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Research Article

Combinatorial effects of splice variants modulate function of Aiolos

Rosalia Caballero1,2, Fernando Setien1, Lidia Lopez-Serra1, Manuel Boix-Chornet 1,3, Mario F. Fraga1, Santiago Ropero1, Diego Megias4, Miguel Alaminos5, Eva M. Sanchez-Tapia2, Maria C. Montoya4, Manel Esteller1, Rogelio Gonzalez-Sarmiento2, * and Esteban Ballestar1, *

1Cancer Epigenetics Laboratory, Molecular Pathology Programme, Spanish National Cancer Research Centre (CNIO), Melchor FernándezAlmagro 3, 28029 Madrid, Spain
2Molecular Medicine Unit-Department of Medicine, Center for Cancer Research (CIC), University of Salamanca, Salamanca, Spain
3Leukaemia Research Fund Centre at the Institute of Cancer Research, London, UK
4Confocal Microscopy and Cytometry Unit, Biotechnology Programme, Spanish National Cancer Research Centre (CNIO), Madrid, Spain
5Department of Histology (University of Granada) and Fundación Hospital Clínico, Granada, Spain
**Authors for correspondence (e-mails: gonzalez@usal.es; eballestar@cnio.es)*
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The transcription factor Aiolos (also known as IKZF3), a member of the Ikaros family of zinc-finger proteins, plays an important role in the control of B lymphocyte differentiation and proliferation. Previously, multiple isoforms of Ikaros family members arising from differential splicing have been described and we now report a number of novel isoforms of Aiolos. It has been demonstrated that full-length Ikaros family isoforms localize to heterochromatin and that they can associate with complexes containing histone deacetylase (HDAC). In this study, for the first time we directly investigate the cellular localization of various Aiolos isoforms, their ability to heterodimerize with Ikaros and associate with HDAC-containing complexes, and the effects on histone modification and binding to putative targets. Our work demonstrates that the cellular activities of Aiolos isoforms are dependent on combinations of various functional domains arising from the differential splicing of mRNA transcripts. These data support the general principle that the function of an individual protein is modulated through alternative splicing, and highlight a number of potential implications for Aiolos in normal and aberrant lymphocyte function.

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