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Effects of insulin-like growth factor 1 on proliferation of different cell lines

O.A. Kachalova[1,2], T. Moiseieva[2], A.G. Portnychenko[1,3]

[1] O.O. Bogomoletz Institute of Physiology, NAS of Ukraine
4, Akademika Bohomoltsia Str., Kyiv, Ukraine, 01024
[2] Tallinn University of Technology
5, Ehitajate tee, Tallinn, Estonia,19086
[3] ICAMER, NAS of Ukraine
27, Akademika Zabolotnoho Str., Kyiv, Ukraine, 03143
olenakachalova@gmail.com

Background/Aim. Targeting cell proliferation may be an important therapeutic purpose in tumor growth, tissue remodeling or degenerative diseases. Insulin-like growth factor IGF-1 is known as a proliferative agent, but its effect in different cellular models may be contradictory due to crosstalk of multiple cellular regulatory pathways [1, 2], and need to be elucidated. The aim was to characterize the proliferative effects of IGF-1 in cells with high and low proliferative activity. **Methods.** In cultivated tumor U2OS cells or RPE cells with low proliferative activity, dose- and time-dependent effects of recombinant IGF-1 were studied. Proliferative effects were assayed using S-phase analysis with EdU uptake by fluorescence-activated cell sorting (FACS), DNA fiber analysis, and evaluation of ATR-CHK1 kinase signaling activity by immunoblotting. **Results.** The assay of EdU incorporation by FACS showed an increase in proliferative response after 24 h incubation with IGF-1 in attached ($P < 0.0001$), but not suspended ($P = 0.8607$) RPE cells. In contrast, IGF-1 did not increase the proliferation ($P = 0.3713$) in the attached U2OS cells, and suppressed in suspended cells ($P = 0.0064$). DNA fiber analysis demonstrated decreasing replication fork velocity in response to 24h IGF-1 treatment in both attached RPE or suspended U2OS cells compared to control ($P < 0.0001$). Evaluation of the cell cycle kinases activation demonstrated that U2OS cells had a higher expression of pChk-1 than RPE cells, and IGF-1 caused an increase the indicators in both cell lines. The proliferative response to IGF-1 inversely depended on cell concentration in the culture. An increase of IGF-1 dose/time resulted mainly in suppression of proliferative response, more pronounced in U2OS cells, which is consistent with previous data obtained on mesenchymal stem cells with high proliferative capacity [2]. In RPE, IGF-1 may shift cell population to have more proliferative capacity [3] that can be important for the treatment of retinopathies, especially related to aging. **Conclusions.** IGF-1 causes different proliferative response in the cells with high and low proliferative capacity with nonlinear dependence on time and dose. The tumor U2OS cell proliferation was most suppressed in suspended cells especially with the IGF-1 overdose. In RPE, IGF-1 may be used in low concentrations to increase proliferative capacities and prevent cellular senescence.

Keywords: cell culture, U2OS, PRE, IGF-1, cell proliferation.

REFERENCES

1. *Kemp MG et al.* Insulin-like Growth Factor 1 Receptor Signaling Is Required for Optimal ATR-CHK1 Kinase Signaling in Ultraviolet B (UVB)-irradiated Human Keratinocytes. *J Biol Chem.* 2017; **292**(4): 1231–9.
2. *Huang YL et al.* Effects of insulin-like growth factor-1 on the properties of mesenchymal stem cells *in vitro*. *J Zhejiang Univ Sci B.* 2012; **13**(1):20–8.
3. *Gupta S et al.* Retinal Pigment Epithelium Cell Development: Extrapolating Basic Biology to Stem Cell Research. *Biomedicines.* 2023; **11**(2):310.