**PROTEOMIC PROFILING OF THE AGED MDX-4CV HEART MODEL OF DYSTROPHINOPATHY-RELATED CARDIOMYOPATHY**

S. Murphy, P. Dowling, **K. Ohlendieck**

Maynooth University, Maynooth, Co. Kildare, Ireland

*Objectives*: In order to improve our general understanding of the molecular pathogenesis of muscular dystrophy-associated cardiomyopathy and to identify new marker candidates of cardiac changes in dystrophinopathy, we have carried out a comparative proteomic study of the mdx-4cv mouse model of Duchenne muscular dystrophy.

*Background*: Cardiomyopathy is a serious complication in X-linked muscular dystrophy, which is triggered by primary abnormalities in the dystrophin gene. The almost complete loss of the membrane cytoskeletal protein dystrophin triggers progressive muscle wasting and impaired cardiorespiratory functions.

*Methods*: In order to directly correlate the deficiency in dystrophin to secondary abnormalities in the dystrophic heart, this study has used label-free mass spectrometry to compare protein expression patterns in the aged mdx-4cv heart model of dystrophinopathy versus wild type heart. Bioinformatics was used to determine major changes in protein families and establish potential alterations in cardiac protein networks. Immunoblotting was employed to verify key findings from proteomic surveys.

*Results*: The mass spectrometric profiling of whole heart preparations has identified the reduction in the dystrophin-glycoprotein complex and a large variety of secondary changes in the dystrophic heart. Cardiac proteins with a changed abundance were shown to be involved in fiber contraction, energy metabolism, cellular signaling, the cytoskeletal network, the extracellular matrix and the stress response.

*Conclusions*: The proteomic findings indicate that the molecular pathogenesis of muscular dystrophy-associated cardiomyopathy is highly complex and involves alterations of energy metabolism, molecular chaperoning and ion homeostasis, as well as the maintenance of the contractile apparatus, the intracellular cytoskeleton and the extracellular matrix.