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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\section*{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.

\section*{OBJECTIVES}
\begin{itemize}
\item Collect sufficient number of disease-specific images to input in FDNA system in order to establish an accurate composite phenotype.
\item Assess Face2Gene technology’s capability to recognize the unique facial phenotype of MPS III.
\end{itemize}

\section*{DIAGNOSTIC DELAY}
\begin{itemize}
\item Average age of diagnosis: US: 7 years old\textsuperscript{1}; Spain: 3-4 years old\textsuperscript{2}
\item Symptom onset typically age 2-4 years old: (examples include)
  \begin{itemize}
  \item Behavioral disturbances
  \item Autistic features
  \item Recurrent ear infections
  \item Poor sleep
  \item Loose stools
  \end{itemize}
\item No current Newborn screening
\item Clinical trials targeting very young children (<4 years old)
\end{itemize}

\textbf{NEED TO IDENTIFY CHILDREN WITH MPS III EARLIER}

\section*{METHODS}
\begin{itemize}
\item Collaboration between Cure Sanfilippo Foundation, Jonah’s Just Begun and FDNA was established
\item Campaign targeted MPS III patient families through social media, email, webinar, conferences, personal communications
\item Photographs were uploaded via HIPAA-compliant online portal
\item Data collected through online portal over 8 week period
\item Statistical analyses of the receiver operating characteristic (ROC) curve was performed to calculate the area under curve (AUC) to determine classification accuracy
\item 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
\item Excessive storage of heparan sulfate. Excessive storage of heparan sulfate.
\item MPS IIIB.
\item 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).
\item Composite images of the groups participating in this study are represented in Fig.1
\end{itemize}

\section*{RESULTS}
\begin{itemize}
\item Total of 614 photos from 64 patients were received
\item 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
\item 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).
\item Composite images of the groups participating in this study are represented in Fig.1
\end{itemize}

\section*{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.

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\section*{REFERENCES}