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EPIGENETICS PREDICTORS OF ATRIAL FIBRILLATION

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The analysis of contemporary literature about epigenetic predictors of atrial fibrillation – the so-called small RNAs (miR) is presented. Article provides information about the expression of miR, controlling the activity of genes of ion channels, which play an important role in atrial fibrillation. Database miRWalk To determine the possible (predicted) and confirmed (validated) RNA-bonds, was used.

Key words: atrial fibrillation, miR, target genes, ion channels, database miRWalk

Atrial fibrillation (AF) is a highly prevalent arrhythmia with pronounced morbidity and mortality. The occurrence of AF in the general population is 1.0-2.0 % [5].

Recent studies have uncovered an important role of epigenetic regulators of genes of ion channels , in particular, some of the micro - RNA (miR). Especially interesting is the possible role of genetic predictors of AF in the remodeling of ion channels.

This work presents data of the literature about the role of the expression of miRNAs that control the activity of certain ion channels in condition of AF.

Materials and methods

In our analysis, we mainly focused on the already validated RNA- bonds to identify potential miR, which expression affects the development of AF, using the standard algorithm of database miRWalk [4].

Results and discussion

It is known that during AF the expression of several miR leads to dysregulation of genes of ion channels and electrical remodeling of the atria. For example, [3] in the experimental work suggested that miR- 328 promotes electrical remodeling in patients with AF. Computer analysis indicated the possible role of miR- 328 in the regulation of target genes CACNA1C and CACNB1, thus, an important role in the process of atrial electrical remodeling . Proved the directly proportional link between the levels of miR- 328 and subunits in L-type Ca2 channel proteins. It is shown that miR- 328 is involved in the regulation of α1c- and 1β- protein subunits of Ca2 + channels of the heart, and thus may reduce the action potential.

In another study, it was suggested that the violation of miR- 1 expression in the target gene KCNJ2 can play the key role in the development of AF [2]. MiR- 1 regulates the internal currents of K+ channels (Kir)2.1. These studies provided the influence of the bond miR- 1 with Kir2.1 over I (K1) channel in patients with persistent AF . The experiment obtained considerable reduction of miR- 1 in patients with AF(86 %), which in turn led to up-regulation of Kir2.1 subunit , and increasing activity of I (K1).

Development of interstitial myocardial fibrosis is a predictor of AF [1]. MiR-21 plays a key role in the development of fibrosis in the atria and affects SPRY1 gene, which is an antagonist of fibroblast growth factor [6]. Increased expression of miR-21 leads to increased levels of collagen expression of connective tissue growth factor (CTGF) and to decreased expression of the gene SPRY1. Increased expression of miR-21 leads to a structural remodeling of the myocardium.

The following table shows the miR, which expression (data base miRWalk) relates to the regulation of Ca2 + and K+ ion channels and development of interstitial myocardial fibrosis.

Table 1. MiRNAs (miR), affecting on the development of atrial fibrillation in humans.

MiR, controlling the slow Ca^{++}channels (CACNA1C, CACNB1)	MiR, controlling the K^{+} channel (KCNJ2)	MiR, regulating aortic fibrosis (by connective tissue growth factor CTGF)
miR-223 miR-101 (101-2) miR-499-3h miR-499-5p miR-328 miR-101 (101-1) miR-664	miR-1 (1-1) miR-1 (1-2)	miR-21

Conclusions

Thus, the available data indicate a clear correlation between the miR expression and some genes which encoding ion channels and response for the formation and impulse conduction. There is a direct correlation between the expression of miR- 328 and genes CACNA1C and CACNB1, coding work of slow Ca2 + channels in atrial fibrillation. Consequently the normalization of the expression of miR-328 may lead to the restoration of sinus rhythm.

It is known that variations of the internal currents are an important factor in the development of AF. Interesting results were obtained in the study of the

connection of micro- RNA and potassium channels, including miR- 1 and Kir2.1 subunit, and increasing activity of I (K1), in patients with AF . It is assumed that the role of miR- 21 is in the influence of epigenetic factors on the formation of interstitial fibrosis with subsequent development of AF.

Study of the influence of different miRs on the development AF one of the most promising methods for prediction of the development of AF, and methods of RNA interference may play an important role in the treatment of this pathology.

Literature

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ЕПІГЕНЕТИЧНІ ПРЕДИКТОРИ ВИНИКНЕННЯ ФІБРИЛЯЦІЇ ПЕРЕДСЕРДЬ

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У роботі проведено аналіз даних сучасної літератури про епігенетичні предиктори виникнення фібриляції передсердь – так званих малих РНК (miR). Наведено відомості про експресію miR, що контролюють роботу генів іонних каналів, які відіграють важливу роль у виникненні фібриляції передсердь. Для визначення можливих (прогнозованих) і підтверджених (доведених) РНК-зв`язків нами використана база даних miRWalk.

Ключові слова: *фібриляція передсердь, miR, гени-мішені, іонні канали, база даних miRWalk*

ЭПИГЕНЕТИЧЕСКИЕ ПРЕДИКТОРЫ ВОЗНИКНОВЕНИЯ ФИБРИЛЛЯЦИИ ПРЕДСЕРДИЙ

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В работе проведен анализ данных современной литературы об эпигенетических предикторах возникновения фибрилляции предсердий – так называемых малых РНК (miR). Представлены сведения об экспрессии miR, контролирующих работу генов ионных каналов, играющих важную роль в возникновении фибрилляции предсердий. Для определения возможных (прогнозируемых) и подтвержденных (доказанных) РНК-связей нами использована база данных miRWalk.

Ключевые слова: *фибрилляция предсердий, miR, гены-мишени, ионные каналы, база данных miRWalk*