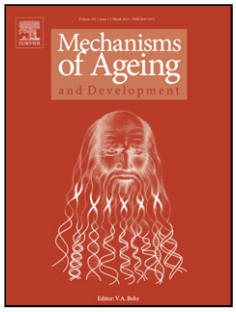


Title: Epigenetic mechanisms in amyotrophic lateral sclerosis: a short review

Authors: Ana Dolinar, Metka Ravnik-Glavač, Damjan Glavač

PII: S0047-6374(17)30225-7
DOI: https://doi.org/10.1016/j.mad.2018.03.005
Reference: MAD 11036

To appear in: *Mechanisms of Ageing and Development*

Received date: 20-9-2017
Revised date: 8-3-2018
Accepted date: 11-3-2018

Please cite this article as: Dolinar, Ana, Ravnik-Glavač, Metka, Glavač, Damjan, Epigenetic mechanisms in amyotrophic lateral sclerosis: a short review.Mechanisms of Ageing and Development https://doi.org/10.1016/j.mad.2018.03.005

# Epigenetic mechanisms in amyotrophic lateral sclerosis: a short review

Ana Dolinar[a], Metka Ravnik-Glavač[a, b], Damjan Glavač[a]

[a] Department of Molecular Genetics, Institute of Pathology, Faculty of Medicine, University of Ljubljana, Slovenia

[b] Institute of Biochemistry, Faculty of Medicine, University of Ljubljana, Slovenia

## Highlights

- Epigenetic mechanisms – DNA methylation, miRNA, histone modifications – contribute to the development of both sporadic and familial ALS.
- Changes in DNA methylation patterns and histone modifications lead to reduced gene expression.
- Dysregulated expression of various miRNAs affect many biochemical pathways, involved in ALS.

Abstract

Amyotrophic lateral sclerosis is a rapidly progressing neurodegenerative disease. Decades of research show that the etiology of this disease is affected by genetic, epigenetic and environmental factors rather than limited by a patient's genotype. The interaction between these factors is complex, and research has only begun to unravel this issue. The main epigenetic mechanisms, DNA methylation, miRNA, and histone modifications, can explain a portion of the disease complexity. However, the interplay among the epigenetic mechanisms themselves and with genetic factors remains largely uncharacterized. Epigenetic changes affect numerous cell processes, from transcription and translation to protein metabolism and cell junctions. In this review, we briefly summarize the main epigenetic mechanisms and outline recent research on the role of these epigenetic mechanisms in amyotrophic lateral sclerosis.

Keywords: amyotrophic lateral sclerosis, DNA methylation, miRNA, histone modifications

## Introduction

Amyotrophic lateral sclerosis (ALS) is one of four clinical phenotypes of motor neuron (MN) disease and has two subtypes [1]. The classification of MN disease phenotypes depends on the type of MNs affected; in ALS, the upper and lower MNs are affected [1]. The upper MNs originate in the cerebral cortex and form synapses with the lower MNs that are located in the brainstem and spinal cord [2]. The lower MNs receive input signals, form sensory neurons and interneurons, and innervate the face and neck muscles (branchial MNs), the smooth muscles and glands (visceral MNs), and the skeletal muscles (somatic MNs) [2]. The clinical phenotype of ALS is divided into two subtypes based on the initial symptoms, which can be either muscle weakness in the upper and lower limbs (limb onset) or tongue spasticity and speech difficulties (bulbar onset) [1]. European population-based ALS registers have revealed an incidence rate of 2.6/100 000 persons per year and a mean life expectancy of 30