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LETTER

Comment on 'CFTR gene mutations in sarcoidosis'

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We read with interest the recent article by Schurmann *et al*,[1] who examined a number of Cystic Fibrosis Transmembrane conductance Regulator (CFTR) gene mutations in a panel of families with two or more siblings affected by sarcoidosis. They refer to our previous studies, which reported an increased frequency of CFTR gene mutations in sarcoidosis, and suggested a trend towards disease progression in mutation carriers.[2,3] To the best of our knowledge, no other paper on this topic is available in the literature, therefore we think it is important to discuss the results. In their study, mutation R75Q was investigated first, because it was detected in 3/26 patients of our published series: the mutation was present in 7/63 families, but it did not segregate with the disease. Also, 34 functional CFTR mutations usually associated with cystic fibrosis were screened in couples concordant for at least one parental copy of the CFTR gene: three patients carrying mutation DF508 were found in two families, one of which was concordant, and one discordant, with disease segregation. Therefore, they could not confirm our results.

We now wish to report here further data, which we more recently obtained after a complete CFTR gene mutation screening in a new series of sarcoidosis patients by denaturing gradient gel electrophoresis (DGGE) which, when compared to a similar complete mutation analysis of the CFTR gene in unaffected individuals from the same population,[4] indicate a loss of the significant difference we had previously reported. In 19 Italian sarcoidosis patients, three coding and three splicing variants were observed, as detailed in Table 1(a): this is not significantly different from controls carrying coding and splicing variants (18/50).

Summarizing present results and the data we have previously reported, in a total of 53 unrelated Italian sarcoidosis patients, 21 had a CFTR gene missense or splicing mutation, as shown in Table 1(b) and (c). This frequency is not significantly different from healthy Italian controls after the same complete gene screening, as mentioned above.

In conclusion, our cumulative case control data obtained by a complete gene screening of 53 Italian sarcoidosis patients are in accordance with the segregation study of R75Q and CF-causing mutations in German families, and support the conclusion that CFTR gene mutations do not appear to have a major influence on the pathogenesis of sarcoidosis. Considering the high frequency of CFTR gene variant carriers in the population, and the unknown role of the great majority of these gene variants as possible clinical modifiers, it might still be of interest to consider performing a complete gene screening of the sarcoidosis families, in order to better define genotype–phenotype correlations.

Table 1 CFTR gene mutations in Italian sarcoidosis patients

	No. of patients	*Missense and splicing mutations*
(a)	1	D513G
	1	R31C
	1	G576A-R668C (d)
	3	IVS85T
	13	- -
(b)	1	R347P
	1	R75Q , 1898+3 A/G (e)
	2	R75Q
	1	621+3 A/G
	1	1991V
	1	L997F
	1	G1069R
	2	IVS85T
	16	- -
(c)	1	DF508
	1	L997F
	1	V754M
	1	E826K
	1	4382delA
	3	- -
Total	53	21

(a) present report, 19 patients.
(b) Bombieri *et al*,[2] 26 patients.
(c) Bombieri *et al*,[3] eight patients.
– – : No mutation found.
(d) -: Mutation in the same allele.
(e) -: Phase unknown.

References

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Cristina Bombieri*, Francesca Belpinati, Pier Franco Pignatti
Department of Mother and Child and of Biology-Genetics, Section of Biology and Genetics, University of Verona, Verona, Italy

Maurizio Luisetti,
Institute of Respiratory Diseases, IRCCS S.Matteo, University of Pavia, Pavia, Italy

**Correspondence: Cristina Bombieri, Department of Mother and Child and of Biology-Genetics, Section of Biology and Genetics, University of Verona, Verona, Italy. Tel: +39 45 802 7673; Fax: +39 45 802 7180*
E-mail: cristina.bombieri@univr.it