This dataset provides a clinical description along with extensive biochemical and molecular characterization of a patient with a homozygous mutation in PEX16 with an atypical phenotype. This patient described in Molecular Genetics and Metabolism Reports was ultimately diagnosed with an atypical peroxisomal disorder on exome sequencing. A clinical timeline and diagnostic summary, results of an extensive plasma and fibroblast analysis of this patient's peroxisomal profile is provided. In addition, a table of additional variants from the exome analysis is provided.

© 2016 Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
How data was acquired
Blood samples and a skin biopsy were obtained from the patient. DNA, plasma and cultured fibroblasts were analyzed in the context of the patient’s diagnostic course. LC–MS/MS, Enzyme activity using radioactive substrates, colorimetric assays, next-generation sequencing.

Data format
Analyzed datasets, Excel, Tif files.

Experimental factors
Unique genotype (n=1)

Experimental features
Plasma samples and cultured fibroblast from a skin biopsy were used for peroxisomal biochemical analysis. Genomic DNA was utilized for whole-exome sequencing.

Data source location
Houston Texas

Data accessibility
Date is included with this article

Value of the data

- A profile of a patient with an atypical peroxisomal biogenesis disorder which can be compared with other patient’s with these phenotypes.
- Clinical review of diagnostic considerations for atypical peroxisomal biogenesis disorders.
- Comprehensive set of functional consequences of F332del allele of PEX16.

1. Data

See Table 1.

1. Plasma VLCFA – plasma was collected at ages 10 years, 11 years and 22 years for VLCFA analysis. Values shown in µg/ml. C24/C22 and C26/C22 ratios shown. Z-scores of the patient’s sample measurement as compared to a set of normal controls shown.
2. Fibroblast VLCFA – patient fibroblasts were cultured and analyzed for VLCFA analysis. Values shown are in µg/mg protein. Z-scores of the patient’s sample measurement as compared to a set of normal controls shown.
3. Catalase Distribution – cultured cells were analyzed for Catalase Distribution (expressed in % soluble). A Z-score of the patient’s sample is shown.
4. Plasmalogen synthesis assay from radiolabel enzyme assay is shown.
5. Plasma pipecolic acid (expressed in µmole/L).
6. Lyso-PC – LC MS/MS of lysophospholipids for the patient’s blood sample at 22 years.
7. 14C oxidation assays for Phytanic and Pristanic acid (in % of the mean of controls) shown.

Table 1
Comprehensive plasma and fibroblast biochemical analysis.

| Analyte                          | Control fibroblasts | Zellweger syndrome | Patient@22 years |
|----------------------------------|---------------------|--------------------|------------------|
| Phytanic acid oxidation (% mean of control value) | 100                 | 5.7                | 73               |
| Pristanic acid oxidation (% mean of control Value) | 100                 | 4.9                | 156.9            |
List of variants in disease-causing genes including heterozygous and homozygous variants which were verified by Sanger sequencing. The Gene, position, specific isoform, nucleotide, protein change (predicted), and zygosity are shown. AR=Autosomal recessive. Comments contain segregation information from the parents or other populations (Table 2). A clinical and diagnostic timeline for the patient showing clinical events and gene diagnostic tests. WES=Whole-exome sequencing (Figs. 1 and 2).

Table 2
Candidate variants table from Whole-exome sequencing.

