SUMMARY

The *FRA10AC1* gene is mapped in the rare fragile site *FRA10A*, which is induced in the absence of folic acid in the cell culture medium, in the human chromosomal region 10q23.3. *FRA10A* is the most prevalent among the rare folate-sensitive autosomal fragile sites in the human genome, and its expression is estimated about 1 in 500 individuals. *FRA10A* carriers exhibit mental and developmental disabilities, such as dysmorphic features, short stature, hypospadias and speech difficulty. The molecular basis of its cytogenetic expression is the expansion (~200 repeat units) of trinucleotide repeats of the type (CGG)n which are located in the 5' untranslated region of the *FRA10AC1* gene. The expansion results in hypermethylation of this region results in and the transcriptional repression of the corresponding allele.

The *FRA10AC1* gene is transcriptionally active in all adult tissues, exhibiting higher levels of expression in organs with high transcriptional activity such as brain, heart, skeletal muscles and liver. The major transcript of the *FRA10AC1* gene encodes a protein of 315aa, which exhibits exclusively nuclear topology. FRA10AC1 is a conserved protein as it presents orthologs in a number of eukaryotic, multicellular or unicellular organisms, but not in prokaryotic organisms. The FRA10AC1 protein has been repeatedly identified as a component of the major spliceosome and its subcomplexes, B *act* (activated), C and P. Also, genetic experiments in *Chlamydomonas reinhardtii* indicate that FRA10AC1 contributes in splice site recognition, and, its protein-protein interactions with spliceosomal components (DGCR14, SF3B2) were identified by different biochemical methods. Based on the data mentioned above, it is indicated that FRA10AC1 involves in mRNA processing.

To understand the functional role of FRA10AC1, in a first place, its protein-protein interaction network was constructed, and, then, the protein-protein interaction network of whole spliceosome. PICKLE meta-database, DroID and Worm Interactome Database, which include protein-protein interaction data in human and in model organisms, *D. melanogaster* and *C. elegans*, respectively, were used for network reconstruction. Only direct protein-protein interactions were retrieved from these databases. A key criterion for the integration of one interaction in the protein-protein interaction network of spliceosome was the biochemical identification of proteins as components of the spliceosome and its subcomplexes. The analysis of the network topological parameters performed by computational methods, and gene ontology analysis of the FRA10AC1 broader 'neighborhood' within the spliceosome network contributed to imply possible biological function of FRA10AC1. At the same time, a *HeLa* cell model with stable suppressed expression of the *FRA10AC1* gene was developed, through the use of shRNA clones which target the coding region of the endogenous *FRA10AC1* gene. In this cell model, omic approaches were applied on three basic levels of cellular function (transcriptomics, proteomics, metabolomics) in order to investigate the effects of suppression of *FRA10AC1* gene expression in cell physiology. The study of these changes in the context of the protein-protein interactions of the spliceosome, but also beyond this context, also contributed to the construction of proposed FRA10AC1 functional models within spliceosome.