

Reply

Reply to Letter to the editor: Unique genetic profile of hereditary haemochromatosis in Russians: High frequency of C282Y mutation in population, but not in patients

Our study [1] was neither designed to address the genetic penetrance of C282Y in Russian population nor did we conclude that the penetrance in Russia is lower than in Western countries. Our major finding is that the proportion of C282Y homozygotes among Russian patients with biochemical and clinical features of HH is dramatically lower than in Western countries. Lower penetrance of C282Y in Russia as compared to Western countries is just one potential explanation of these findings, which has to be tested using appropriate methods. Since there are no published data documenting ethnic or geographical variation of C282Y penetrance, we rather favor an alternative explanation, suggesting that in Russia ethiologically “orphan” cases of idiopathic iron overload are more common than classical HFE-related and other known monogenic forms of HH.

Though the selection criteria of our patients could be improved by direct assessment of iron overload, we strictly excluded all patients whose symptoms could be explained by conditions other than HH. It would be of major interest to compare our data on the frequency of C282Y in Russian HH patients with the results of confirmatory testing for HH mentioned by Drs. C.A. McCune and M. Worwood. Immediate comparison of two studies is hampered by the lack of information about clinical indications for genotyping and ethnic

background of their patients, which both strongly influence the proportion of C282Y-related cases. However, the data of Drs. C.A. McCune and M. Worwood suggest that non-classical forms of primary iron overload may be significantly more frequent in Western countries than currently believed, thus necessitating further research into the mechanisms of “orphan” hemochromatosis.

Reference

- [1] E.S. Potekhina, A.V. Lavrov, L.M. Samokhodskaya, A.Y. Efimenko, A.V. Balatskiy, A.A. Baev, M.L. Litvinova, L.A. Nikitina, G.A. Shipulin, N.P. Bochkov, V.A. Tkachuk, V.N. Bochkov, Unique genetic profile of hereditary hemochromatosis in Russians: high frequency of C282Y mutation in population, but not in patients, *Blood Cells Mol. Diseases* 35 (2005) 182–188.

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