Drosophila models of *ABCD1*-related X-linked Adrenoleukodystrophy show possible implications in peroxisomal biogenesis

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X-linked adrenoleukodystrophy (X-ALD) is a progressive neurodegenerative disorder caused by a loss-of-function (LOF) mutation in the *ATP binding cassette subfamily D member 1* (*ABCD1*) gene, leading to the accumulation of very long-chain fatty acids (VLCFAs). This disorder exhibits striking heterogeneity; some male patients develop a neuroinflammatory demyelination disorder, while other patients, including most affected women, experience chronic progressive myelopathy. All patients are born asymptomatic, and it is currently impossible to predict symptoms based on genetics, complicating clinical decision-making. Previous fruit fly models highlighted an upstream deficiency in VLCFA synthetases, leading to reduced lifespan, retinal degeneration, and VLCFA accumulation. Here, we present a study of LOF of *ATP binding cassette subfamily D member 1* (*Abcd1*) as a *Drosophila* model of X-ALD. First, we used UAS-$Abcd1^{RNAi}$, *which*, when overexpressed ubiquitously and spacio-temporally, showed a severe reduction in survival, abnormal peroxisomal biogenesis, abnormal eye formation, and retinal degeneration. We also utilized a known LOF allele $Abcd1^{\Delta 4}$ and observed locomotion defects compared to the control. When we performed biochemical analysis of VLCFAs observed an accumulation of the signature hexatonic acid (C26:0). Next, we generated the fly model for the human *ABCD1 (*$ABCD1^{Ref}$*)* along with the known X-ALD-causing variant $ABCD1^{R518Q}$ under the UAS promoter. When overexpressed ubiquitously and spacio-temporally, the human $ABCD1^{Ref}$ causes abnormal peroxisomal biogenesis and late larval lethality. However, the $ABCD1^{R518Q}$ variant also shows peculiar peroxisomal biogenesis that notably differs from the reference and causes partial larval lethality. $ABCD1^{R518Q}$ variant expressing flies fail to behave as reference animals, thus proving a LOF mechanism for the variant. This research in the fly model partially recapitulates the biochemical manifestations of X-ALD observed in humans. These results identify a potential link between *Abcd1* function and peroxisomal biogenesis in the fly's simplified mechanism of VLCFA import in peroxisomes.