Transgenic Screens for Modulators of Brain-Derived Neurotrophic Factor Production

(VA Reference No. 01-113)

Unique drug screening tool for identifying potential therapeutic agents for neurological disorders

Technology
Drug screening tool for identifying potential neurological disorder treatment agents

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Key Features
- Fluorescent labeled transgenic screening tool
- Identifies specific mechanism by which BDNF is increased
- High precision in identifying potential drug candidates

Stage of Development
Reduced to practice with successful demonstration

Keywords
Drug Screening Tool
- Brain-derived neurotrophic factor (BDNF)
- High-throughput screening
- Transgenic screens
- Drug discovery

Patent Status
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Technology
The Department of Veterans Affairs has developed a transgenic screening tool to rapidly screen drug candidates for their ability to influence the production of brain-derived neurotrophic factor (BDNF). The method also promises to be useful in identifying the complex genetic pathway affecting BDNF expression and thus in identifying new targets for drug discovery efforts.

Description
This transgenic screening tool developed by the VA uses a zebrafish BDNF promoter sequence inserted upstream of a fluorescent marker gene to mark the BDNF promoter by fluorescence. This transgene is injected into zebrafish embryos at the 1- to 8-cell stage of embryonic development to create a founder line, which is developed using standard breeding and analysis methods. The embryos are exposed to a test substance of biological or chemical nature, after which the level of fluorescent protein reporter is compared to controls using a fluorescent image analysis system. In this manner, factors that affect the promoter activity can be determined by alterations in the level of fluorescent signal.

Competitive Advantage
Most established methods of screening for modulators of BDNF production are based on cell culturing and measure the level of BDNF that is secreted into the culture medium before and after the introduction of potential modulators.

This Invention:

- Identifies the specific mechanism by which BDNF is increased.
- Allows researchers to identify factors that affect the activity of specific promoter genes.
- Results in drug candidates that are likely to be more useful because of the precision of the method.

Status
The Department of Veterans Affairs is looking for a partner for further development and commercialization of this technology through a license, and the VA inventors are available to collaborate with interested companies through a Cooperative Research and Development Agreement (CRADA).