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CentoMD®: Genetic variants-related biomarker knowledge database

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Clinical symptoms in lysosomal storage diseases (LSDs) are caused by the deficiency of specific enzymes function and resultant substrate accumulation in the lysosomes. Several biomarkers are already in use as indicators of the presence and monitoring of LSDs: lyso-Gb3 (Gb3) in Fabry disease (FD), lyso-Gb1 (Gb1) in Gaucher disease (GD) and NP509 in Niemann-Pick (NP) disease. CentoMD® is a browser-based tool that enables access to a high-quality repository of genetic, biochemical and human phenotype ontology (HPO)-based clinical information. All patients provided informed consent before inclusion in the DB. We measured lyso-Gb3, lyso-Gb1 and NP509 in the DBS samples obtained from 5,603 patients (57.6% females, 39.1% males, 3.3% unknown) undergoing biochemical and genetic testing for verification of FD (71.7%), GD (15.8%) or NP (12.5%). The pathological cut-off for biomarker measurements was set to 1.8 ng/ml for Gb3, to 4.8 ng/ml for Gb1; and to 0.9 ng/ml for NP509. Biomarker levels were correlated with clinical severity of the individual patients.

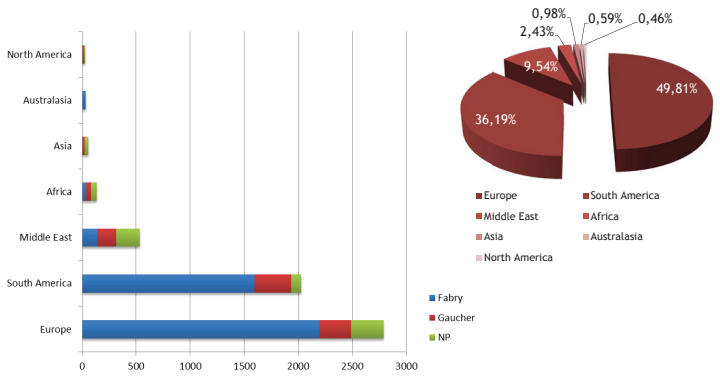

Figure 1: Distribution of LSD cases by geographical region

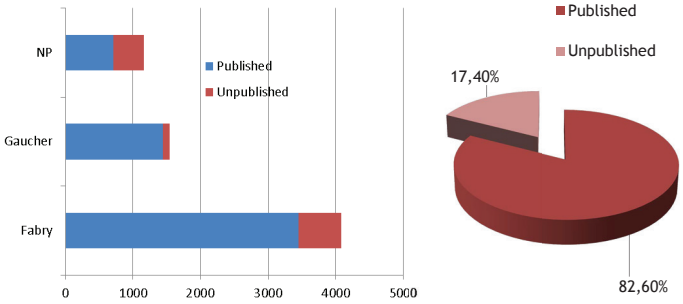

Figure 3: Ratio of newly detected relevant variants vs previously published variants related to Fabry, Gaucher and NP diseases

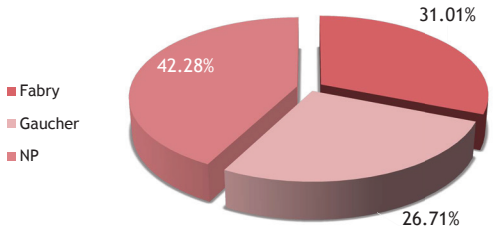

Figure 4: Amount of novel genetic variants described for the first time and associated with epidemiological information, clinical symptomatology and biomarker levels in CentoMD®

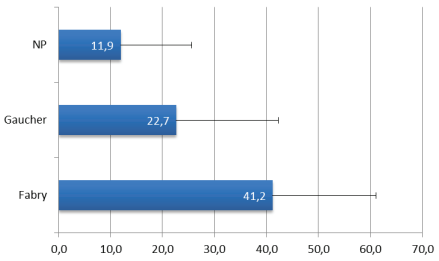

Figure 2: Age at diagnosis (years, months) of Fabry, Gaucher and NP cases (expressed as mean +STD)

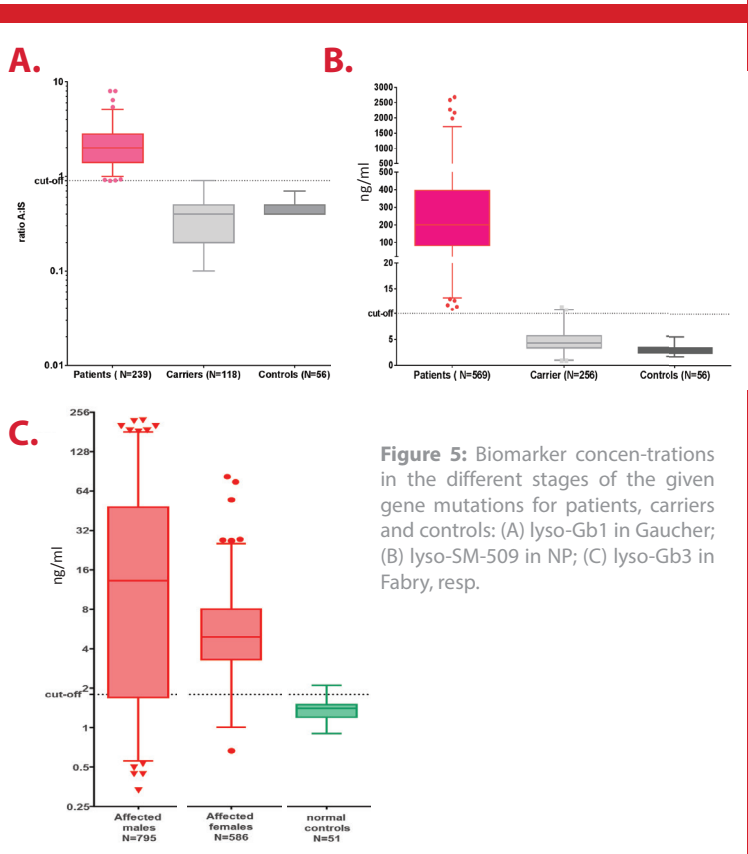

Figure 5: Biomarker concen-trations in the different stages of the given gene mutations for patients, carriers and controls: (A) lyso-Gb1 in Gaucher; (B) lyso-SM-509 in NP; (C) lyso-Gb3 in Fabry, resp.

Disclosure of conflict of interest:
This study was sustained in part by Centogene AG, Rostock, Author of the presentation, Alekhya Narravula, and 3 co-authors are employees of Centogene AG, Rostock, Germany