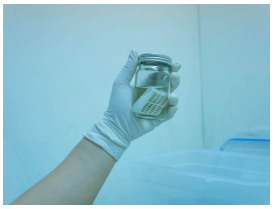

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Project Information

**BRAINBOWAKT**

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Project closed

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1 June 2011

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