Strength in numbers: Exploring muscle regeneration through single-cell and spatial transcriptomics

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scMuscle
McKellar et al, *Comms Bio*, 2021

STRS
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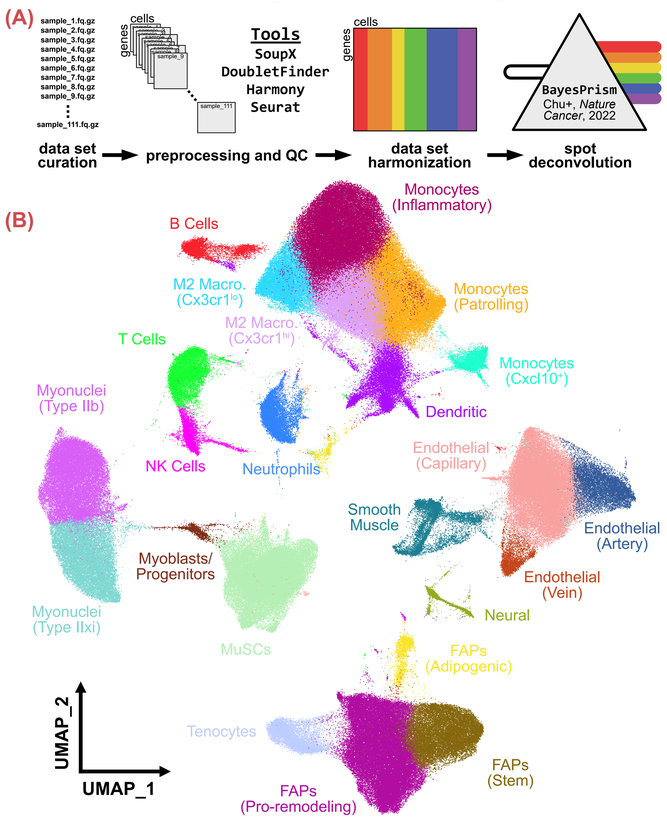
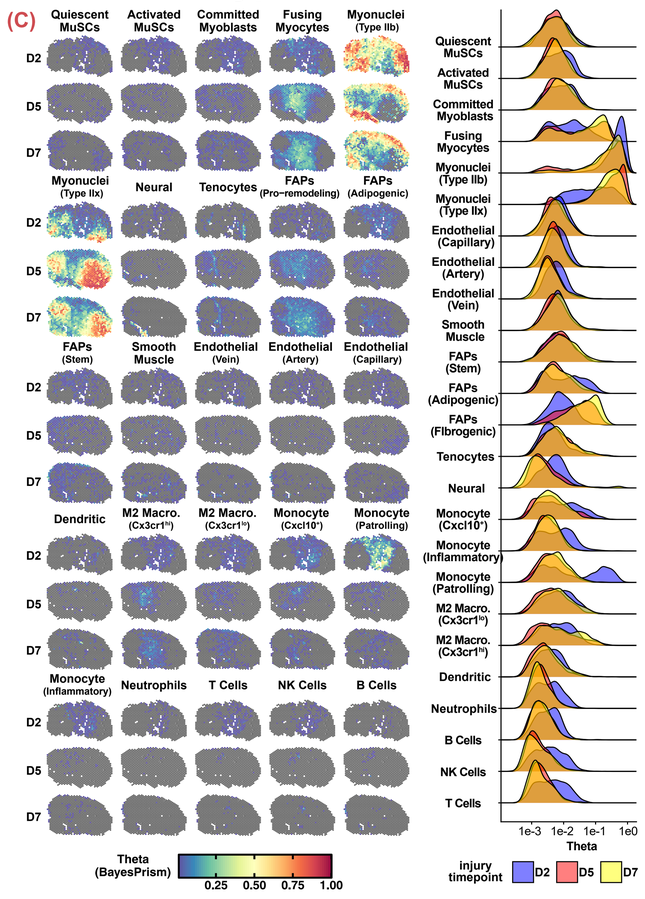
Abstract

