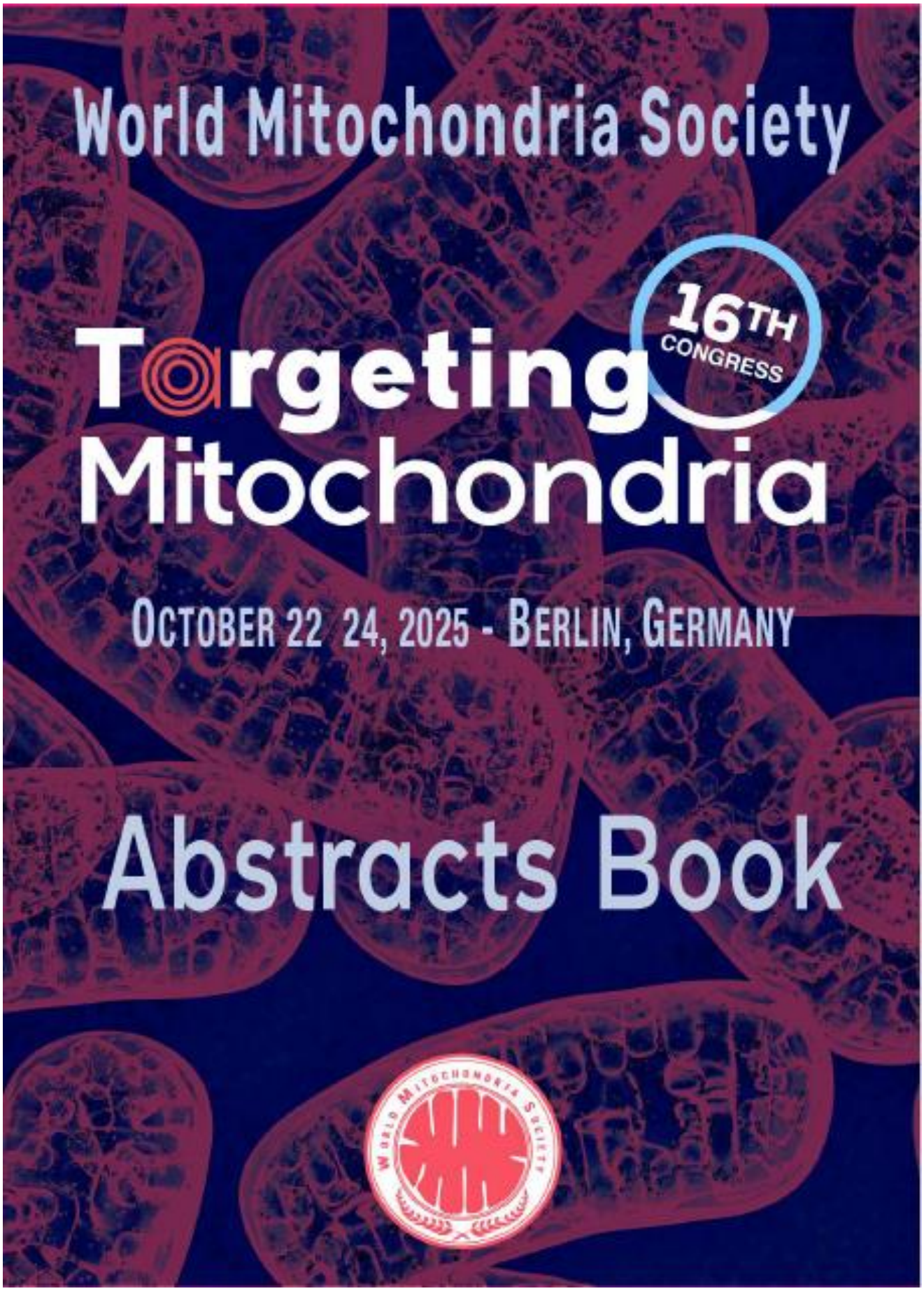
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16th World Congress on

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INSIGHTS INTO MITOCHONDRIAL DYSFUNCTION IN SPINAL AND BULBAR MUSCULAR ATROPHY THROUGH IPSC-DERIVED SKELETAL MUSCLE MODELS

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Spinal and bulbar muscular atrophy (SBMA), is a rare X-linked neuromuscular disorder caused by a CAG repeat expansion in the androgen receptor (AR) gene, producing a protein with an elongated poly Q tract (ARpolyQ)1. This mutation leads to progressive degeneration of lower motor neurons and skeletal muscle dysfunction. Many evidence indicates that mitochondrial/metabolic dysfunction are critical points to disease progression2. This study aims to characterize mitochondrial abnormalities in skeletal muscle cells.
We differentiated induced pluripotent stem cell (iPSC)-derived from SBMA patients into skeletal muscle cells (SkMuCs)3, and used this model to investigate mitochondrial structure and function.

In SBMA myoblasts, mitochondria displayed alterations, appearing more rounded and smaller, which indicated fragmentation. They showed fewer branches per mitochondrion, suggesting an impaired mitochondrial network. Electron microscopy (EM) confirmed a reduced mitochondrial size in SBMA cells. Flowcytometry analysis assessment using JC-1 dye revealed a reduction in mitochondrial membrane potential. Furthermore, EM showed that SBMA cells has a diminished number and a smaller size of lipid droplets.

Our findings demonstrate that SBMA muscle cells have significant mitochondrial defects, supporting mitochondrial dysfunction as a contributor to disease pathogenesis.These results support the use of patient-derived iPSC models for investigating disease mechanisms and potential therapeutic targets.

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