

Statins as Treatment for Cognitive Dysfunction Associated with RASopathies

Tech ID: 20191 / UC Case 2004-598-0

SUMMARY

Professor Alcino Silva and colleagues at the UCLA department of Neurobiology have repurposed HMG-CoA reductase inhibitors (statins) to reverse cognitive dysfunction associated with RASopathies, such as neurofibromatosis type 1 and Noonan syndrome.

BACKGROUND

RASopathies comprise a group of developmental syndromes arising from germline mutations in genes resulting in dysregulation of the Ras-MAPK signaling pathway. Among the RASopathies, Noonan syndrome and neurofibromatosis type 1 (NF1) alone account for an estimated 9 million cases worldwide. In addition to the physical symptoms associated with these diseases, physicians also observe cognitive defects, with patients exhibiting a decreased capacity to learn and form memories. Families with NF1 patients cite these as the most pernicious part of this disorder, and there are currently no treatments available to alleviate this cognitive dysfunction.

INNOVATION

Professor Alcino Silva and colleagues at the UCLA department of Neurobiology have repurposed HMG-CoA reductase inhibitors (or statins) to reverse the cognitive dysfunction associated with RASopathies. By blocking HMG-CoA reductase, the drug prevents overactivation of the Ras protein, which leads to deficits in long term potentiation, a mechanism of learning and memory. Using in vivo models of NF1 and Noonan Syndrome, the researchers have shown that lovastatin is able to restore both LTP deficits and cognitive function to wild-type levels.

APPLICATIONS

- Treatment of cognitive dysfunction associated with NF1
- Treatment of cognitive dysfunction associated with Noonan syndrome
- Treatment of other disorders driven by hyperactivation of the Ras-MAPK pathway

ADVANTAGES

- Statins would represent the first and only drug available to treat the cognitive defects observed in NF1, Noonan and other RASopathies
- Statins have already been approved by the FDA as a cholesterol-lowering drug, demonstrating an amenable safety profile in humans
- Effectiveness in restoring cognitive function has been demonstrated in vivo

STATE OF DEVELOPMENT

The researchers first demonstrated the ability of statins to restore cognitive function in a mouse model of NF1. More recently, a phase I clinical trial demonstrated that lovastatin is safely tolerated in children, with provisional results from the same trial indicating some improvements in memory. Research adequately powered to fully assess therapeutic effects is ongoing in a phase II, multi-institutional protocol.

RELATED MATERIALS

- ▶ [The HMG-CoA reductase inhibitor lovastatin reverses the learning and attention deficits in a mouse model of neurofibromatosis type 1.](#)
Curr Biol. (2005)

PATENT STATUS

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INVENTORS

- ▶ Silva, Alcino J.

OTHER INFORMATION

KEYWORDS

Neurofibromatosis, NF1, attention deficit, ADD, ADHD, repositioning, statins, learning, memory, rasopathy, ras protein

CATEGORIZED AS

- ▶ **Biotechnology**
 - ▶ Health
- ▶ **Medical**
 - ▶ Disease: Central Nervous System
 - ▶ Therapeutics

RELATED CASES

2004-598-0

Country	Type	Number	Dated	Case
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