CONNECTIVITY ANALYSIS OF ATRIAL FIBRILLATION RELATED STROKE BASED ON CO-EXPRESSION STRUCTURE NETWORK

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Atrial fibrillation (AF) significantly increases stroke risk, but the risk factors and predictors of AF-stroke are rarely discovered. Hence, it is necessary to identify novel biomarker and therapeutic targets. Our study aimed to find effective pathogenic targets and elucidate the underlying molecular mechanism. First, we conducted weighted co-expression network analysis (WGCNA) in stroke-related dataset and AF-related dataset. The pink module that was highly associated with stroke (r = 0.78, p = 2e−20) and the red module that was correlated with AF (r = 0.71, p = 4e−05) was identified. The male-specific lethal homolog 3 (MSL3) was selected by taking the intersection between top 5 genes in stroke-related dataset and top 5 genes in AF-related dataset. Next, the expression of key gene and the receiver operating characteristic curve (ROC) analysis were also validated in other two datasets. Single sample gene set enrichment analysis (ssGSEA), single sample gene set variation analysis (ssGSVA) and correlation between genes in the key modules were exploited to investigate the function of MSL3. In addition, Gene Ontology (GO), Kyoto Encyclopedia of Genes and Genomes (KEGG) and immune cells infiltration were conducted in key modules. At last, 10 small molecular drugs that have the potential to treat AF-stroke were filtered. In conclusion, our research find MSL3 can be as a novel biomarker and several candidate molecular drugs for treating AF-stroke.

Key words: *atrial fibrillation, stroke, weighted co-expression network analysis, hub gene, drugs.*

АНАЛІЗ ПОВ'ЯЗАНОСТІ ІНСУЛЬТУ НА ТЛІ ФІБРИЛЯЦІЇ ПЕРЕДСЕРДЬ НА ОСНОВІ МЕРЕЖІ СТРУКТУРИ КОЕКСПРЕСІЇ

Фібриляція передсердь (ФП) значно підвищує ризик виникнення інсульту, проте виявити фактори ризику й предиктори інсульту на тлі ФП вдається рідко. Отже, необхідно ідентифікувати нові біомаркери й терапевтичні цілі. Метою нашого дослідження був пошук ефективних патогенетичних мішеней та з'ясування молекулярних механізмів, що лежать в їхній основі. По-перше, ми провели аналіз зваженої мережі коекспресії (WGCNA) у наборі даних, по-в'язаних з інсультом, і в наборі даних, пов'язаних з ФП. Було виявлено рожевий модуль, який був тісно пов'язаний з інсультом (r = 0,78, p = 2e−20), і червоний модуль, який корелював з ФП (r = 0,71, p = 4e−05). Специфічний чоловічий летальний гомолог 3 (MSL3) було обрано на перетині між топ-5 генів у наборі даних, пов'язаних з інсультом, і топ-5 генів у наборі даних, пов'язаних з ФП. Далі експресію ключового гена та аналіз робочої характеристичної кривої (ROC) також перевірили у двох інших наборах даних. Для дослідження функції MSL3 було використано аналіз збагачення набору генів однієї вибірки (ssGSEA), аналіз варіацій набору генів однієї вибірки (ssGSVA) та кореляцію між генами в ключових модулях. Крім того, в ключових модулях були використані онтологія генів (GO), Кіотська енциклопедія генів і геномів (KEGG) та інфільтрація імунними клітинами. Зрештою було відфільтровано 10 низькомолекулярних препаратів, які мають потенціал для лікування інсульту при ФП. Отже, наше дослідження показало, що MSL3 може бути як новим біомаркером, так і кількома молекулярними препаратами-кандидатами для лікування інсульту при ФП.

Ключові слова: фібриляція передсердь, інсульт, зважений аналіз мережі коекспресії, хаб-ген, лікарські засоби.

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