A novel functional polymorphism in the fatty acid desaturase 2 gene (*Fads2*): possible role in basal metabolic rate

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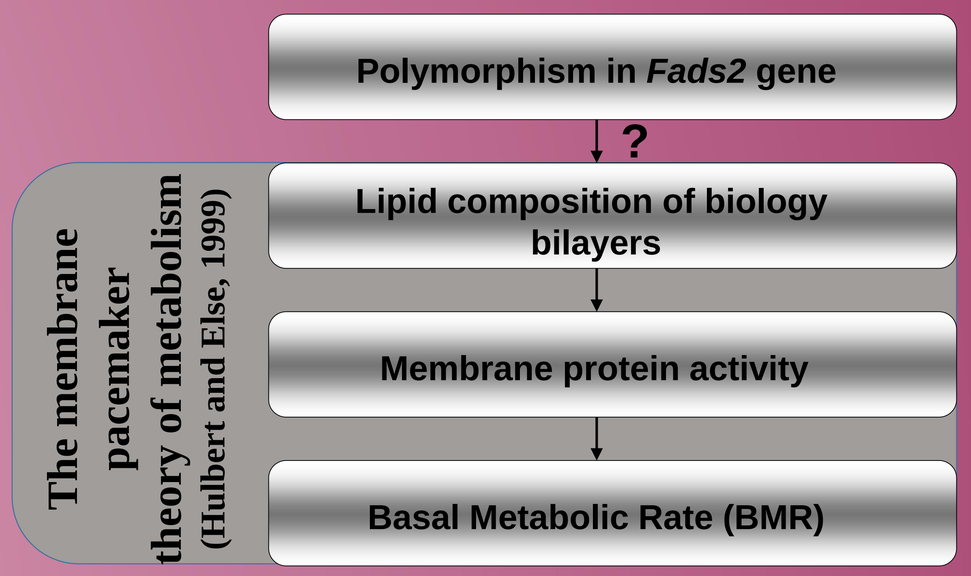
Introduction

As membrane components, polyunsaturated fatty acids (PUFAs), play an important role in cellular processes and have been shown to be associated with basal metabolic rate - BMR. The physical characteristics of PUFAs increase flexibility of bilayers and modulates the molecular activity of many membrane proteins and thus lead to increase of BMR. While the link between BMR and membrane lipid composition is clear on an interspecific level, the underlying mechanism linking them on an intraspecific level is not well understood.

Here we present a new polymorphism in the fatty acid desaturase 2 (*Fads2*) gene for Δ-6 desaturase (D6D) in mice, a key enzyme for PUFA synthesis.

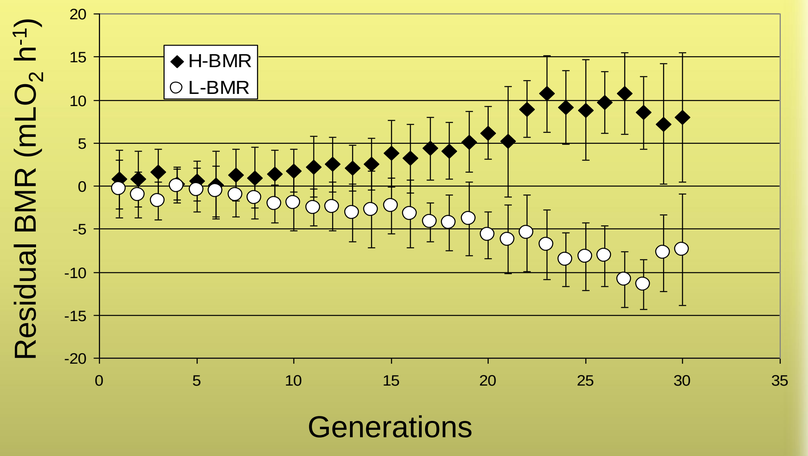


Aim

The goal of this study was to verify a possible association between *Fads2* genotypes and BMR.

Material

Outbred Swiss-Webster laboratory mice lines divergently selected for high and low BMR in the Institute of Biology, University of Bialystok, Poland.

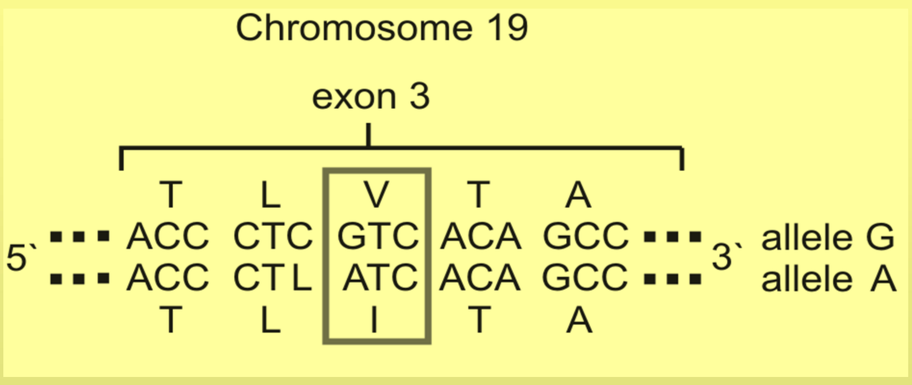


Changes in basal metabolic rate (body mass-corrected) for laboratory mice due to selection for H-BMR and L-BMR with generations.

