THE LIMITS OF NIPT SENSITIVITY AND SPECIFICITY

Harsanyova, Maria[1,2]; Duris, Frantisek[1,3]; Budis, Jaroslav[1,3,4]; Turna, Jan[3,2,5]; Hyblova, Michaela[6]; Minarik, Gabriel[6]; Szemes, Tomas[1,7,5]

[1]Geneton Ltd., Bratislava, Slovakia, [2]Faculty of Natural Sciences, Comenius University, Bratislava, Slovakia, [3]Slovak centre of scientific and technical information, Bratislava, Slovakia, [4]Faculty of mathematics, physics and informatics, Comenius University, Bratislava, Slovakia, [5]Comenius University Science Park, Bratislava, Slovakia, [6]Medirex Inc., Bratislava, Slovakia, [7]Faculty of Natural Sciences, Comenius University, Bratislava, Slovakia,

Introduction: Non-invasive prenatal testing for aneuploidies has rapidly become a part of clinical management of pregnant women, thanks to relatively risk-free sampling of peripheral blood of pregnant women. However, the DNA present in maternal plasma is of placental, not directly fetal origin. Different available non-invasive prenatal tests vary in many aspects, including determined abberations or techniques used, but there are differences also in their key performance indicators, which are sensitivity or specificity. However, these figures do not consider the possibility of fetoplacental mosaicism, thus the reported sensitivity and specificity may not be totally credible. Most of the commercial tests declare the sensitivity and specificity over 99%. However, there are hard limits given by natural occurrence of fetoplacental mosaicism phenomenon.Results: We devised mathematical model for sensitivity and specificity, which includes prevalence of fetoplacental mosaicism, with sufficient amount of present placental DNA, the theoretical limit for sensitivity is approx. 98,6% and specificity 99,98%. According to the model, theoretical positive predictive value is 90,91 and negative predictive value is 99,99 incorporating the prevalence of trisomy 21.Conclusion: We have shown that limits of NIPT tests are not just fetal fraction and the sample itself, but there are hard limits to their values due to natural occurrence of fetoplacental mosaicism and it should be considered when sensitivity and specificity is measured or declared.