| Gene  | Position | Isoform | Nucleotide | Protein | Zygosity | Disease                        | Disease inheritance | Comment                        |
|-------|----------|---------|------------|---------|----------|--------------------------------|---------------------|--------------------------------|
| CTC1  | Ch17:8134658 | NM_025099 | c.2605C>T  | p. Q869X | Het      | Cereboretinal microangiopathy with calcifications and cysts | AR                  | Father also heterozygous       |
| SYNE1 | Chr6:152730222 | NM_033071 | c.6542C>T  | p. T2181I | Het      | Spinocerebellar ataxia, autosomal recessive 8 | AR                  | Mother also heterozygous       |
| C5orf42| Chr5: 37185062 | NM_023073 | c.4309A>G  | p. I1437V | Het      | Joubert syndrome              | AR                  | Novel variant                  |
| CLN3  | Chr16:28493901 | uc010vcx.1 | c.583C>G   | p. P195A  | Het      | Ceroid lipofuscinosis         | AR                  | rs146839771                   |
| VPS13A| Chr9:79902873 | NM_033305 | c.3356G>A  | p. G1119E | Het      | Choroeacanthocytosis          | AR                  | rs144358567                   |
| PSAP  | Ch10:73588801 | NM_002778 | c.409C>G   | p.L137V  | Het      | Combined SAP deficiency       | AR                  | Novel variant                  |
| MAN1B1| Chr9: 140002934 | NM_016219 | c.1991C>T  | p. T664M  | Het      | Mental retardation, autosomal recessive 15 | AR                  | Reported in ESP5460 and or Thousand Genomes |
| NPC1  | Chr18:21166261 | NM_000271 | c.47G>A    | p.C16Y   | Het      | Niemann–Pick disease, type D  | AR                  | Novel variant                  |
| BRAT1  | Chr7:2579447 | NM_152743 | c.1471G>A  | p. G491S  | Het      | Rigidity and multifocal seizure syndrome, lethal neonatal | AR                  | Father also heterozygous       |
| BRAT1  | Chr7: 2582935 | NM_152743 | c.826G>A   | p. D276N  | Het      | Rigidity and multifocal seizure syndrome, lethal neonatal Zellweger syndrome, complementation 9 | AR                  | Mother heterozygous, rs146546197 |
| PEX16 | Chr11:45931818 | NM_004813 | c.995_997delTCT | p. F332del | Hom      |                           | AR                  | Novel variant, both parents heterozygous |

Fig. 1. Clinical timeline for the patient.
2. Experimental design, materials and methods

2.1. Ethics statement

Informed consent for the research and for publication was obtained prior to participation for the subject who was recruited under an Institutional Review Board approved protocol at Baylor College of Medicine.

2.2. Peroxisomal biochemical studies

Plasma samples and cultured fibroblast from a skin biopsy were used for peroxisomal biochemical analysis.

- Plasma pipecolic acid was measured by electron capture negative ion mass fragmentography [1].
- Very-long-chain fatty acid levels and total lipid fatty acid profile were measured as described [2,3].
- The plasmalogen assay was performed using C14 radioactivity incorporation and H3 counts to measure microsomal plasmalogen steps [4].

Fig. 2. Peroxisomal biochemical studies. (A) C26:0 Lyso PC measured by LC-MS-MS for the Patient’s plasma compared to Normals and other disease populations. (B) Catalase Distribution in cultured fibroblasts (expressed as % soluble). (C) Bile acid measurements in pmoles/10μl plasma for the Patient, controls and other disease populations.
Fibroblast oxidation assays were performed using radioactive substrates to assay enzyme activity [5,6].

Measurement of C26:0-lyso-PC was performed as described [7] and bile acid quantitation was performed by tandem mass spectrometry [8].

Catalase distribution in cultured cells was performed and quantified (% soluble catalase) [9,10].

2.3. Whole-exome capture, sequencing and data analysis

The patient underwent WES through the Whole Genome Laboratory (https://www.bcm.edu/research/medical-genetics-labs/index.cfm?PMID=21319) using methods described [11].

Produced sequence reads were aligned to the GRCh37 (hg19) human genome reference assembly using the HGSC Mercury analysis pipeline (http://www.tinyurl.com/HGSC-Mercury/). Variants were determined and called using the Atlas2 [12] suite to produce a variant call file (VCF [13]).

High-quality variants were annotated using an in-house developed suite of annotation tools [14].

Acknowledgments

The authors thank Ann Snowden at KKI for cell culture technical support. Cell culture work funded by the Intellectual and Developmental Disability Research Center 1 U54 HD079123-01A1 at KKI PI. Wayne Silverman funded by: NICHD, M.W. was supported by NIH K08NS076547 funded by NINDS, and funding from the Simmons Family Foundation Collaborative Research Fund and the Clayton Murphy Peroxisomal Disorders Research Fund at Baylor College of Medicine.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.dib.2015.12.011.

References

[1] R.M. Kok, L. Kaster, A.P. de Jong, B. Poll-The, J.M. Saudubray, C. Jakobs, Stable isotope dilution analysis of pipecolic acid in cerebrospinal fluid, plasma, urine and amniotic fluid using electron capture negative ion mass fragmentography, Clin. Chim. Acta 168 (2) (1987) 143–152.

