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## REVIEW

of PhD thesis by Agnieszka Chabowska-Kita, M.Sc.

**“Genetic and environmental interactions in the acquisition of the brown adipocyte phenotype during postnatal development”**

**Supervisor: Prof. Leslie P. Kozak, Ph.D.**

In addition to the better-known white adipose tissue (WAT) that specializes in lipid storage and undergoes pathological expansion during obesity, mammals are also equipped with brown adipose tissue (BAT). BAT is a key thermogenic tissue in rodents and other small mammals, including newborn humans, that defends core body temperature in cold weather. Recent studies unambiguously demonstrate that healthy adult humans have significant depots of metabolically active BAT. It is of special interest because it has been shown that the activities of brown and beige fat cells reduce metabolic disease, including obesity, in mice and correlate with leanness in humans. Many genes and pathways that regulate brown and beige adipocyte biology have now been identified, providing a variety of promising therapeutic targets for metabolic diseases. Therefore, the main aims of the reviewed Ph.D. thesis, i.e. establishing the effects of ambient temperature during the early postnatal period and evaluating whether variation in ambient temperature during early postnatal period affected the brown adipocyte phenotype in white adipose tissue and interscapular BAT in adult mice is timely and fully justified.

Dissertation was written in English and contains of 26 pages and the copies of two published articles which co-author is Agnieszka Chabowska-Kita. The dissertation is starting with “Table of Contents”. Then, “List of articles comprising the monothematic cycle of publications” and a table showing total number of publications and value of Impact Factor of already published by Ms.

Chabowska-Kita papers are presented. Next, there are 2 pages of “Abbreviations list” and 5 pages of “Introduction”, that contains all the information necessary for the understanding of the research, i.e. data about structural and functional characterization of WAT and BAT, the origin of brown and white adipocytes and stimulation of the brown adipocyte phenotype in WAT has been described. It is worth to underline that this part of dissertation was published in extended version as the review paper: **Agnieszka Chabowska-Kita, Leslie P. Kozak “The critical period for brown adipocyte development: genetic and environmental influences” Obesity (doi:10.1002/oby.21376)**, that is a part of presented PhD thesis. Then “Description of articles included in doctoral dissertation” is presented. Unfortunately, this part just repeated information which were described in the review and original manuscripts presented as PhD achievement. Having privilege of unlimited space available in PhD thesis Agnieszka Chabowska-Kmita should use this opportunity to present extended results description and discussion of obtained results. Method section should be also updated, e.g. sequences of probes and primers used in the study should be added, Western blot method should be described in details not just linked to appropriate reference etc. The first part of dissertation is ended with Abstracts (in English and in Polish) and with a list of 81 items of references, predominantly published in recent years. As a minor remark I have to mention that titles of the journals are cited in different manner: usually as whole titles but sometimes as abbreviated titles. It is also not necessary to present information when cited papers were indexed by PubMed.

The most valuable part of the dissertation is paper by **Agnieszka Chabowska-Kita, Anna Trabczynska, Agnieszka Korytko, Monika M. Kaczmarek, Leslie P. Kozak** entitled **“Low ambient temperature during early postnatal development fails to cause a permanent induction of brown adipocytes” published in FASEB Journal 29: 3238-3252 (2015)**. The main findings of this article are that: (1) low ambient temperature during early postnatal development reduced fat mass and adiposity in developing and adult mice fed a high-fat diet for 8 weeks, (2) the development of brown adipocytes in white adipose tissue and their thermogenic potential is determined by a genetic program that is independent of ambient temperature, (3) the realization of the complete brown adipocyte phenotype in white cells during the early postnatal period in response to cold stimulation, a process that is recapitulated in adult animals, depends on the development of sympathetic responsiveness to low ambient temperatures in white adipose tissue between 10 and 21 days of age. These findings contribute significantly to our knowledge in the subject of adipocytes metabolism and function. The study was well rationalized, logically designed and clearly presented. The obtained results are well illustrated on very carefully prepared figures and tables.



One of the main conclusion of the presented study is that the development of brown adipocytes in WAT is determined by a genetic program that is independent of ambient temperature. I would like this issue to be elaborated during the defense of the PhD thesis. Please discuss what are the molecular mechanisms, what transcription factors are involved in starting of such "genetic program" and how it could be regulated.

In both mentioned above papers which constitute major part of PhD thesis Agnieszka Chabowska-Kita is the first author. According to the attached statements of co-authors Agnieszka Chabowska-Kita was the leading author. My only concern relates to the lack of description of contribution of Agnieszka Chabowska-Kita to the papers presented as PhD achievement, especially to the second one. It is unclear to me, what was the exact contribution of Agnieszka Chabowska-Kita to the study presented in this article. I assume that PhD candidate performed most of presented analysis but it is not clearly indicated in the attached statements. In my opinion in the case of complex papers, a contribution of the PhD candidate should be described in more details.

Summarizing, all of the above-mentioned remarks do not diminish the great value of the presented PhD thesis. Agnieszka Chabowska-Kita has proved a very good knowledge of the literature, as well as a wide range of research methods and demonstrated his leading role in the research performed and her great scientific possibilities and abilities.

I conclude that the dissertation presented for evaluation meets the requirements of the LAW ABOUT SCIENTIFIC DEGREES AND TITLE OF SCIENTIFIC AND THE GRADE AND TITLE IN THE FIELD OF ART and recommend to the Scientific Council of the Medical University of Bialystok admission of Ms. Agnieszka Chabowska-Kita to the further stages of Ph.D. proceedings.

Stwierdzam, że przedstawiona do oceny rozprawa doktorska spełnia wymogi stawiane przez **USTAWĘ z dnia 14 marca 2003 r. O STOPNIACH NAUKOWYCH I TYTULE NAUKOWYM ORAZ O STOPNIACH I TYTULE W ZAKRESIE SZTUKI** (Dz. U. z 2003 roku Nr 65, poz. 595 z późniejszymi zmianami) i wnoszę do Rady Wydziału Lekarskiego Uniwersytetu Medycznego w Białymstoku o dopuszczenie mgr Agnieszki Chabowskiej-Kita do dalszych etapów przewodu doktorskiego.

*Paweł Dobry*