

Ultrastructural Retinal Neuronal Changes in Juvenile Miniature Ossabaw Pigs Fed a Western Diet

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DR is the main cause of irreversible blindness associated with diabetes mellitus in young adults. More than 642 million people are estimated to be diabetic by year 2040, with 90% of them being type 2 diabetic (T2DM), and an increasing proportion of the T2DM reported in children younger than 14 years of age. An average 10% of patients will be afflicted with some form of retinopathy within 10 years of having diabetes. As a result, one-third of the economic cost from eye disorders was predicted to be incurred by adults younger than 40 years of age. Current DR treatments target mostly in the late stages of DR and involves anti-angiogenic drug injections into the eye, and laser photocoagulation surgery. However, there is no treatment for the early non-proliferative stage of the disease, and early signs of DR are impossible to detect or visualize with modern advanced imaging techniques. One of the major limitations to characterize the early events in DR is the unavailability of a suitable animal model especially in the early stages of disease pathogenesis. Additionally, there are no translational large animal model currently available which represents the physiological and clinical development of juvenile diabetes expressing DR features. This is the first study to examine retinal changes in the Ossabaw pigs, which are a breed of wild boar with a “thrifty phenotype”, making them a good model for diet-induced obesity. Using a JEOL JEM 1400 transmission electron microscope at 80 kV on a Gatan Ultrascan 1000 CCD, we found that juvenile Ossabaw pigs fed a western diet exhibit early signs of DR including neuronal defects and basement membrane thickening, hence making it a novel translational animal model for DR.

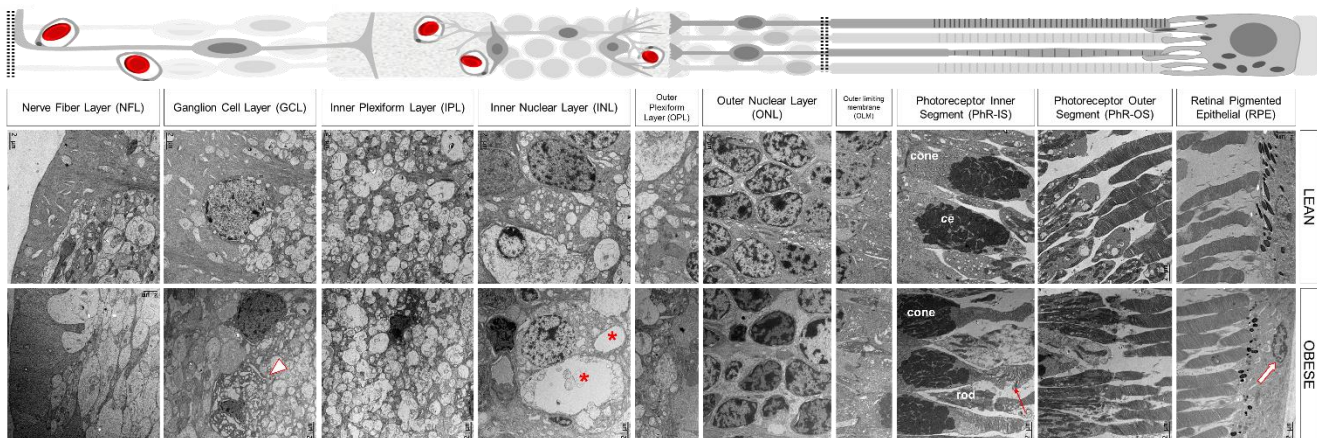


Figure 1. Ultrastructural defects in western diet fed Ossabaw pig retina. Numerous ganglion cells (**block arrowhead**) in the GCL of Ossabaw pigs were vacuolated and in the process of disintegration. Similar vacuolations can be seen in the INL (**asterisks**). ONL comprising of photoreceptor cell bodies were less organized in the obese pig, with increased gaps between PhR nuclei, which were of uneven sizes and shapes compared to lean control. PhR in both lean and obese Ossabaw pigs were largely well organized, however disarrangement of cone discs (**arrow**) were seen in the obese pig. RPE in both groups was in good contact with the PhR, but nuclear distortion (**block arrow**) was observed in the western fed Ossabaw pig. Scale bar, 2µm.