**IN SILICO IDENTIFICATION OF MARS/SARS IN DNA SEQUENCES.**

GLAZKO G.V.+, ROGOZIN I.B., GLAZKOV M.V.\*

Institute of Cytology and Genetics, Siberian Branch of the Russian Academy of Sciences, 10 Lavrentiev Ave., Novosibirsk, 630090, Russia, e-mail: rogozin@bionet.nsc.ru

\*N.I. Vavilov's Institute of General Genetics, RAS, Moscow, Russia, e-mail: glazkov@vigg.ru

+Corresponding author

Keywords: Identifications of matrix/scaffold attachment regions, linear discriminant analysys

The loop hypothesis for the organization of DNA arose largely from observations of loops emanating from histone-depleted chromosomes and nuclei using electronic microscope [1,2]. This organization is brought about by the anchorage of specific DNA sequence landmarks to a network of protein cross-ties, termed nuclear matrix at interphase or chromosomal scaffolds at mitosis. The sites of DNA attachment named MARs/SARs (Matrix/Scaffold Attachment Regions) are relatively short (100-1000 bp) sequences. They are known to facilitate the expression of genes and supposed to punctuate chromosomal DNA into functional units of topologically constrained loop domains (for review see [3,4]).

It is well known, that the nuclear matrix (it consists of a complex nuclear pore - nuclear lamina, a residual nucleolus and internal fibrillar-globular network) can include or not include such nuclear structures as residual nucleoli and internal fibrillar-globular network depending on the method of isolation (the high concentration of salt, LIS detergent, electroelution). It is probable, that the characteristics of DNA sequences, named as "the sequences, associated with nuclear matrix", will depend on method of matrix isolation.

For MARs/SARs, there are no cytological data, directly indicating on their anchoring to specific components of nuclear matrix (residual nuclear structure). At the same time, there are the set of samples of DNA fragments, isolated from various residual chromosome/nuclear substructures - nuclear lamina, cores of rosette-like structures (elementary chromomers) and synaptonemal complex, which are also the sites of the DNA attachment, and for which in each case there are cytological data about the residual nuclear structure with which these fragments are associated. It can be suggested, that each components of nuclear matrix can be associated with specific context properties of these DNA sequences.

We had lead the computer analysis of the nucleotide sequences presumably participating in the loop organization of somatic and meiotic chromosomes. From the results of linear discriminant analysis one can see, that lamDNA, crDNA, scDNA show a greater similarity among themselves, then when compared to MARs/SARs, which, in turn, are closer to 5’flDNA and randDNA (Figure 1).

We have calculated a matrix of coefficients for discriminant function and created the calculation program "ChrClass". Given work presents the results of classification some DNA fragments with the use of our program ChrClass and with the use of the program MarFinder [5], developed for the same purpose. Comparison of ChrCLass and MarFinder results suggested that the accuracy of the methods of MARs/SARs prediction could be improved not only via accumulation the information about MARs-specific nucleotide motifs, but also via consideration of the internal heterogeneity of nuclear matrix structures and peculiarities of the localization of the analyzed DNA fragments in various structural-functional regions of genomes.

**References**

1. P.R. Cook and I.A. Brazell, “Conformational constraints in nuclear DNA.” J. Cell Sci. 22, 287-302 (1976).
2. J.R. Paulson and U.K. Laemmli, “The structure of histone-depleted metaphase chromosomes.” Cell 12, 817-828 (1977).
3. T. Boulikas, “Chromatin Domains and Prediction of MAR Sequences” International Review of Cytology 162A, 279-388 (1995).
4. S.M. Gasser, B.B. Amati, M.E. Cardenas and J.F.X. Hoffman, “Studies on Scaffold Attachment Sites and Their Relation to Genome Function” Int. Rev. of Cytology 119, 57-96 (1989).
5. G.B. Singh, A.K. Jeffrey and S.A. Krawetz, “Mathematical model to predict regions of chromatin attachment to the nuclear matrix” Nucleic Acids Res. 25, 1419-1425 (1997).



Fig 1. Clustering of the samples of the chromosomal DNA fragments, participating in the loop organization of somatic and meiotic chromosomes on the base of Mahalanobis’s distances between samples (MARs/SARs - Matrix/Scaffold Attachment Regions; sc1DNA, sc2DNA - fragments from synaptonemal complexes of chinese hamster and rat respectively; lamDNA - fragments from nuclear lamina; crDNA - fragments from core of rosette-like structures; control samples: 5'flDNA - 5' flanking regions of genes; randDNA - random sequences).