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Title:	Nutrient Dependent Regulation Of The Transcriptomic Dynamics In Hematopoietic Progenitors Of Drosophila And Humans
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Abstract:	The study presented in this thesis unravels a tapestry where miRNAs are not mere bystanders but active players in dictating how blood cells react to their environment, particularly under varying nutrient states. The results of this study provide a comprehensive analysis of microRNAs (miRNAs) in hematopoiesis, focusing on the influence of the amino acid “Leucine.” I elucidate how cells maintain phenotypic stability and robustness in response to environmental fluctuations, particularly nutrient availability. Employing Drosophila larval blood progenitors, my work highlights how leucine, a branch-chain amino acid, becomes a critical messenger, influencing the interplay between miRNA and messenger RNA (mRNA) in autophagy. Through molecular, genetics and pharmacological approaches, I demonstrate how autophagy through leucine sensing directly affects the dynamics of miRNA and mRNA hybrids, thereby influencing the proliferation process in blood cell progenitors. Extending this investigation to human blood stem and progenitor cells (HSPCs), I translate these findings to a human context. This leap from Drosophila blood cells to humans is not just a change in scale but underscores a potentially conserved nature of “Leucine dependent miRNA autophagy”, hinting at an evolutionarily conserved mechanism from simple to complex organismal systems. My study critically examines the molecular pathways identified in Drosophila blood progenitors and demonstrates its conservation in human hematopoietic stem and progenitor cells (HSPCs) and similar blood cell lines. This comparative analysisemphasizes the potential conservation of leucine-dependent miRNA autophagy across species, suggesting a broader relevance of these mechanisms in mammalian hematopoiesis. Findings from my work may have significant implications for understanding the molecular foundations of blood cell formation and function, with potential translational applications in addressing diseases related to blood cell development and nutrient metabolism disorders.
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