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Identification of muscular dystrophy-specific biomarkers using fluorescence two-dimensional difference in-gel electrophoresis

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Duchenne muscular dystrophy is a highly progressive X-linked inherited disorder of childhood and represents one of the most common genetic disorders of the neuromuscular system. In the most severe cases of dystrophinopathy, primary abnormalities in the dystrophin gene cause the almost complete absence of this crucial membrane cytoskeletal protein. The secondary reduction in dystrophin-associated glycoproteins renders muscle fibres more susceptible to necrosis and triggers abnormal calcium handling and disintegration of the muscle surface membrane. Muscle wasting affects both skeletal muscles and the heart, warranting large-scale investigations into the molecular mechanisms that underlie fibre degeneration in striated muscle tissues. In order to generate a comprehensive biomarker signature of X-linked muscular dystrophy, our laboratory has initiated a proteomic screening program to identify global changes in dystrophin-deficient muscle fibres. For comparative studies, fluorescence difference in-gel electrophoresis was employed and established as an excellent biomarker discovery tool in the field of muscular dystrophy research. This advanced method of gel-based proteomics is an ideal analytical tool for studying the majority of muscle-associated proteins, such as contractile proteins and metabolic enzymes. With the help of mass spectrometry and a variety of biochemical and cell biological verification experiments, distinct changes in muscle proteins associated with cellular signaling, the excitation-contraction-relaxation cycle, the cytoskeleton, the extracellular matrix, ion homeostasis, metabolite transport, glycolysis, mitochondrial metabolism and the cellular stress response were established. These new biomarker candidates of muscular dystrophy may be useful for improving diagnostic, prognostic and therapeutic methodology.

Biography

Kay Ohlendieck has an undergraduate degree in Biology from the University of Konstanz, Germany (1985), a PhD in Biochemistry from University College Cork, Ireland (1989) and a DSc in Muscle Biology from University College Dublin, Ireland (2011). He has worked as a postdoctoral associate at the University of Iowa, Iowa City and at the State University of New York, Stony Brook, as well as a Lecturer in the Department of Pharmacology, University College Dublin (1995-2001). Since 2002, he is Chair of Biology at the National University of Ireland, Maynooth, and his research focuses on skeletal muscle proteomics.

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