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Animal models are reliably mimicking human diseases? A morphological study that compares animal and human NAFLD

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Nonalcoholic fatty liver disease (NAFLD) affects up to 20% of western population and, when untreated, it can progress from simple fatty liver or steatosis to a more severe condition, such as NASH (non alcoholic steatohepatitis) and cirrhosis (1). NAFLD is a clinical-pathological syndrome that include a wide spectrum of morphological alteration but such studies on humans are not copious, as human samples are difficult to obtain because of ethical limitations. Experimental models are crucial to study steatosis' progression, not only for elucidating the pathogenesis of NAFLD but also in examining therapeutic effects of various agents. Animal models may be developed on genetic or nutritional basis, or a combination of both. It is important to select the best model fitted to the aim of the study. But the question that arises is: can the animal model reflect hepatic histopathology and pathophysiology of human NAFLD? This question is always neglected as well as the evaluation of ultrastructural features of NAFLD. In order to overcome this lack of investigations we compared ultrastructural features of NAFLD in an animal model and in human samples of NAFLD patients. NAFLD animal model was obtained using Sprague Dawley rats fed by a high fat diet (HFD) (71% of energy from fat), while control rats were fed by a standard diet (35% of energy from fat). Diets were given *ad libitum* and rats were killed after 1, 2, 3, and 4 weeks. Human specimens were obtained from patients with fatty liver disease undergoing to liver biopsies. Normal liver was taken from patients undergoing surgery for other pathologies. Hepatic steatosis and normality of the liver were assessed by parallel examinations at light microscopy, transmission and high resolution scanning electron microscopy. Light microscopy results showed that different degrees of NAFLD observed in human samples corresponded to similar morphological changes in treated rats. Ultrastructural examination revealed that in the HFD model the histopathology closely reflected that of human NAFLD, although the first did not replicate the full spectrum of the disease in humans. In summary, we showed that, at least morphologically, HFD model overlays to human NAFLD. This could point out for reliability in evaluating other pathological features in animal models. Moreover, animal HFD mimics human nutritional dysregulation that may induce the same biochemical and molecular modifications observed in human patients and might represent a more appropriate tool for studying the pathogenesis of NAFLD over genetic models (2).

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References

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Key words

Animal model, NAFLD, electron microscopy.