# Supplementary Table 1. Common Infantile and Pediatric Leukodystrophies

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|  | Pathophysiology | Diagnosis | Clinical manifestations |
| Krabbe disease\* (globoid cell leukodystrophy)1 | Lysosomal storage disorder: Deficiency of the enzyme galactocerebrosidase | Autosomal recessive, biallelic variants in *GALC* gene | Irritability, limb spasticity, truncal hypotonia, absent reflexes, microcephaly |
| Alexander disease2\* | Dysmyelinating disorder with Rosenthal fibers within astrocytes | Autosomal dominant, de novo variants in *GFAP* gene (glial fibrillary acidic protein) | Megalencephaly, psychomotor regression; typically young school age but infantile forms described |
| Metachromatic leukodystrophy3\* | Lysosomal storage disorder: Deficiency of arylsulfatase A | Autosomal recessive, biallelic variants in *ARSA* gene; also detected by low enzyme activity or elevated urine sulfatides | Late infantile form with progressive gait problems (14-16 months) |
| Pelizaeus-Merzbacher disease4\* | Hypomyelinating disorder with axonal degeneration | X-linked pathogenic variant in *PLP1* gene\*\* | Pendular nystagmus, head tremor, hypotonia and motor delays progressing to spasticity and ataxia, optic atrophy, seizures |
| X-linked Adrenoleukodustrophy5\* | Peroxisomal disorder: Abnormal function of protein within the peroxisomal membrane. | X-linked pathogenic variant in *ABCD1* gene\*\*; now included on NBS for many states detected by elevated very long chain fatty acids | Boys (4-8 years of age) presenting with behavior problems and regression |
| Canavan disease6\* | Spongiform degeneration of the brain: Deficiency of aspartoacylase leading to increased *N*-acetylaspartic acid (NAA) causing demyelination | Autosomal recessive pathogenic variants in the *ASPA* gene; also detected by elevated NAA on MR spectroscopy or in urine | Normal development until 3-5 months of age, followed by lethargy, hypotonia, optic atrophy that progresses to spasticity, feeding difficulties, and seizures |

\*Listed in American Board of Psychiatry and Neurology (ABPN) Certification Examination Content Specifications

\*\*X-linked disorders would be less likely in female patients

# Supplementary References

1. Orsini JJ, Escolar ML, Wasserstein MP, Caggana M. *Krabbe Disease*.; 2018.

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3. Gomez-Ospina N. *Arylsulfatase A Deficiency*. University of Washington, Seattle; 2017.

4. Hobson GM, Kamholz J. *PLP1-Related Disorders*. University of Washington, Seattle; 2013.

5. Raymond G V, Moser AB, Fatemi A. X-Linked Adrenoleukodystrophy. GeneReviews. https://www.ncbi.nlm.nih.gov/books/NBK1315/. Published February 15, 2018. Accessed June 26, 2019.

6. Matalon R, Delgado L, Michals-Matalon K. *Canavan Disease*. University of Washington, Seattle; 2018.