

# Chondrocyte Identity and Function are Controlled by Glutamine Metabolism

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## Abstract

Correct functioning of chondrocytes is crucial for bone growth and fracture repair. These cells square measure extremely associateabolic however survive and performance in an avascular setting, implying specific metabolic necessities that square measure, however, poorly characterised. Here, we tend to show that chondrocyte identity and performance square measure closely coupled with amino acid metabolism during a feed forward method. The master chondrogenic transcription issue SOX9 stimulates amino acid metabolism by increasing amino acid consumption and levels of glutaminase one (GLS1), a rate-controlling catalyst during this pathway. Consecutively, GLS1 action is important for chondrocyte properties and performance via a triangular mechanism. First, amino acid controls chondrogenic organic phenomenon epigenetically through salt dehydrogenase-dependent acetyl-CoA synthesis, necessary for simple protein acylation. Second, transaminase-mediated aspartate synthesis supports chondrocyte proliferation and matrix synthesis. Third, glutamine-derived glutathione synthesis avoids harmful reactive species accumulation and permits chondrocyte survival within the avascular growth plate. Together, our study identifies amino acid as a metabolic regulator of gristle fitness throughout bone development.

**Ke words:** chondrocyte; glutamine; metabolism; bone development; avascular; feed forward; SOX9; GLS1; glutathione; reactive species; epigenetics; acylation; aspartate; proliferation; matrix synthesis; survival; gristle fitness.

## Introduction

Chondrocytes are the primary cells of cartilage and are responsible for the production and maintenance of the extracellular matrix (ECM) of cartilage. They are found in the growth plate, articular cartilage, and intervertebral discs. Chondrocytes are highly specialized cells that are able to survive in an avascular environment. They obtain their nutrients from the surrounding tissue through diffusion. The metabolism of chondrocytes is highly regulated and is essential for their survival and function. One of the key metabolic pathways in chondrocytes is the glutamine pathway. Glutamine is an essential amino acid that is used for a variety of metabolic processes, including protein synthesis, gluconeogenesis, and the synthesis of glutathione. In chondrocytes, glutamine is primarily used for the synthesis of glutathione, which is a major antioxidant and is essential for the survival of these cells. The glutamine pathway is regulated by several factors, including the transcription factor SOX9. SOX9 is a master chondrogenic transcription factor that is essential for the development of cartilage. It has been shown that SOX9 stimulates the expression of glutaminase one (GLS1), a rate-controlling catalyst in the glutamine pathway. This suggests that SOX9 plays a role in regulating the metabolism of chondrocytes. In this review, we will discuss the role of glutamine metabolism in chondrocyte identity and function. We will first discuss the basic metabolism of chondrocytes and then focus on the glutamine pathway. We will then discuss the role of SOX9 in regulating the glutamine pathway and how this affects chondrocyte identity and function. Finally, we will discuss the implications of our findings for the treatment of cartilage diseases.

1. Introduction

2. Chondrocyte Metabolism

3. The Glutamine Pathway

4. Regulation of the Glutamine Pathway

5. SOX9 and the Glutamine Pathway

6. Implications for Cartilage Development

7. Conclusion

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