



# Lyso-SM-509 is a highly sensitive biomarker for Niemann-Pick disease: a three years experience

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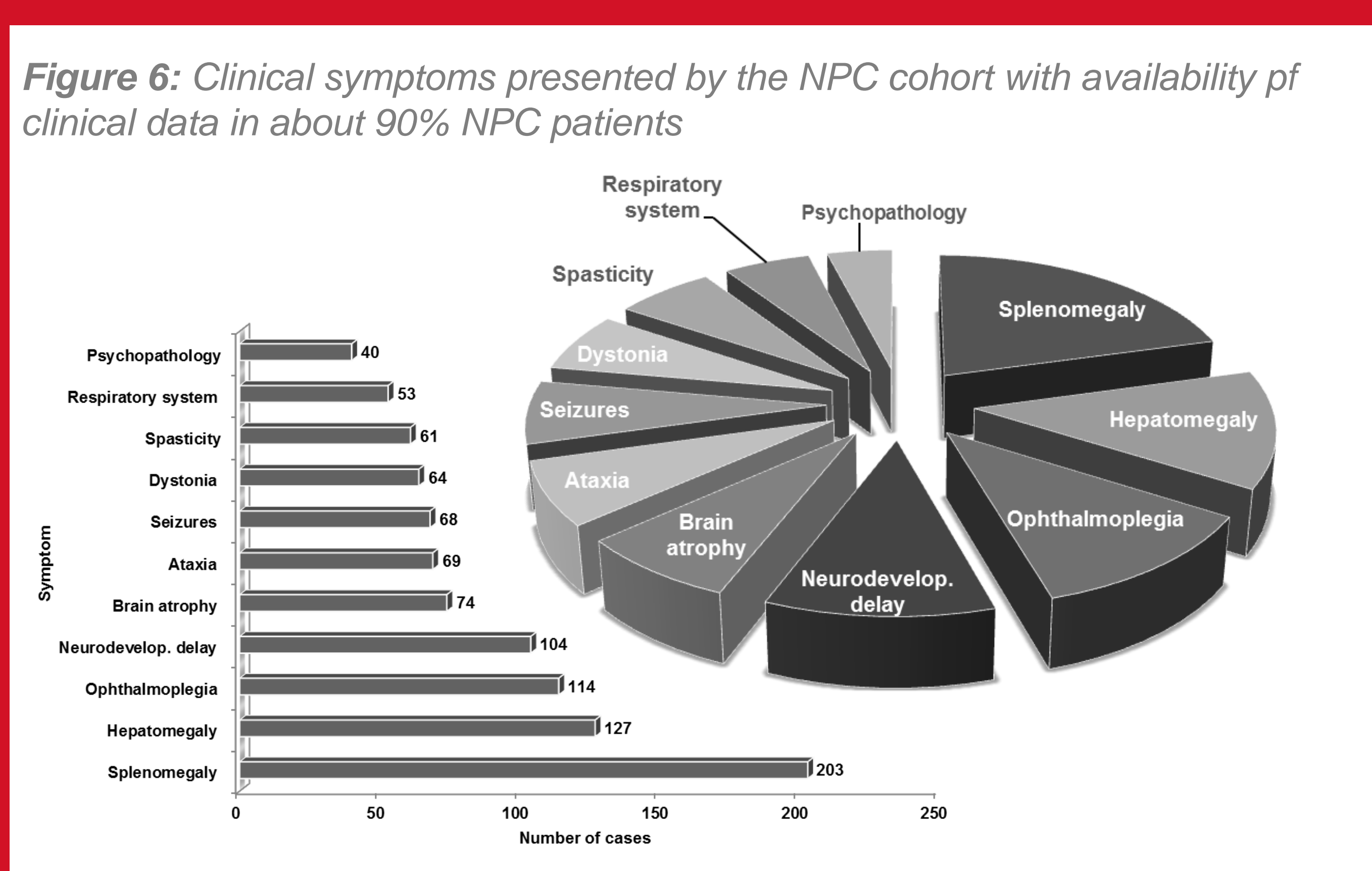
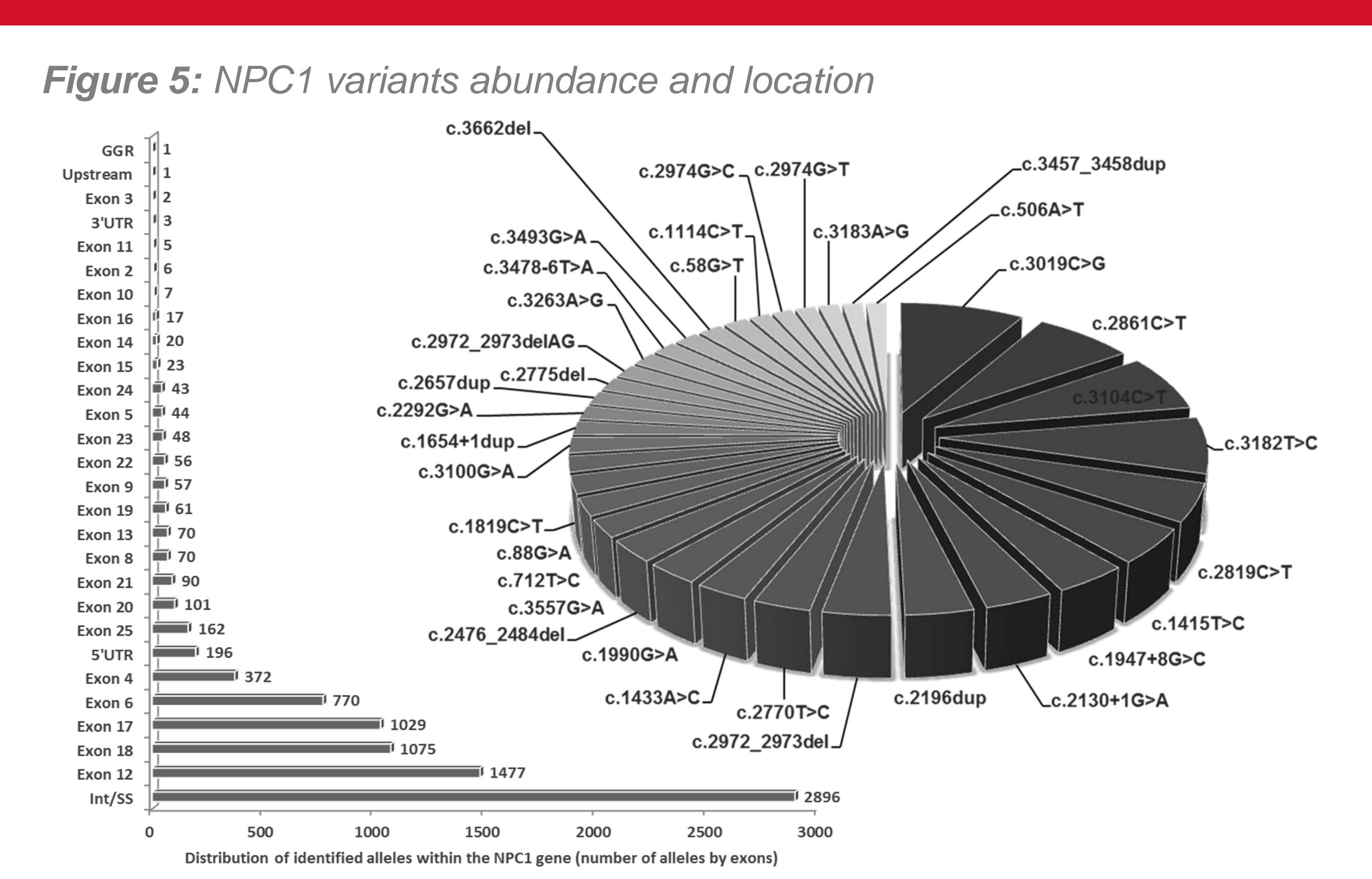
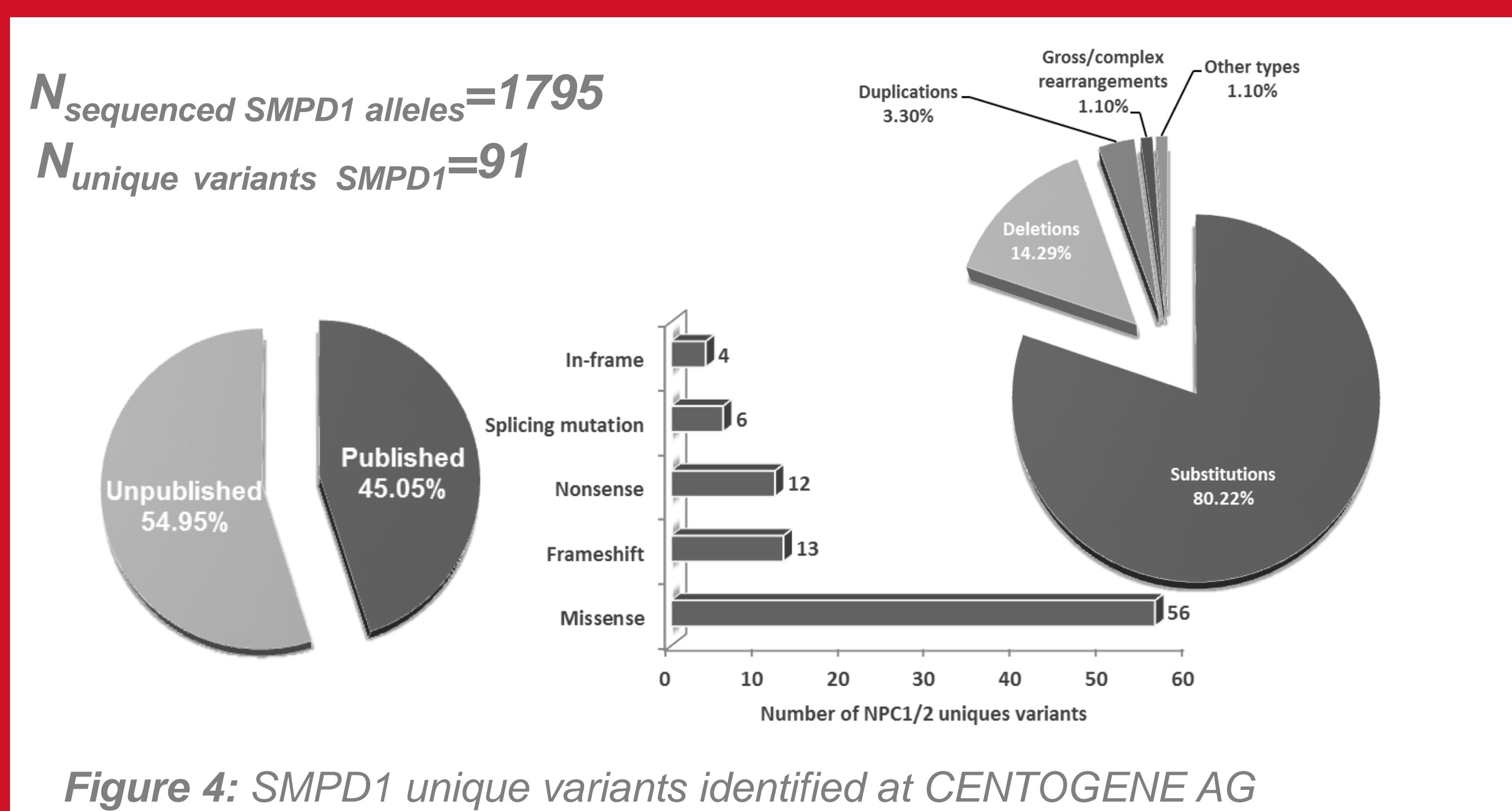
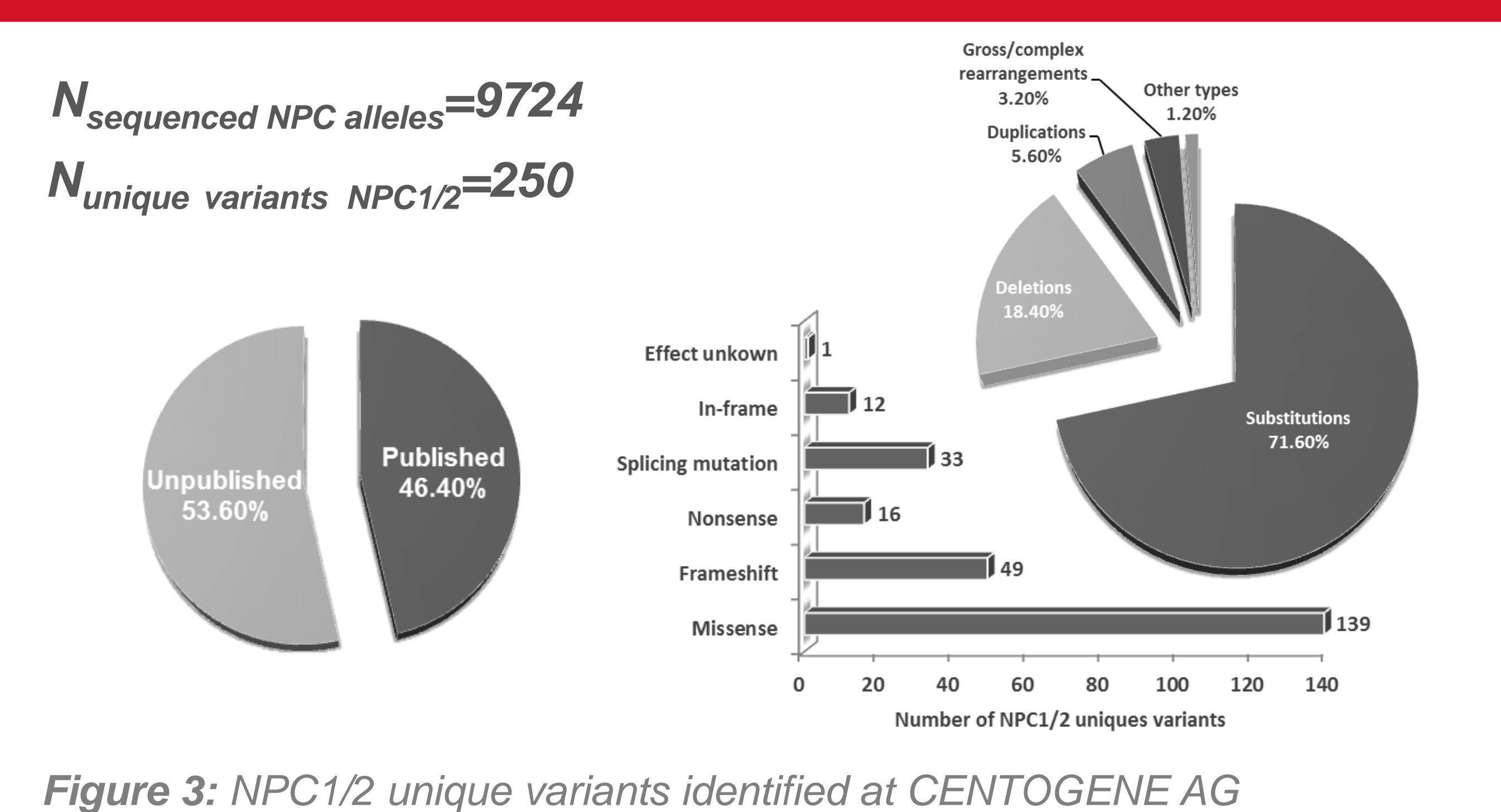
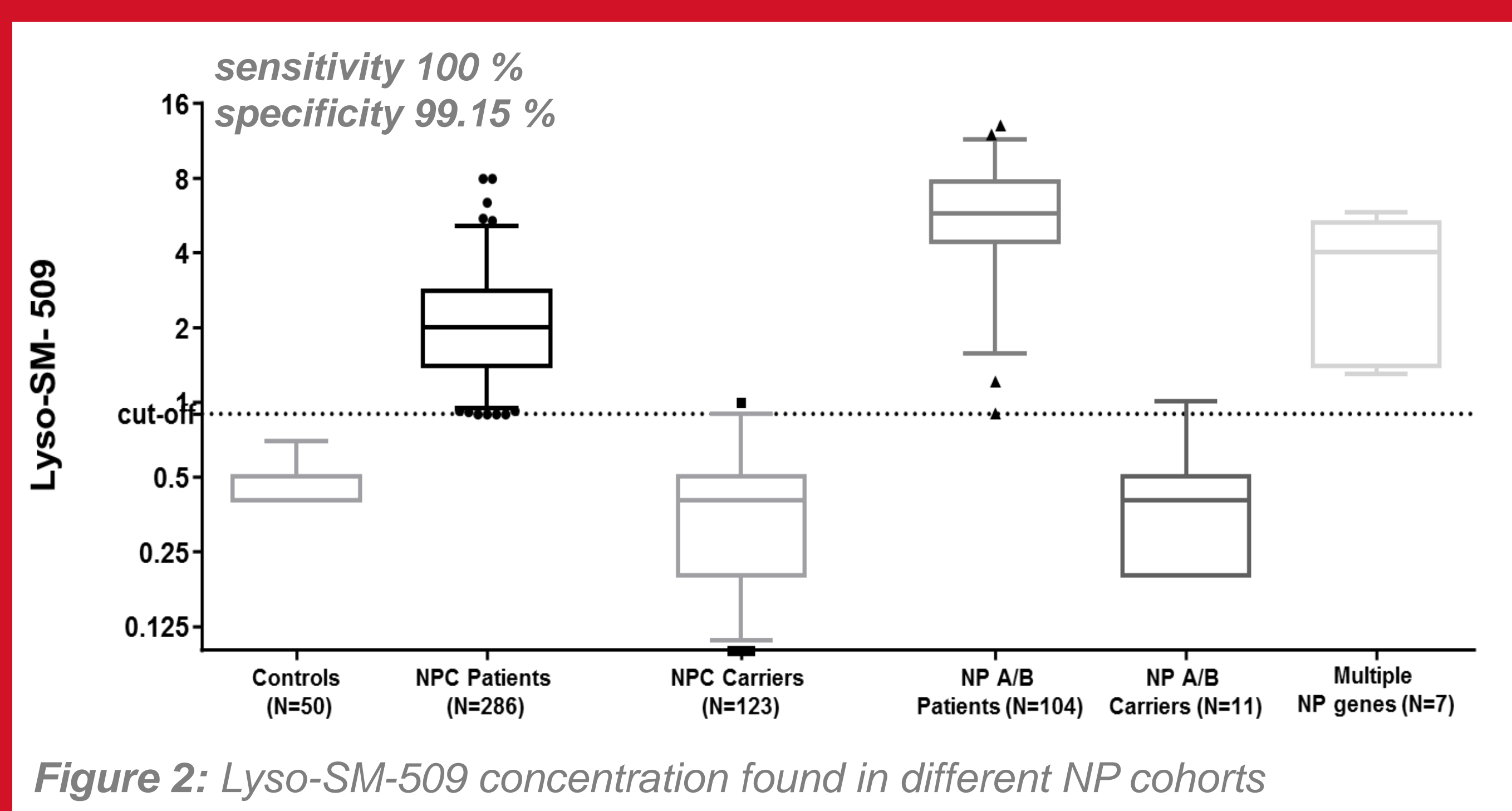
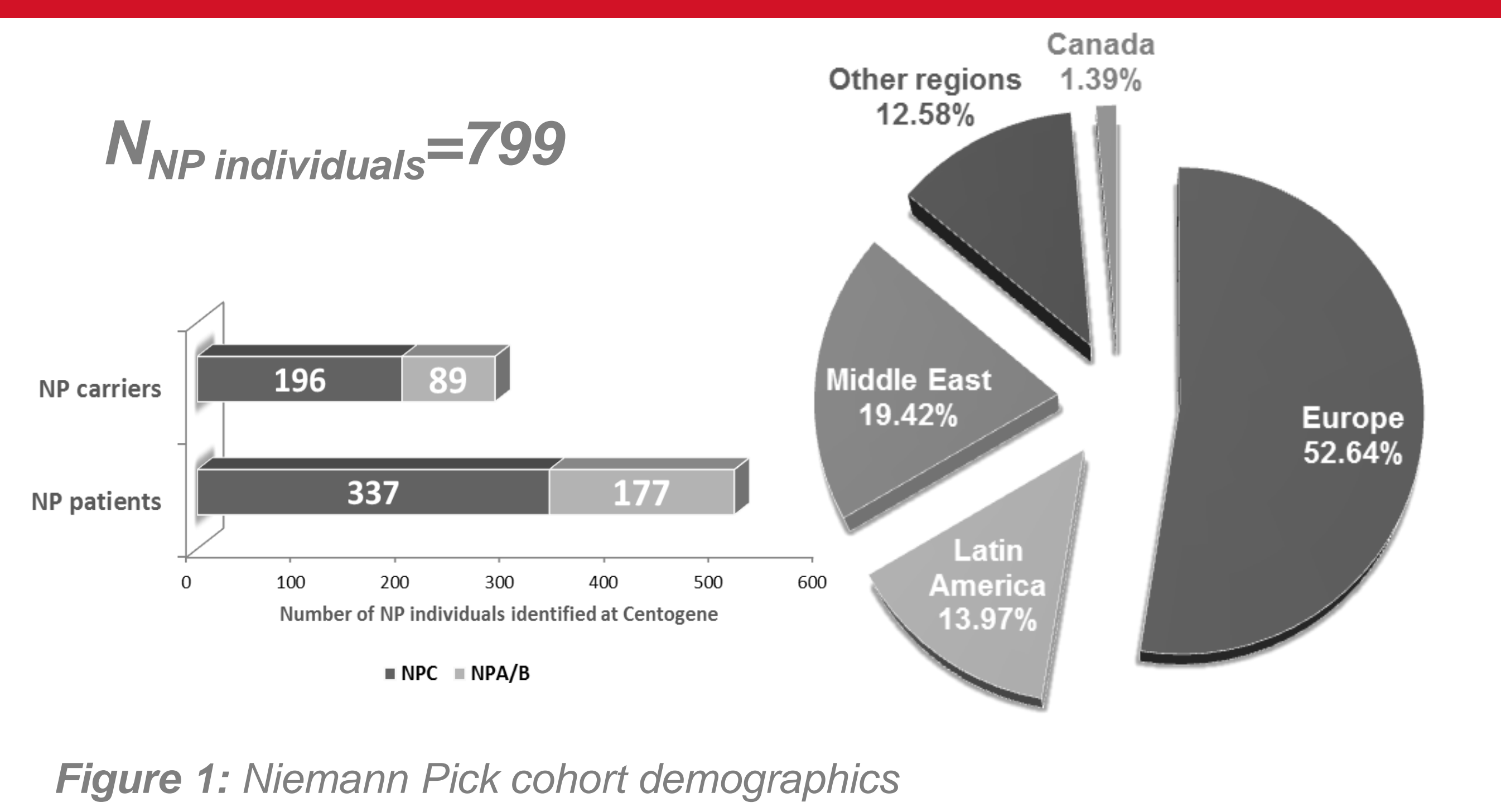
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**Introduction:** Niemann Pick Type C (NPC) disease