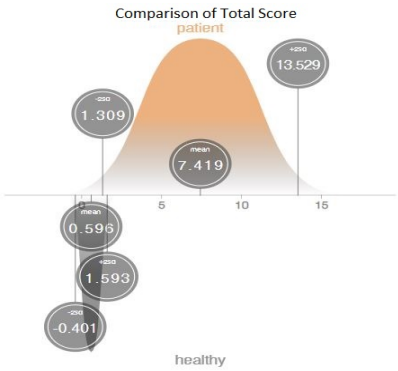
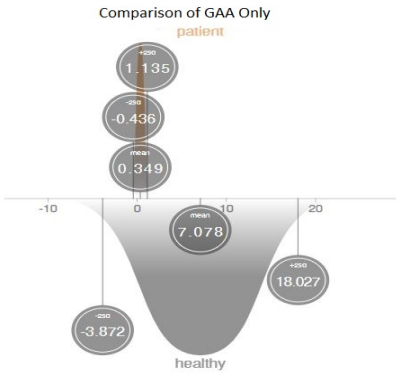
ANALYTICAL SCORING TOOL BASED ON ENZYME ACTIVITY TO GUIDE THE DIAGNOSIS OF POMPE DISEASE SUSPECTED PATIENTS

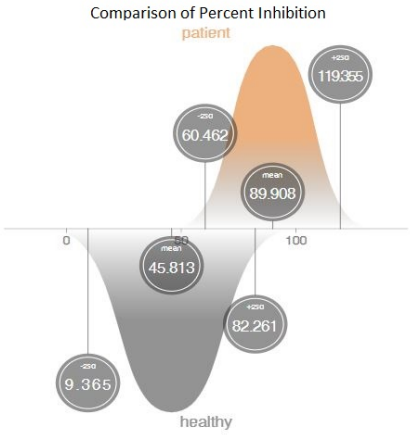
Ibrahim Tanyalcin[1] Mihriban Tijen Tanyalcin[2], [1]Self-Employment;Interuniversity Institute of Bioinformatics ULB/VUB, Structural Biology, VUB 1050 Brussels, Belgium website: https://deogen2.mutaframe.com/ ; http://i-pv.org/; http://lexicon.ibrahimtanyalcin.com
[2]Tanyalcin Medical Laboratory Selective Screening and Metabolism Unit; Izmir,Turkey

AIM: The aim of this study is to create an analytical scoring system based on the results of acid alpha-glucosidase GAA, neutral alpha-glucosidase NAG and maltase-glucoamylase MAG. 3 reactions were performed by fluorometric enzymatic assay:1- GAA, was measured at pH 4.0 in the presence of inhibitor acarbose;2- total GAA (MGA+GAA) measured at pH 4.0 without acarbose; and 3-Neutral a glucosidase activity (NAG), measured at pH 7.3. The tGAA reflects the combined activity of the isoenzyme MGA and GAA and was measured to calculate the percentage of tGAA that was inhibited by acarbose by using the formula (tGAA - GAA)/tGAA.



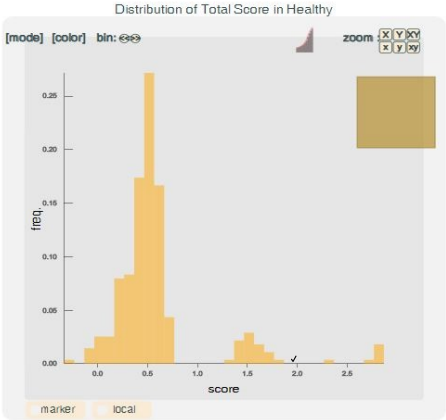


STATISTICAL METHOD
The scoring system is composed of 10 classifiers, several of which were either taken or adapted from Chien et al.,2008. Out of these 10 classifiers, 9 of them are binary with values 0 or 1;the remaining is a floating point classifier that ranges between-1 and 1. Overall,a given patients score can range between -1 to 10;effectively incorporates tGAA, NAA, GAA and percent inhibition into the decision process. The algorithm tested on 301 patients, 276 of whom were healthy. Based on these values a threshold with a score of **1.868 yields excellent diagnostic odds ratio,** classifying all patients correctly. As clearly seen on comparison of percent inhibiton graph; while half percent of the patients overlaps on the mean of healthy subjects , on total score graph, 95 % of the affected subjects are above the mean total score of healthy subjects.



Total Score Table

	Healthy	Patient	ALL
mean	0.596	7.419	1.163
sd	0.499	3.055	2.129
max	2.868	10	10
min	-0.334	2.421	-0.334



CONCLUSION: Our scoring system provides efficient and effective separation between healthy and affected subjects by GAA, tGAA, NAG and inhibition percent combination. Additionally, this system provides basis for: -development for more sophisticated algorithms that incorporates regression analysis;-fine-tuning of the threshold using ROC curves based on dynamic patient databases; and in cases where diagnostic metrics show bimodal/ trimodal distribution, extension of classifiers to incorporate ethnic background to increase reliability.