Patient Advocacy Group and Industry Collaborate to Establish Distinct Sanfilippo Syndrome (MPS IIIB) Facial Phenotype for Use in Facial Dysmorphism Recognition Software Tool

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INTRODUCTION

Sanfilippo Syndrome (MPS III) is a rare genetic disease caused by the deficiency of 1 of 4 lysosomal enzymes required to breakdown heparan sulfate. Excessive storage of heparan sulfate causes relentless neurodegeneration while systemic disease is comparatively milder. MPS III is the most prevalent form of mucopolysaccharidosis (MPS), however there is often a delay in diagnosis due to the less obvious physical features, particularly early in its course. Classic facial features include progressive coarsening facies, prominent eyebrows, and frontal bossing.

Face2Gene is a phenotyping tool utilizing FDNA's (Facial Dysmorphology Novel Analysis) technology to analyze 2D photographs via computer or freely downloadable smartphone app. Facial patterns are detected and matched with composite photos of known conditions to aid clinicians in diagnosis. Effectiveness of FDNA's technology requires input of disease-specific images to establish an accurate composite phenotype.

OBJECTIVES

- Collect sufficient number of disease-specific images to input in FDNA system in order to establish an accurate composite phenotype.
- Assess Face2Gene technology's capability to recognize the unique facial phenotype of MPS III.

DIAGNOSTIC DELAY

- Average age of diagnosis: US: 7 years old[1]; Spain: 3-4 years old[2]
- Symptom onset typically age 2-4 years old: (examples include)
  - •Behavioral disturbances
  - •Autistic features
  - •Poor sleep
  - •Developmental Delay
  - •Recurrent ear infections
  - •Loose stools
- No current Newborn screening
- Clinical trials targeting very young children (<4 years old)

NEED TO IDENTIFY CHILDREN WITH MPS III EARLIER

METHODS

- Collaboration between Cure Sanfilippo Foundation, Jonah's Just Begun and FDNA was established
- Campaign targeted MPS III patient families through social media, email, webinar, conferences, personal communications
- Photographs were uploaded via HIPAA-compliant online portal
- Data collected through online portal over 8 week period
- Statistical analyses of the receiver operating characteristic (ROC) curve was performed to calculate the area under curve (AUC) to determine classification accuracy
- 2 separate analyses conducted: MPS IIIB Images (n=109) vs. Unaffected Controls (n=132); and MPS IIIB Images vs. MPS IIIA (n=59) & MPS IIIC (n=123) Images

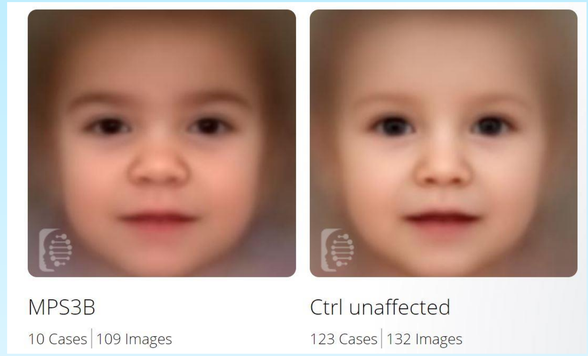

Figure 1. *Composite image of uploaded photos, depicting an average appearance for the analyses run of (a) MPS IIIB Patients vs. unaffected controls; and (b) MPS IIIB vs. MPS IIA and MPSIIIC*

RESULTS

- Total of 614 photos from 64 patients were received
- Training of the technology was conducted during September 2017 yielding an AUC of 0.97 when compared to all other syndromes trained for in version 17.6.1 of Face2Gene
- Comparison with unaffected control subjects and combined MPS IIIA & C syndromic facies yielded an AUC of 0.952 (p = 0.000, SD = .02), and 0.778 (p = 0.03, SD = 0.08) respectively. (Fig. 2).
- Composite images of the groups participating in this study are represented in Fig.1

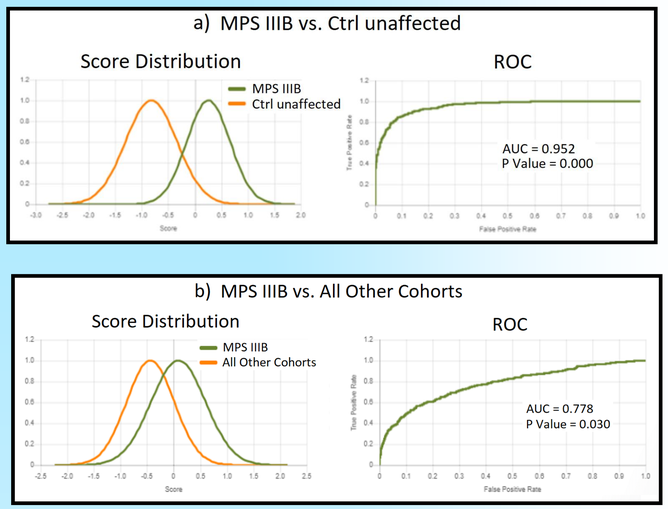

Figure 2. *Detection score and ROC curves obtained for the best performing split in three populations: MPS IIIB patients, non-syndromic/ normal controls and non-MPS IIIB facies/ other syndromes controls. When the AUC is 1 it expresses "perfect" separation between Sanfilippo patient photos and normal control photos.*

CONCLUSIONS

Collaboration between Patient Groups and industry partner FDNA enabled the creation of a disease-specific facial composite image for use in the Face2Gene facial recognition tool. Results here indicate that this collaboration generated a powerful clinical tool to aid in identifying patients with MPS IIIB. This research further highlights the value of patient involvement in the advancement of rare disease diagnosis.

ACKNOWLEDGEMENTS

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REFERENCES

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Jonah's Just Begun
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