

## REDUCED EXPRESSION OF *PEDF* AND *ALDH1A1* DURING SPHEROID TRANSITION OF LUNG CANCER CELLS: AN *IN VITRO* STUDY

M.Y. TERZI<sup>1, 2\*</sup>, H.M. OKUYAN<sup>3, 4</sup>, G.G. DURAN<sup>1, 2</sup>, M.U. KÜÇÜK<sup>1, 2</sup>

<sup>1</sup> Department of Medical Biology, Faculty of Medicine, Hatay Mustafa Kemal University, Hatay, Turkey

<sup>2</sup> Department of Molecular Biochemistry and Genetics, Graduate School of Health Sciences, Hatay Mustafa Kemal University, Hatay, Turkey

<sup>3</sup> Department of Medical Services and Techniques, Vocational School of Health Services, Hatay Mustafa Kemal University, Hatay, Turkey

<sup>4</sup> Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Sakarya University of Applied Sciences, Sakarya, Turkey

E-mail: menderesyusufferzi@gmail.com, myterzi@mku.edu.tr.

«Cancer stem cells» (CSCs), can initiate tumorigenesis and metastasis and show resistance against chemotherapy owing to the expression of prominent stem cell markers. CSCs are a subpopulation of highly heterogenic cancer spheroid cells. Pigment epithelium-derived factor (PEDF) is a neurotrophic, anti-tumorigenic, and anti-metastatic protein and its gene expression levels in A549 spheroids is still unknown. We aimed to compare clonogenicity and mRNA levels of *PEDF*, *Oct4*, and *ALDH1A1* between A549 and spheroid cells. Spheroid and colony formation assays were performed with spheroid and A549 cells. We performed quantitative reverse transcription-polymerase chain reaction (qRT-PCR) for gene expression analysis. The clonogenic ratios for A549 and spheroids were ~60 % and ~1 % respectively. During spheroid formation, *Oct4* mRNA level did not change but *PEDF* and *ALDH1A1* levels decreased significantly. CSCs are characterized by elevated stem cell markers but spheroid cells consist of heterogeneous population including CSCs. In spheroid population, no increase in stem cell markers was observed. The reduced *PEDF* levels during spheroid transition can be a suppression mechanism of spheroid cells.

**Key words:** lung cancer, *PEDF*, A549, spheroid cell, *Oct4*, *ALDH1A1*.

### ЗНИЖЕНА ЕКСПРЕСІЯ *PEDF* ТА *ALDH1A1* ПІД ЧАС УТВОРЕННЯ СФЕРОЇДУ З РАКОВИХ КЛІТИН ЛЕГЕНЬ: ДОСЛІДЖЕННЯ *IN VITRO*

«Ракові стовбурові клітини» (РСК) можуть ініціювати утворення пухлин і метастазів, а також де-

монструвати стійкість до хіміотерапії завдяки експресії важливих маркерів стовбурових клітин. РСК — це субпопуляція ракових сфероїдних клітин високої гетерогенності. Фактор пігментного епітелію (*PEDF*) — це нейротрофічний, протипухлинний і антиметастатичний білок, рівні генної експресії якого у сфероїдах A549 все ще невідомі. Наша мета полягала у порівнянні рівнів клоногенності і мРНК *PEDF*, *Oct4* та *ALDH1A1* між A549 та клітинами сфероїдів. Аналіз утворення сфероїдів і колоній було проведено за використанням клітин сфероїдів і A549. Для аналізу генної експресії нами було проведено кількісну полімеразну ланцюгову реакцію із зворотною транскрипцією (кЗТ-ПЛР). Коефіцієнти співвідношення клоногенності для A549 і сфероїдів становили ~60 % і ~1 %, відповідно. Впродовж утворення сфероїдів рівень мРНК *Oct4* не змінювався, однак рівні *PEDF* і *ALDH1A1* значно знизилися. РСК характеризуються підвищеним рівнем маркерів стовбурових клітин, а клітини сфероїдів складаються з гетерогенної популяції, що включає в себе і РСК. Жодного підвищення рівня маркерів стовбурових клітин не було зафіксовано у популяції сфероїда. Знижені рівні *PEDF* упродовж переходу сфероїда можуть слугувати механізмом пригнічення клітин сфероїду.

**Ключові слова:** рак легень, *PEDF*, A549, клітина сфероїду, *Oct4*, *ALDH1A1*.

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