Запрошуємо відвідати семінар за участю доктора біологічних та медичних наук Фелікса Брехара ("Bagdasar-Arseni" Clinical Emergency Hospital, Бухарест, Румунія), на якому він зробить доклад на тему "*Targeting cancer stem cells self-renewal molecular mechanism inhibits CD133 cells migration and proliferation in glioblastoma*" в рамках проекту науково-технічного співробітництва між Україною та Румунією. Зустріч відбудеться 5-го травня 2017 року в актовому залі Інституту молекулярної біології і генетики НАН України об 11-ій годині. Вхід вільний.

Тези доповіді: «Targeting cancer stem cells self-renewal molecular mechanism inhibits CD133 cells migration and proliferation in glioblastoma»

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Background

Recent evidence shows a role for Lissencephaly-1 (Lis1) protein in regulating the asymmetric division and self-renewal of stem cell population and neural progenitor cell migration. Therefore, we investigated Lis1 expression in CD133+ glioblastoma cells and evaluated its possible role in regulating the CD133+ U87 cells functions.

Material and methods

Lis1 gene expression was silenced in U87 cells by stable transfection using specific shRNA plasmids. U87 and shLis1-U87 cells were cultivated for 5 days with serum-free neural stem cell medium to enrich the CD133+ U87 population. CD133+ cells were isolated from U87, shLis1-U87 and primary glioblastoma cultures using magnetic MicroBeads and columns. Lis1 and CD133 gene expression in cells was assessed by Real-Time PCR in CD133+ and CD133- glioblastoma cells. Cell adhesion and migration tests were performed using xCELLigence Real-Time Cell Analysis instrument. For invasion experiments, organotypic mouse-brain slices were inoculated with 10^4 GFP-U87, respectively 10^4 shLis1GFP-U87 cells per each slice. Images of the slices were captured at 1, 3, 5 and 7 days.

Results

Lis1 is overexpressed up to 60-fold in CD133+ cells isolated from U87 cells and primary glioblastoma cultures, compared with CD133- cells suggesting a key role of Lis1 in CD133+ glioblastoma cells function. CD133+ cells percentage was six-fold greater in U87 culture compared with shLis1-U87 culture, suggesting a deregulation of self-renewal mechanism involved in expansion/maintaining the pool of CD133+ cells population in shLis1-U87 cells. CD133+ U87 cells are two times more adhesive and migratory, as compared with shLis-U87 CD133+ cells. After inoculation of the organotypic brain slices at the level of corpus callosum, GFP-U87 cells migrate and infiltrate both hemispheres. shLis1GFP-U87 cells show a decreased migratory tendency, the majority of cells remaining at the inoculation site at day 7.

Conclusions

The self-renewal is a crucial mechanism for maintaining the stem cell population in normal and tumor tissue. To our knowledge this is the first report about the role of Lis1 in regulating the self-renewal and invasion of CD133+ U87 cells. These preliminary results suggest that Lis1 could become a promising target for glioblastoma therapy.

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