Author's response to reviews

Title: Genome-wide expression profiling and functional characterization of SCA28 lymphoblastoid cell lines reveal impairment in cell growth and activation of apoptotic pathways.

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Author’s response to reviews:

Dear Editor,

We are submitting to BMC Medical Genomics our paper entitled “Genome-wide expression profiling and functional characterization of SCA28 lymphoblastoid cell lines reveal impairment in cell growth and activation of apoptotic pathways” by Mancini et al.

SCA28 is one of the more recently identified forms of autosomal dominant spinocerebellar ataxia, and it is associated with mutations in the AFG3L2 gene (ATPase family gene 3-like 2) on chromosome 18p. We studied the genome-wide expression profile and characterized the cellular phenotype of
human SCA28 lymphoblastoid cell lines (LCLs), highlighting alterations in specific pathways and functions correlated to the disease.

Concerning consent and ethical approval, we stated in the methods section that all patients/controls received and signed an informed consent (in case of children, it was signed by a parent). We added a statement that the research was carried out in compliance with the Helsinki Declaration. The samples were collected within the SPATAX network to study the genetics basis and pathogenesis of hereditary spinocerebellar ataxias and spastic paraplegia. The protocols used were approved by the local ethical committee as specified in the text. All control cell lines used in the study were anonymized with an ID code.

Differentially expressed transcripts in SCA28 LCLs clustered in five major functional categories: (1) regulation of cell proliferation; (2) regulation of programmed cell death; (3) response to oxidative stress; (4) cell adhesion, and (5) chemical homeostasis. Alterations of these pathways are often reported in neurodegeneration.

Functional analyses led to the identification of specific and measurable aspects, such as cell cycle blockage, decreased cell growth and increased apoptosis characterizing SCA28 cells. An increased lipid damage due to ROS was also detected. Overall our findings showed altered pathways in SCA28 connected with the disease, that may be used as readout for high-throughput screenings of potential drugs.

Microarray data included in this study are deposited in the GEO database with Accession Number GSE42406.

To allow referees to review record GSE42406 while it remains in private status, the following private link has been created:


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The Authors declare that they have no competing interests.

We hope that our paper is suitable for publication in BMC Medical Genomics.

Yours sincerely,

Alfredo Brusco, PhD