Skeletal muscle repair is driven by the coordinated self-renewal and fusion of myogenic stem and progenitor cells. Single-cell gene expression analyses of myogenesis have been hampered by the poor sampling of rare and transient cell states that are critical for muscle repair, and do not provide spatial information that is needed to understand the context in which myogenic differentiation occurs. Here, we demonstrate how large-scale integration of new and public single-cell and spatial transcriptomic data can overcome these limitations. We created a large-scale single-cell transcriptomic dataset of mouse skeletal muscle by integration, consensus annotation, and analysis of ~365,000 cells. We used this data build a densely sampled model of myogenesis and identified rare, short-lived transitional states of progenitor commitment and fusion that are poorly represented in individual datasets. We paired this deep profiling with spatial RNA-sequencing of mouse muscle at three time points after injury and used the integrated dataset as a reference to achieve a high-resolution, local deconvolution of cell subtypes. This analysis identified the temporal variation in cell subtype colocalization during injury recovery. Finally, we extended these data with a new molecular strategy to broaden the repertoire of RNAs which can be captured by existing spatial transcriptomics platforms. Together these data provide insight into the spatiotemporal patterns of gene expression and regulation during skeletal muscle regeneration.

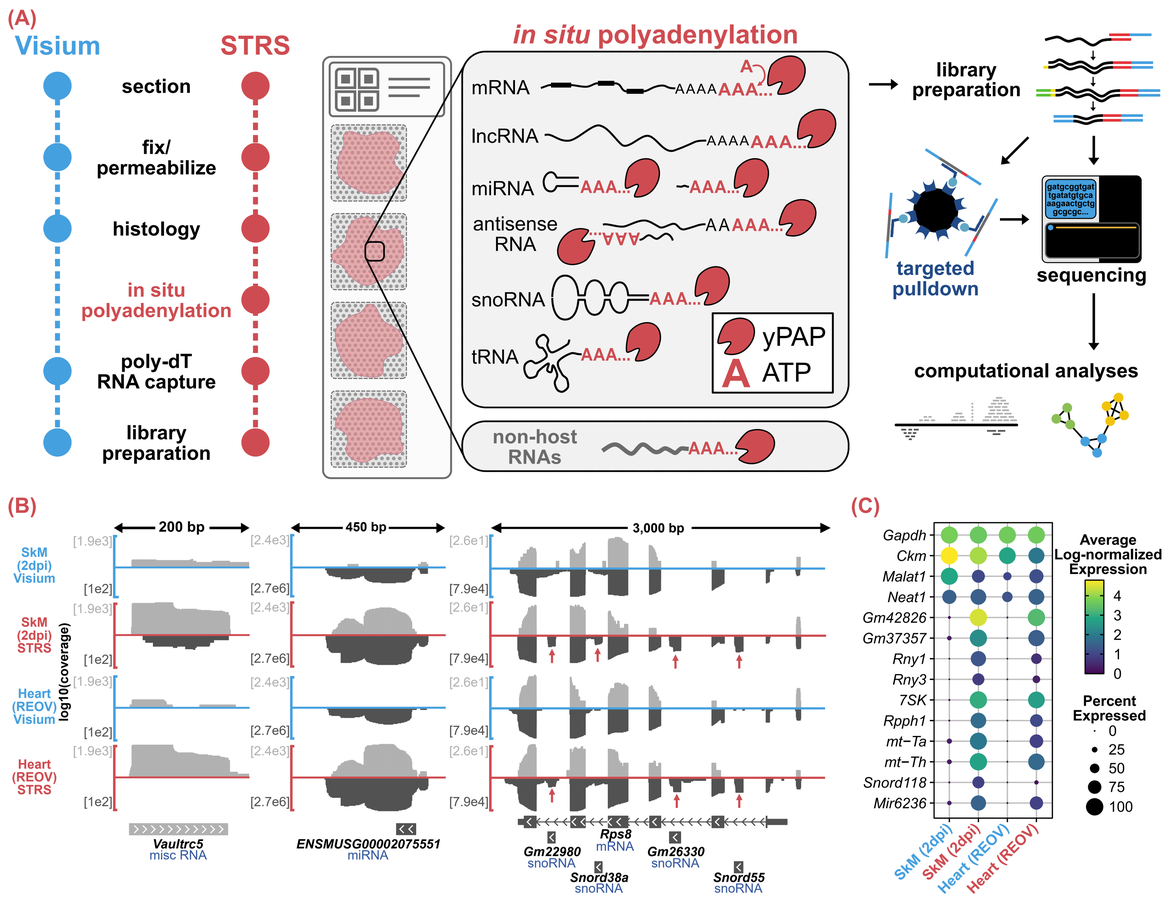
scMuscle: Large-scale integration reveals cell subtypes in skeletal muscle