[2] A.B. Moser, N. Kreiter, L. Bezman, S. Lu, G.V. Raymond, S. Naidu, H.W. Moser, Plasma very long chain fatty acids in 3,000 peroxisome disease patients and 29,000 controls, Ann. Neurol. 45 (1) (1999) 100–110.

[3] S.A. Lagerstedt, D.R. Hinrichs, S.M. Batt, M.J. Magera, P. Rinaldo, J.P. McConnell, Quantitative determination of plasma c8–c26 total fatty acids for the biochemical diagnosis of nutritional and metabolic disorders, Mol. Genet. Metab. 73 (1) (2001) 38–45.

[4] A. Roscher, B. Molzer, H. Bernheimer, S. Stockler, I. Mutz, F. Paltauf, The cerebrohepatorenal (Zellweger) syndrome: an improved method for the biochemical diagnosis and its potential value for prenatal detection, Pediatr. Res. 19 (9) (1985) 930–933.

[5] A. Poulos, Diagnosis of Refsum’s disease using [1-14C]phytanic acid as substrate, Clin. Genet. 20 (4) (1981) 247–253.

[6] R.J. Wanders, S. Denis, J.P. Ruiter, R.B. Schutgens, C.W. van Roermund, B.S. Jacobs, Measurement of peroxisomal fatty acid beta-oxidation in cultured human skin fibroblasts, J. Inherit. Metab. Dis. 18 (Suppl 1) (1995) S113–S124.

[7] W.C. Hubbard, A.B. Moser, A.C. Liu, R.O. Jones, S.J. Steinberg, M.J. Magera, P. Rinaldo, J.P. McConnell, Rapid and quantitative analysis of unconjugated C(27) bile acids in plasma and blood samples by tandem mass spectrometry, J. Lipid Res. 42 (1) (2001) 9–16.

[8] D.W. Johnson, H.J. ten Brink, R.C. Schuit, C. Jakobs, Rapid and quantitative analysis of unconjugated C(27) bile acids in plasma and blood samples by tandem mass spectrometry, J. Lipid Res. 42 (1) (2001) 9–16.

[9] B.T. Poll-The, P.A. Watkins, Complementation analysis of patients with intact peroxisomes and impaired peroxisomal beta-oxidation, Biochem. Med. Metab. Biol. 49 (2) (1993) 228–242.

[10] P.A. Watkins, M.C. McGuinness, G.V. Raymond, B.A. Hicks, J.M. Sisk, A.B. Moser, H.W. Moser, Distinction between peroxisomal bifunctional enzyme and acyl-CoA oxidase deficiencies, Ann. Neurol. 38 (3) (1995) 472–477.
[11] J.R. Lupski, C. Gonzaga-Jauregui, Y. Yang, M.N. Bainbridge, S. Jhangiani, C.J. Buhay, C.L. Kovar, M. Wang, A.C. Hawes, J. G. Reid, C. Eng, D.M. Muzny, R.A. Gibbs, Exome sequencing resolves apparent incidental findings and reveals further complexity of SH3TC2 variant alleles causing Charcot–Marie–Tooth neuropathy, Genome Med. 5 (6) (2013) 57.

[12] P. Danecek, A. Auton, G. Abecasis, C.A. Albers, E. Banks, M.A. DePristo, R.E. Handsaker, G. Lunter, G.T. Marth, S.T. Sherry, G. McVean, R. Durbin, The variant call format and VCFtools, Bioinformatics 27 (15) (2011) 2156–2158.

[13] M.N. Bainbridge, W. Wiszniewski, D.R. Murdock, J. Friedman, C. Gonzaga-Jauregui, I. Newsham, J.G. Reid, J.K. Fink, M. B. Morgan, M.C. Gingras, D.M. Muzny, L.D. Hoang, S. Yousaf, J.R. Lupski, R.A. Gibbs, Whole-genome sequencing for optimized patient management, Sci. Transl. Med. 3 (87) (2011) 87re3.

[14] A. Untergasser, I. Cutcutache, T. Koressaar, J. Ye, B.C. Faircloth, M. Remm, S.G. Rozen, Primer3 – new capabilities and interfaces, Nucleic Acids Res. 40 (15) (2012) e115.