THE GRADUATE COLLEGE OF THE
UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER

ANNOUNCES THE FINAL EXAMINATION OF

Chengyi Sun

FOR THE DEFENSE OF THE DOCTOR OF PHILOSOPHY DEGREE
GRADUATE COLLEGE
Department of Cell Biology

May 5, 2017, 10 a.m.
Oklahoma Medical Research Foundation
Wileman Learning Center

Functional analysis of PDGFRα/PDGFRβ in adipogenesis

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ABSTRACT: Adipose tissue is distributed in depots throughout the body with specialized roles in energy storage and thermogenesis. Platelet-derived growth factor receptor α (PDGFRα) and PDGFRβ are both used as markers of adipocyte precursors, but the function of PDGFRα/PDGFRβ during adipose tissue organogenesis and adult adipogenesis is still not well understood. Here, by analyzing mice with juxtamembrane or kinase domain point mutations that increase PDGFRα activity (V561D or D842V), we found that PDGFRα activation inhibited embryonic white adipose tissue organogenesis in a tissue autonomous manner. PDGFRα inhibited the formation of adipocytes from collagen-expressing precursors while favoring the formation of stromal fibroblasts. Recent analysis in our lab also indicates that increased PDGFRβ signaling causes juvenile adipose tissue atrophy. For analysis in adult adipogenesis, we use a new Cre/LoxP and Flp/FRT based approach for mosaic mutant analysis, which allow us to track scattered PDGFRα or PDGFRβ mutant cells at the single cell level during adipogenesis. This approach identifies different contribution of PDGFRα or PDGFRβ positive precursors between different fat depots. Mosaic activation of PDGFRα blocks adipogenesis while knockout of PDGFRα promotes adipogenesis at the single cell level. Our data implicate PDGFRα as predominantly negative regulator of adipogenesis, and indicate that regulation of PDGFRα activity may change the determination of cell fate during adipocyte development. Recent evidence has shown adipose tissue as a promising source for clinical stem cell therapy. Our study focusing on PDGFR in adipocyte precursors may provide a better understanding of the cellular mechanism involved in adipose tissue formation and also may contribute to the application of stem cell therapy in the future.