3.5 Logistics over Long Distances: Nascent Proteomes in Nerve Axons

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Their long axonal processes present a significant logistics challenge for neuronal cells, requiring integration of local translation and motor dependent transport mechanisms to support axon growth and maintenance. I will present new approaches to study regulation and dynamics of local translation in axons, and the roles of these mechanisms in supporting neuronal growth, survival and regeneration.

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3.6 Temporal dynamics of the multi-omic response to endurance exercise training across tissues

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Repeated endurance exercise induces a robust multi-tissue response that promotes whole-body health while reducing the risk of chronic disease and premature death. While the effects of exercise on metabolism, immune responses, and tissue function are recognized, the underlying molecular mechanisms of exercise training adaptation are incompletely understood. The Molecular Transducers of Physical Activity Consortium (MoTrPAC) profiled the longitudinal molecular adaptation to 8 weeks of endurance exercise training in whole blood, plasma, and 18 solid tissues in the mammalian model Rattus norvegicus. We employed a multi-omic approach for complete molecular characterization through proteomics, phosphoproteomics, acetylproteomics, ubiquitylproteomics, transcriptomics, metabolomics, DNA methylation, chromatin accessibility, and multiplexed immunoassays. This compilation of 211 datasets across 19 tissues, 25 molecular assays, and 4 training time points in young male and female animals represents the most comprehensive resource to explore the tissue-specific response to exercise training to date. We identified 34,244 analytes that significantly changed over the training time course in at least one sex (5% false discovery rate). Next, using a graphical approach for temporal multi-omic and multi-tissue integration, we identified the main differential trajectories of the selected features over the training time course and interpreted corresponding biological pathway enrichments. The heart and skeletal muscle shared similar temporal responses, reflecting a concerted adaptation of mitochondrial biogenesis and metabolism. Extensive changes in heart signaling were observed through kinase activity prediction analysis of phosphoproteomics data, revealing altered activity of tyrosine kinases. The predicted regulation of Src was linked to remodeling of the extracellular matrix and intercellular interactions critical for heart structural adaptation to training. We performed a metabolism-focused analysis across tissues, revealing global regulation of liver lipid metabolism that suggests improved liver health. Integration with acetylproteomics data indicated that changes in lipid metabolism were linked to a previously unobserved robust acetylation of the mitochondrial proteome. Substantial sex differences in training adaptation were discovered, including male-specific recruitment of immune cells to adipose tissues and female-specific immune enrichments in the small intestine. Altogether, this MoTrPAC resource provides an unprecedented view of the effects of exercise across an organism, revealing mechanistic details of how exercise impacts mammalian health.

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