Reviewers report

Title: The Facioscapulohumeral muscular dystrophy region on 4qter and the homologous locus on 10qter evolved independently under different evolutionary pressure.

Version: 2 Date: 31 October 2006
Reviewer: Rossella Tupler

Reviewers report:

General

In this manuscript, the authors present a wide study regarding the distribution and the composition of D4Z4 alleles at the subtelomeric region of chromosomes 4q and 10q in 106 healthy control individuals and 70 FSHD subjects. FSHD, a frequent myopathy, has been causally associated with deletion of D4Z4 repetitive elements at 4q35. In this manuscript, the authors report that 33% of the healthy individuals and 27% of FSHD subjects do not present the “canonical” distribution of D4Z4 alleles at 4q and 10q. Moreover the authors analyze the structural organization of variant 4q and 10q alleles in healthy subjects and FSHD patients. From their data the authors infer that D4Z4 loci at 4q and 10q are under a different evolutionary pressure.

In summary, the manuscript presents a study that highlights the high frequency of recombination events between almost identical sequences at 4q and 10q. The authors discuss possible mechanisms underlying the high number of recombination events occurring at 4q and 10q. The authors list numerous possibilities without an articulate analysis. The discussion should be deeply revised also considering the data obtained in this study regarding the 4qA/4qB polymorphism.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Methods

The methodology used to analyze the structural organization of variants 4q and 10q should be described clearly.

Results

The authors observed that among the healthy subjects they analyzed, two displayed alleles within the FSHD range.

FSHD familial cases

The authors observed four FSHD patients who were heterozygotes for two 4q alleles shorter than 39 kb. They refer that only one allele segregates with the disease within those families. It would be interesting to know the size of the family investigated and clinical data to evaluate the statistical significance of this observation. Associated with the observation of healthy subjects carrying one “short “ 4q allele, this data can be relevant for genetic counseling and the identification of factors that can modify the disease onset.

Telomeric markers

The second paragraph is not clear. The authors should explain the meaning of allelotyping and their results. The procedures used to perform it should also be described in materials and methods.

Minor observations (page are not numbered)

Background

First paragraph, line 2: “biological process” should be “biological processes”.
First paragraph, line 24: “allowed” should be “allows”.
First paragraph, line 26: “at the” should be “between”.

Methods
Patients and control
First paragraph, line 10: “consense” should be “consent”.

Southern blot analysis
First paragraph, line 12: “as described in a previously described paper” should be “as previously described”.

Results
Second paragraph, line 1: “will name” should be “named”.
Second paragraph, line 3: “will define” should be “defined”.
Second paragraph, line 5: “detect” should be “detected”.
Second paragraph, line 7: “we represent schematically the 4q and 10q subtelomeric region” should be “the 4q and 10q subtelomeric region are schematically represented”.

Figures
Figure 3A Positioning of the 20 kb Molecular weight marker should be corrected

What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes

Declaration of competing interests:
I declare that I have no competing interests.