is an autosomal recessive disease caused by mutations in NPC1 or NPC2 genes translated in defects of the lysosomes cholesterol transport system leading to abnormal accumulation of cholesterol and glycolipids in the lysosome. Recently developed treatment renders early NPC diagnosis of high most importance. Niemann Pick (NP) type A/B is an autosomal recessive disease caused and characterized by acidic sphingomyelinase deficiency. We present data from a 3 year global cohort of Niemann Pick patients using lyso-SM-509 biomarker determination, followed by sequencing of SMPD1 and/or NPC1/2 genes. The levels of lyso-SM-509 in blood reflect the burden of the NP disease and it can be used for the easy diagnosis of NPC patients and for the monitoring of the disease progression.

**Materials and methods:** Analysis of lyso-SM-509 is performed by LC/MRM-MS in plasma, serum, EDTA blood and dried blood spots (DBS). We identified in a world-wide study using lyso-SM-509 as primary screening in DBS samples over 337 patients and NPC A/B patients 177 NP. For the cases where the screening was started with Lyso-SM-509 determination, the diagnosis was confirmed by sequencing of the NPC1/2 genes by Sanger gene sequencing, NGS, or MLPA. In NPC1/2 sequencing negative patients with increased lyso-SM-509 concentrations the sequencing of sphingomyelinase (SMPD1) gene was done from the same sample. Lyso-SM-509 has a sensitivity of 100 % and specificity of 99.15 % for NPC1/2, and a sensitivity and specificity of 100% for SMPD1. Most of the NPC cases were diagnosed in the age of 3 to 10 years (30.65 %). From over 9,700 sequenced NPC1 and NPC2 alleles, we identified 514 NPC cases (patients and carriers). 47% of the unique variants identified in this study have not been previously described. The most common symptoms within the patients are: hepatomegaly (65%), splenomegaly (57%), neurodevelopment delay (54%), ataxia (34%), psychopathology (32%), brain atrophy (30%), ophthalmoplegia (30%), spasticity (30%), dystonia (25%), seizures (20%). From over 1,740 sequenced alleles, we identified 250 NPA/B individuals (affected patients and carriers).

**Summary:** Lyso509 is an easy and specific tool for screening of Niemann-Pick disease.



## References

1. Giese et al, 2015
2. CENTOGENE AG, WO2013072060
3. www.centomd.com

## Disclosure of conflict of interest:

This study was sustained in part by CENTOGENE AG, Rostock, Author of the presentation, Claudia Cozma, and 3 co-authors are employees of CENTOGENE AG, Rostock, Germany