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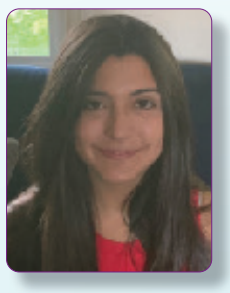

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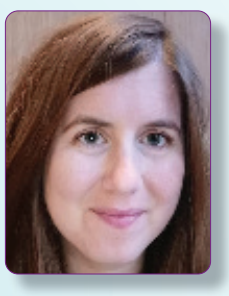

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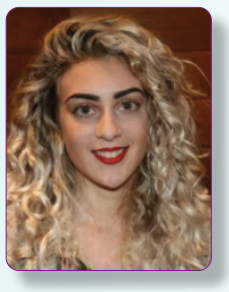

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Application of ATAC-Seq for genome-wide analysis of the chromatin state at single myofiber resolution

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Myofibers are the main components of skeletal muscle, which is the largest tissue in the body. Myofibers are highly adaptive and can be altered under different biological and disease conditions. Therefore, transcriptional and epigenetic studies on myofibers are crucial to discover how chromatin alterations occur in the skeletal muscle under different conditions. However, due to the heterogenous nature of skeletal muscle, studying myofibers in isolation proves to be a challenging task. Single-cell sequencing has permitted the study of the epigenome of isolated myonuclei. While this provides sequencing with high dimensionality, the sequencing depth is lacking, which makes comparisons between different biological conditions difficult.

Here, we report the first implementation of single myofiber ATAC-Seq, which allows for the sequencing of an individual myofiber at a depth sufficient for peak calling and for comparative analysis of chromatin accessibility under various physiological and disease conditions. Application of this technique revealed significant differences in chromatin accessibility between resting and regenerating myofibers, as well as between myofibers from a mouse model of Duchenne Muscular Dystrophy (mdx) and wild-type (WT) counterparts. This technique can lead to a wide application in the identification of chromatin regulatory elements and epigenetic mechanisms in muscle fibers during development and in muscle-wasting diseases.

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