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Title: Understanding the importance of branched chain amino acids in blood cell development

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Abstract:

Hematopoiesis is the process of production of blood cells. During both the stages of primitive and definitive hematopoiesis in vertebrates, hematopoietic stem and progenitor cells (HSPCs) are formed which have the potential to give rise to all the blood cell types. There are several intrinsic and extrinsic factors that can influence hematopoiesis, one of them being carbon source in nutrients. Both in vivo studies across model organisms as well as in vitro cell culture assays, have shown that nutrients play an important role in blood cell proliferation and differentiation. Manipulation in one or more nutrition sources such as carbohydrates, lipids, amino acids or micronutrients, have an impact in the physiology of these cells. When it comes to specific amino acid sources, such as branched chain amino acids (BCAAs), not much is evidenced on their role in hematopoiesis. Here, we have used two mammalian blood cell lines HL-60 and K-562 to observe the effect of manipulations in BCAA concentrations in cell culture media on their cell growth. We found that BCAA starvation, both in terms of dosage and exposure, leads to reduced cell proliferation and size, thus indicating the importance of BCAA in cell growth. Next we tried to figure out the molecular underpinnings with which BCAAs affect our phenotype. BCAAs are reported to be involved in 'proteostasis' of cells which is majorly regulated by: protein synthesis and autophagy. Here in our study, we found heightened autophagic initiation upon BCAA starvation, affecting the proliferation rate and size of the cells at a time point where we observe no change in protein synthesis, thereby proposing the importance of autophagy in BCAA's regulation of hematopoiesis.

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