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КОНФЛИКТ ИНТЕРЕСОВ

Авторы заявляют, что у них нет конфликта интересов.

СПИСОК ЛИТЕРАТУРЫ

Духовлинов И.В., Богомолова Е.Г., Добровольская О.В., Федорова Е.А., Кляус А.М., Ищук С.А., Климов Н.А., Симбирцев А.С. 2017. Продукция *in vivo* инсулиноподобного фактора роста 1 (ИФР-1), кодируемого плазмидной ДНК. Мед. академ. журнал. 17(3) : 47–52. (Dukhovlinov I.V., Bogomolova E.G., Dobrovolskaya O.A., Fedorova E.A., Klyaus A.M., Ischuk S.A., Klimov N.A., Simbirtsev A.S. 2017. Production of insulin-like growth factor 1 (IGF-1) encoded by plasmid DNA *in vivo*. Med. Acad. J. (Russ.) 17(3) : 47–52).

Bake S., Selvamani A., Cherry J., Sohrabji F. 2014. Blood brain barrier and neuroinflammation are critical targets of IGF-1-mediated neuroprotection in Stroke for Middle-Aged Female Rats. PLoS ONE. 9 : e91427. https://doi.org/10.1371/journal.pone.0091427

Bonadio J., Smiley E., Patil P., Goldstein S. 1999. Localized, direct plasmid gene delivery *in vivo*: Prolonged therapy results in reproducible tissue regeneration. Nat. Med. 5 : 753–759.

Davis H.L., McCluskie M.J., Gerin J.L., Purcell R.H. 1996. DNA vaccine for hepatitis B: Evidence for immunogenicity in chimpanzees and comparison with other vaccines. Proc. Natl. Acad. Sci. USA. 93 : 7213–7218.

Draper N.R., Smith H. 2016. Applied regression analysis. Wiley. 3rd ed. 736 p.

Dyer A.H., Vahdatpour C., Sanfeliu A., Tropea D. 2016. The role of insulin-like growth factor 1 (IGF-1) in brain development, maturation and neuroplasticity. Neurosci. 325 : 89–99.

Horn N.A., Meek J.A., Budahazi G., Marquet M. 1995. Cancer gene therapy using plasmid DNA: purification of DNA for human clinical trials. Hum Gene Ther. 6 : 565–573.

Kooijman R., Sarre S., Michotte Y., De Keyser J. 2009. Insulin-like growth factor I a potential neuroprotective compound for the treatment of acute ischemic stroke? Stroke. 40 : e83–e88. https://doi.org/10.1161/STROKEAHA.108.528356

Laviola L., Natalicchio A., Perrini S., Giorgino F. 2008. Abnormalities of IGF-I signaling in the pathogenesis of diseases of the bone, brain, and fetoplacental unit in humans. Am. J. Physiol. Endocrinol. Metab. 295 : E991–E999.

Liu X.F., Fawcett J.R., Thorne R.G., Frey W.H. 2001. Non-invasive intranasal insulin-like growth factor-I reduces infarct volume and improves neurologic function in rats following middle cerebral artery occlusion. Neurosci. Letters. 308 : 91–94.

Nishijima T., Piriz J., Duflot S., Fernandez A.M., Gaitan G., Gomez-Pinedo U., Verdugo J.M., Leroy F., Soya H., Nuñez A., Torres-Aleman I. 2010. Neuronal activity drives localized blood-brain-barrier transport of serum insulin-like growth factor-I into the CNS. Neuron. 67 : 834–846.

O'Kusky J., Ping Y. 2012. Neurodevelopmental effects of insulin-like growth factor signaling. Front. Neuroendocrinol. 33 : 230–251.

Reinhardt R.R., Bondy A. 1994. Insulin-like growth factors cross the blood-brain barrier. Endocrinol. 135 : 1753–1761.

Romero N.B., Benveniste, O., Payan C., Braun S., Squiban P., Herson S., Fardeau M. 2002. Current protocol of a research phase I clinical trial of full-length dystrophin plasmid DNA in Duchenne/Becker muscular dystrophies. Part II: Clinical protocol. Neuromus. Disord. 12 (Suppl. 1) : S45–S48.

Tsurumi Y., Kearney M., Chen D., Silver M., Takeshita S., Yang J., Symes J.F., Isner J.M. 1997. Treatment of acute limb ischemia by intramuscular injection of vascular endothelial growth factor gene. Circulation. 96 (Suppl. 9) : 382–388.

Wolff J.A., Malone R.W., Williams P., Chong W., Acsadi G., Jani A., Felgner P.L. 1990. Direct gene transfer into mouse muscle *in vivo*. Science. 247 : 1465–1468.

STUDY OF PHARMACOKINETICS OF TWO RECOMBINANT INSULIN-LIKE GROWTH FACTOR 1 FORMS IN BLOOD

I. V. Dukhovlinov[a], O. A. Dobrovolskaya[b], I. V. Evsyukov[a, *], E. G. Bogomolova[b], N. N. Kolmakov[b], A. A. Lukovenko[c], E. A. Fedorova[c], S. A. Ishuk[b], A. I. Orlov[d], E. V. Vorobeychikov[e], and A. S. Simbirtsev[b]

[a]Limited Liability Company "ATG Service Gene" St. Petersburg, 199034 Russia

[b]Institute of Experimental Medicine, St. Petersburg, 197376 Russia

[c]Limited Liability Company "Biochemical Agent", St. Petersburg, 190005 Russia

[d]Limited Liability Company "Dakra Medical", St. Petersburg, 197101 Russia

[e]Limited Liability Company "Polifarm", St. Petersburg, 197101 Russia

**E-mail: evsyukov007@mail.ru*

The paper discusses the pharmacokinetics of two substances containing recombinant insulin-like growth factor 1 as the active agent. The first substance (IGF_1) contains the recombinant IGF1 itself, the second (IGF_2) – IGF1 translated from the plasmid DNA encoding the *IGF-1* gene. It has been established that with intramuscular administration of IGF_1, the delay time of its entry into the bloodstream is 1.5–2 hours, whilst IGF_2 – 24–25 hours. This indicates the presence of various mechanisms of accumulation of these substances in the bloodstream. The maximum concentration of IGF_1 in the blood is determined 5 hours after the administration, and IGF_2 – 125 hours after the administration. The maximum values of the concentrations of these substances are comparable. The concentration

of IGF_1 in the blood decreases to the initial value 12 hours after its introduction, and the concentration of IGF_2 – after 216 hours. The clearance (Cl) and elimination constants (*Kel*) parameters of these substances also have significant differences, which confirms the presence of fast and slow dynamics of their maximum concentrations decrease after intramuscular administration. The different dynamics of accumulation of substances in the blood and their elimination from the bloodstream after administration, as well as different values of the parameters of the area under the pharmacokinetic curve (AUC_t, AUC_∞), demonstrate that IGF_2 has been in the systemic circulation for a longer time than IGF_1. This is essential for the formation and severity of pharmacodynamic effects.

Keywords: pharmacokinetics, insulin-like growth factor, recombinant protein, plasmid DNA, *IGF-1* gene, intramuscular administration