2021 ESMO congress

16-21 SEPTEMBER 2021

Presentation number: 301P

Integrins in different subsets of circulating tumor cells in breast cancer

Grigoryeva E.S.[1], Savelieva O.E.[2], Alifanov V.V.[2], Tashireva L.A.[2], Zavyalova M.V.[2], Tarabanovskaya N.A.[3], Perelmuter V.M.[2]

TOMSK NATIONAL RESEARCH MEDICAL CENTER
THE RUSSIAN ACADEMY OF SCIENCES

Background

Circulating tumor cells (CTCs) are released from tumor tissue and provide tumor progression. The presence of stem and epithelial-mesenchymal transition (EMT) features in CTCs makes population extremely heterogenous and determines their invasiveness, adaptability to the microenvironment, and resistance to proapoptotic signals and chemotherapy. Integrins (ITGs), adhesion molecules, can determine organotropic metastasis when expressed on exosomes, as was shown in a study conducted by Hoshino A. et al. (2015). Herewith, as authors postulated, ITGB3 promoted brain metastasis, ITGB4 and ITGAvB5, lung and liver metastasis in vivo, correspondently. Here we assessed integrins expression on different subsets of CTCs.

Methods

The prospective study included 38 breast cancer patients with stage T2-4N0-3M0, admitted for treatment to Cancer Research Institute, Tomsk NRMC. CTCs phenotypes assessment was carried out by flow cytometry using monoclonal antibody cocktail.

The study was supported by the Russian Science Foundation (grant #21-15-00140).

Results

Only 18 out 38 blood samples contained enough CTCs (CD45-Epcam+) for following analysis. Total CTC quantity detected in 18 blood samples was 314 cells per 1 ml of whole blood. We have previously shown the association of CD45-Epcam+CD44-CD24-N-cadherin+ CTCs (metastasis-associated CTCs, MA-CTCs) with the occurrence of distant metastases. In this study, MA-CTCs were detected in 27,78% of samples (5/18) (Figure 1).

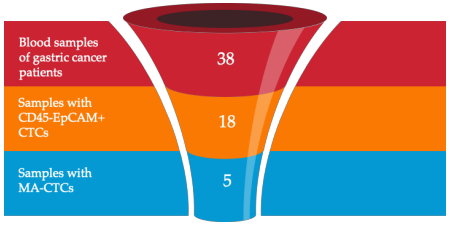

Figure 1. Quantity of samples during screening procedure.

Expression of ITGs was detected in 75% of MA-CTCs and in 69,6% of total CTCs. The incidence of ITGB4 expression was higher in MA-CTCs compared to the total CTC population (p=0.0014), while the expression of ITGB3 and ITGAvB5 was not statistically different (Table 1).

	MA-CTCS	Total CTCS
ITGB3	3/6	218/378
ITGB4	4/6	71/378
ITGAvB3	2/6	30/378

Table 1. Frequency of occurrence of integrins on the surface of circulating tumor cells

All of the MA-CTCs expressing ITGs possessed stemness features (CD133+ and/or ALDH1A1+). Positive expression of ALDH1A1 was observed in 83,3% of MA-CTCs (5/6), positive expression of CD133 was detected in 50% of MA-CTCs (3/6), while co-expression of both stem markers was observed in 33,3% MA-CTCs (2/6).

Conclusion

The detected MA-CTCs with stem-like features and positive ITGB4 expression in three patients allow us to expect lungs metastasis in follow-up period.