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Promotionsverfahren von **Herrn M.Sc. Marten Schouwink**
Auslage der Dissertation und Gutachten sowie Termin der mündlichen Prüfung
Anlage: Einseitige Zusammenfassung der Dissertation

Sehr geehrte Damen und Herren,

in dem oben genannten Promotionsverfahren wird die Annahme der Dissertation

Fetal programming of adipocyte development by exposure to an obesogenic intrauterine milieu

von den Berichterstattenden Prof. Dr. H. Al-Hasani und Prof. Dr. med. Regina Ensenauer beantragt. Sie kann zusammen mit den Gutachten in der Zeit

vom 02.12.2024 bis 11.12.2024

eingesehen werden. Bitte wenden Sie sich zur Einsicht an das Promotionsbüro (promotionmnf@hhu.de).

Einsprüche gegen diese Dissertation können nur zwei Tage nach der vorgenannten Frist geltend gemacht werden. Erfolgt kein Einspruch, so gilt die Dissertation als angenommen (§ 7 Ziffer (5) PO).

Sofern die Dissertation angenommen wird, findet die mündliche Prüfung am

16.12.2024 um 15.00 Uhr

im **Raum 26.24.U1.020** statt. Als Prüferinnen bzw. Prüfer sind vorgesehen:
Prof. Dr. S. Prömel, Prof. Dr. O. Ebenhöh und Prof. Dr. T. Klein.

Die Öffentlichkeit ist bei der Befragung nicht zugelassen.

Mit freundlichen Grüßen
im Auftrag

Daniela Schleiffer

Abstract

The escalating prevalence of overweight and obesity, affecting 55% of women and 67% of men, and up to 38% and up to 40% of girls and boys aged 5-19 years in high-income western countries, respectively, underscores a pressing public health concern with profound implications for future generations. Maternal factors such as gestational weight gain, gestational diabetes mellitus, and increased pre-pregnancy weight negatively affect offspring health. Furthermore, previous studies on mouse models of our research group revealed sex-specific impacts of maternal obesity on adipose tissue development, with disturbances, particularly in females. Processes that cause these effects are called *fetal programming* and include epigenetic alterations like DNA methylation.

This thesis aims to study underlying mechanisms by which the intrauterine obesogenic environment influences offspring adipocyte development focusing on embryonic female adipocytes. Utilizing an NMRI mouse model for maternal obesity in pregnancy established in our group, *ex vivo* differentiated E13.5 mouse embryonic fibroblasts were analyzed regarding their adipogenic differentiation capacity, transcriptome, proteome, and methylome. Subsequently, candidate genes' role in adipogenesis was investigated *in vitro* in the 3T3-L1 preadipocyte cell line using RNA interference-mediated knockdown.

Maternal obesity during pregnancy altered female fetal adipocytes' transcriptome, proteome, and methylome, affecting genes and proteins associated with regulating commitment to the adipogenic lineage and lipid metabolism. Transcriptomic analysis revealed a downregulation of several genes including aldehyde dehydrogenase family 1 subfamily A7 (Aldh1a7) in female fetal adipocytes by maternal obesity. Remarkably, analysis of the time course of expression and knockdown experiments during adipogenic differentiation uncovered *Aldh1a7* as a novel regulator of adipogenesis and showed its downregulation in female adipose tissue also in adulthood.

These findings highlight the early onset of maternal obesity's impact on female offspring adipocyte development, predisposing offspring to adverse fat tissue development, obesity, and long-term adverse health consequences. In this context, the identification of targets such as *Aldh1a7* offers avenues for intervention such as nutritional modifications to alleviate the intergenerational transmission of metabolic dysfunction associated with maternal obesity. In conclusion, this thesis supports the development of preventive interventions aimed at improving health development of future generations by further understanding the intricate sex specific molecular mechanisms underlying adipocyte development and dysregulation in the context of maternal obes