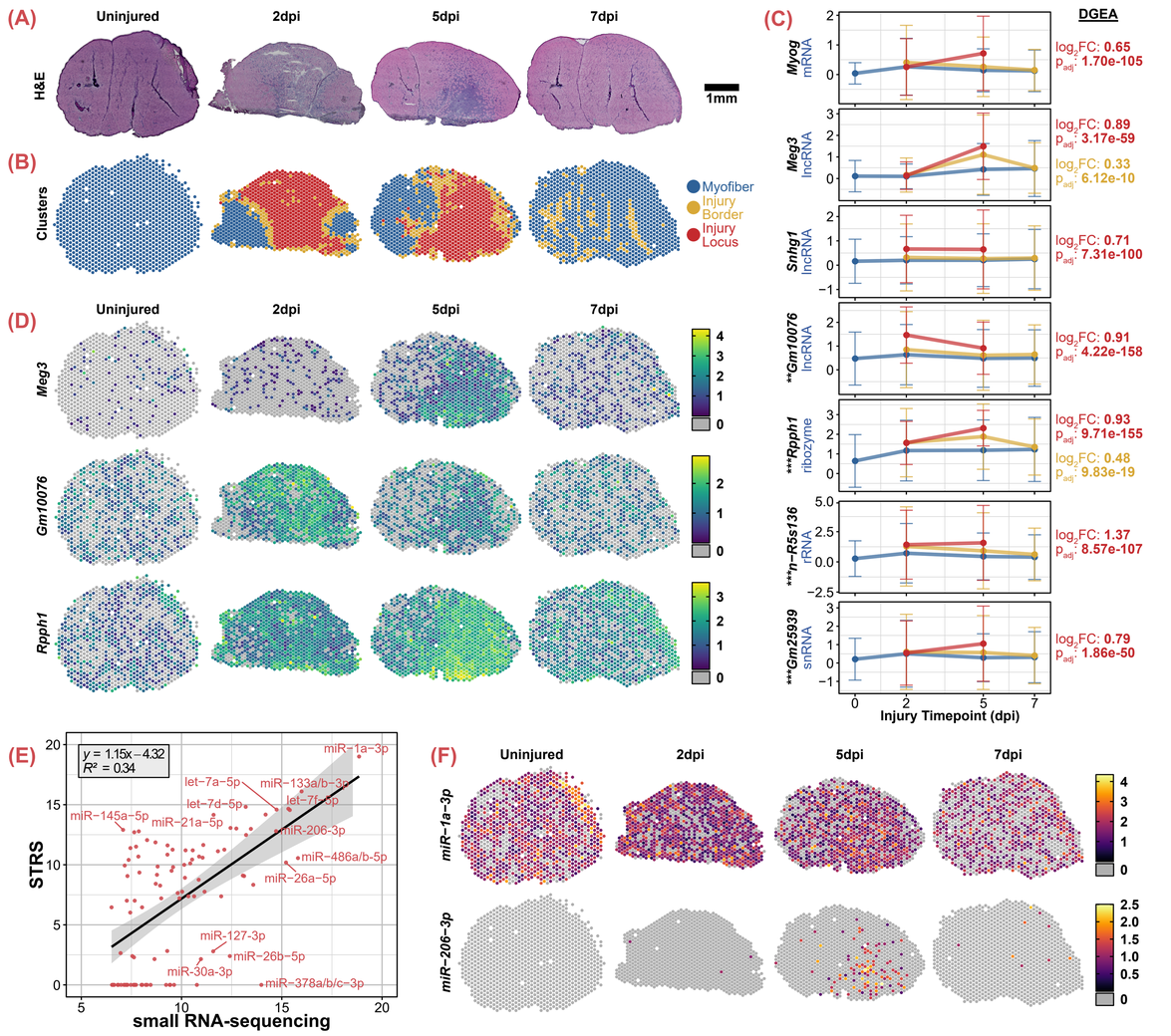


~365k cells/nuclei, 111 data sets (88 public + 23 new), 16 labs

Spatial Total RNA-Sequencing (STRS)



STRS spatially resolves ncRNA expression in regenerating muscle



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STRS enables simultaneous analysis of viral infection and host response