

NON-TECHNICAL ABSTRACT: *(State in layman's terms the application's broad, long-term objectives and specific aims, making reference to the potential public benefits of the project.)*

The long-term goal of my research program is to understand the mechanisms by which undifferentiated cells become restricted to specific fates and subsequently maintain the differentiated state. For example, even though virtually all our cells contain the same genetic blueprints, some cells become bone while others become muscle. Furthermore, once the commitment to become a particular type of cell is made, the decision is rarely ever reversed. At the broadest level, understanding the mechanisms driving distinct differentiation events can likely be exploited for regenerative medical benefit in order to replace diseased or damaged tissue with healthy new cells. The work proposed here aims at understanding the roles two specific factors, Wdr68 and Dyrk1b, play in muscle development. The mouse C2C12 cell line is a well-characterized model for muscle cell differentiation. In mouse C2C12 cells, Dyrk1b acts as a differentiation switch during muscle development. This Dyrk1b-mediated switch results in expression of the myogenin gene that is known to be important for muscle differentiation. We hypothesize that wdr68 is also required for myogenin expression in C2C12 cells. If this hypothesis tests positive, the C2C12 cell culture system can be further exploited to study the molecular mechanism of Wdr68 and Dyrk1b action.