

## Mitochondrial alterations in NASH and Wilson disease: a 3-D study by HRSEM

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Non-alcoholic fatty liver disease (NAFLD) is defined as a constellation of clinical conditions predominantly characterized by macrovesicular steatosis of the liver. By definition, NAFLD occurs in subjects who do not consume enough alcohol to cause *serious* liver problems. The most severe stage of NAFLD is known as nonalcoholic steatohepatitis (NASH), a condition that may progress to fibrosis, cirrhosis and liver failure. Certain other medical conditions, including Wilson's disease (WD) (a genetic disorder of copper metabolism involving liver dysfunction), have also been linked to NASH.

Evidence indicates that mitochondrial impairment plays a critical role in NAFLD initiation and progression to the more serious condition of NASH.

Since three-dimensional (3D) morphological studies of NASH liver mitochondria are lacking, the aim of this preliminary study was to ascertain by High Resolution Scanning Electron Microscopy (HRSEM) if mitochondrial ultrastructure is altered in humans with that disease.

Specimens were obtained from patients with fatty liver disease undergoing to liver biopsies. As WD is associated with hepatic steatosis, we studied mitochondrial morphology in WD patients as well. Normal liver was taken from patients undergoing surgery for pathologies not involving it. Informed consent was obtained from each patient and permission was granted by the local ethical committee (ASL 8, Cagliari). Hepatic steatosis and normality of the liver were assessed by parallel examinations at light microscopy and at transmission electron microscopy.

This study proved that NASH and WD mitochondria have morphological alterations. Normal liver mitochondria, as seen by HRSEM, are spherical or slightly elongated and filled with abundant tubular cristae. In NASH, mitochondria were abnormal. They were pleomorphic, with a few cristae, some of which were not tubular but rather dilated or discoidal. WD liver mitochondria also showed alterations, such as: an elongated or branched shape and few inhomogeneously arranged cristae. Thus, we found very similar mitochondria morphologies in NASH and WD patients and we reasonably believe that mitochondrial abnormality in WD patients is not correlated to a disorder in copper metabolism, but could be related to liver steatohepatitis. The relationship between NASH or WD and mitochondrial abnormalities has to be clarified in the next step of this study.