Author's response to reviews

Title: Deletion of REXO1L1 locus in a patient with malabsorption syndrome, growth retardation, and dysmorphic features: a novel recognizable microdeletion syndrome?

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Author’s response to reviews:

Dear Editor,

we are sending you a covering letter with a point-by-point description of the changes made.

Reviewer 1

- please provide the version in which aCGH data is reported (e.g. GRCh37/hg19)

The hg version used in data presentation was added in the Results section

- please provide a review about MDD syndromes in introduction; e.g. doi:10.1369/0022155412440001.
We added a sentence in Background section and a review about microdeletion and microduplication syndromes.

In fact, the number of microdeletion and microduplication syndromes (MMSs) and the phenotypic consequences is continuously increasing [5].


Reviewer 2

1. Abstract (page 3)

Case presentation. We report a de novo heterozygous 2 Mb deletion at 8q21.2 region which includes the family of REXO1L genes and pseudogenes in a young man affected by global development delay, progeroid signs, and gastrointestinal anomalies. Molecular and cellular analysis showed that the REXO1L1 gene hemizygosity in a patient’s fibroblasts induces genetic instability and increased apoptosis after treatment with different DNA damage-induced agents.

You are spoken of your patient, not any one patient, I think it’s misspelled

We changed the abstract in

Case presentation. We report a de novo heterozygous 271 Kb deletion at 8q21.2 region which includes the family of REXO1L genes and pseudogenes in a young man affected by global development delay, progeroid signs, and gastrointestinal anomalies. Molecular and cellular analysis showed that the REXO1L1 gene hemizygosity in our patient’s fibroblasts induces genetic instability and increased apoptosis after treatment with different DNA damage-induced agents.

2. Keywords: (page 3)

8q21.2 deletion, REXO1L1 gene, aCGH, facial dysmorphisms, inflammation and apoptosis of gastrointestinal mucosa.

I understand that the number of keywords is limited, but CNV seems to me a very important concept in this case report.

We added CNV in keywords.
3. Case presentation (page 5)

The dismorphological description should be more accurate. When was the incomplete spina bifida diagnosed?

What was and at what level was the spina?

The patient had an incomplete spina bifida, diagnosed when he was a newborn. No specific treatment was required.

What type of cleft palate did the patient have? Full, soft…..

The patient had a cleft of the soft palate, without a cleft of the hard palate, treated surgically.

We added these clinical data in the Clinical report section.

4. Cytogenetic and molecular studies page 8

Fluorescence in situ hybridisation (FISH) analysis was performed using RP11-96G1, RP11-133G2, RP11-179B4 BAC clones and centromeric probe of chromosome 8 on metaphase spreads obtained from peripheral blood of our patient and his parents using standard procedures.

Although these clones of FISH probes are explained in the results, you could put here the cytogenetic coordinates to which they correspond.

The cytogenetic coordinates were added in the methods section.

Moreover, by checking carefully the BAC clones coordinates, we defined the new measure of the identified microdeletion in 271kb containing the REXO1L1 gene and 3 REXO1L2P pseudogenes.

Cellular Analysis page 9

Fibroblast cell lines were cultured in DMEM-F12 medium supplemented with 15% foetal calf serum (FCS) and 1% L-glutamine. The HeLa and the HEK293 cell lines were growth in DMEM medium supplemented with 10% FCS. All culture media contains antibiotics. All the cell cultures are growth at 37°C under an atmosphere of 5% CO2.
Here you speak of fibroblast cell lines without saying that line refers and in the next paragraph refers to the line HFFF2 without saying that this is the line of fibroblasts with which they are working.

We accepted your suggestion and we changed in:

Human fibroblast HFFF2 cell line and patient’s fibroblasts were cultured in DMEM-F12 medium supplemented with 15% foetal calf serum (FCS) and 1% L-glutamine. The HeLa and the HEK293 cell lines were growth in DMEM medium supplemented with 10% FCS. All culture media contains antibiotics. All the cell cultures are growth at 37°C under an atmosphere of 5% CO2.

Micronuclei (MN) induction on HFFF2 and patient’s fibroblasts was performed by treatment with either 4-8 J/m2 of UV-C, or with 2-5 #M Hydroxyurea, or 25, 50 and 100 #M t Butil-hydroxiperoxide or 0.25, 0.5 and 1Gy of X-rays, and exposition with cytocalasin B (3 #g/ml) for 72 hrs. Cells were then fixed in situ by the gradual adding of methanol:acetic acid (3:1), slides were air-dried and stained with 3% Giemsa for 10 min. At least 500 binucleate cells (BNC) were scored for MN induction for each experimental point.

We received no comments about this latest point of the review.

Best Regards

Maria Rosaria D'Apice