



Novel EphA4 Agonists for the Treatment of ALS

Tech ID: 33114 / UC Case 2020-246-0

BACKGROUND

Amyotrophic lateral sclerosis (ALS) is caused by the degeneration and death of motor neurons (MN). In patients with rapid ALS progression, the receptor tyrosine kinase, EphA4, is overexpressed. Studies have shown the unbound EphA4 causes pro-apoptotic activity and death in MNs. Additionally, EphA4 overexpression has been noted to correlate with the progression and resistance to chemotherapy of several human cancers including gastric, breast, and pancreatic cancers. The design of potent, selective, and effective EphA4 agonistic peptidomimetics may be desirable as therapies for ALS and cancer.

BRIEF DESCRIPTION

Researchers at the University of California, Riverside (UCR) in collaboration Nationwide Children’s Hospital have developed and characterized small peptidomimetics that act as EphA4 agonists. Given ALS is a heterogeneous disease, astrocytes reprogrammed from the fibroblasts of patients with sporadic and SOD1-linked ALS (iAstrocytes) were cultured with MNs and the UCR/Nationwide EphA4 agonists. As seen in Fig. 1, these small agonistic peptidomimetics decrease MN death in iAstrocytes derived from sporadic ALS (sALS) cells.

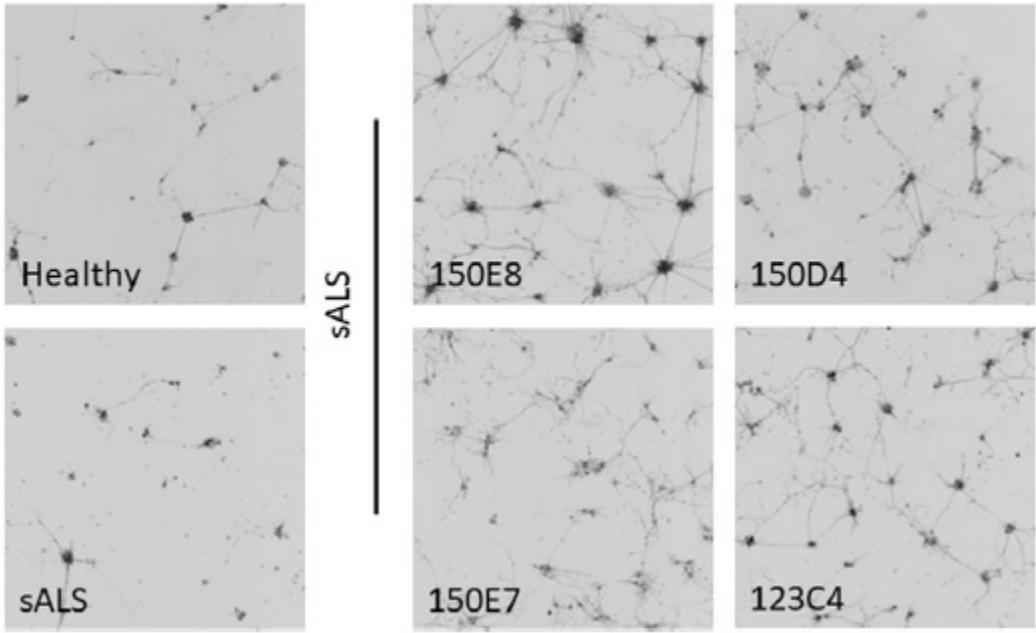


Fig 1: Representative images of motor neurons (black) co-cultured with iAstrocytes and novel EphA4 agonists, 150E8, 150D4, 150E7, and 123C4.

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OTHER INFORMATION

KEYWORDS

EphA4, ALS, AD, cancer therapeutics,
ephrin, diagnostic, Parkinson’s,
Alzheimers, peptide

CATEGORIZED AS

- **Medical**
 - Disease: Cancer
 - Disease: Central Nervous System
 - New Chemical Entities, Drug Leads
 - Research Tools

RELATED CASES

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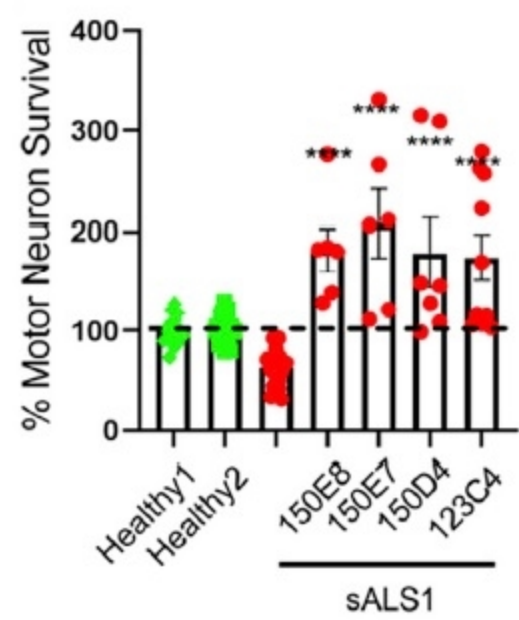


Fig 2: Quantification of MN survival treated with the novel UCR/Nationwide EphA4 agonists. Experiments were run in triplicate.

APPLICATION

- A potential treatment for ALS and cancer

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	20230203096	06/29/2023	2020-246

RELATED MATERIALS

- [Dennys, C.EphA4 targeting agents protect motor neurons from cell death induced by amyotrophic lateral sclerosis -astrocytes. iScience. 2022 Aug 5;25\(9\):104877. doi: 10.1016/j.isci.2022.104877. PMID: 36034213; PMCID: PMC9404653. - 08/25/2022](#)

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