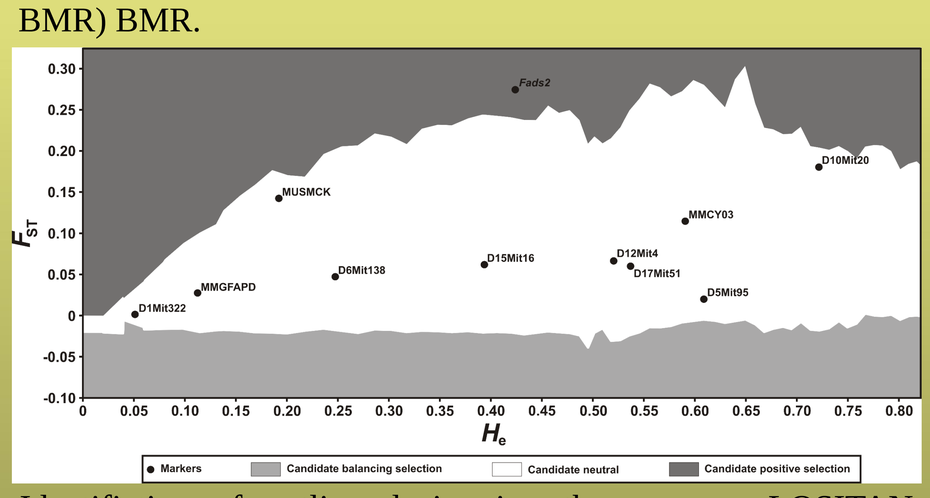
Methods

- measurements of BMR (open – circuit respirometry system; Sable System)
- RNA isolation (RNeasy MiniKit; Qiagen)
- RT – PCR (Qiagen)
- primers design (Primer3, Fast PCR)
- PCR (Qiagen; GeneAmp PCR System, Perkin Elmer)
- sequencing analysis of *Fads2* gene
- analysis of 11 microsatellite loci for *F*st outlier test (LOSITAN)

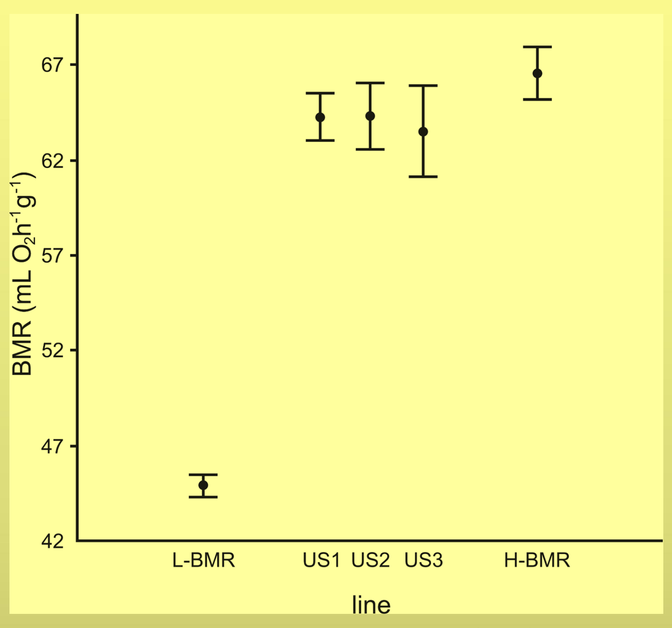
Results



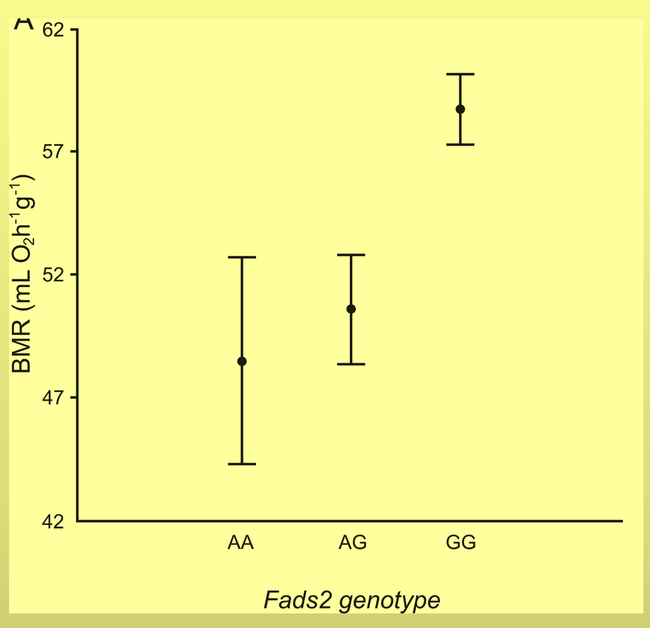
Polymorphism in *Fads2* gene encoding Δ-6 desaturase in lines of mice divergently selected for high (H-BMR) and low (L-BMR) BMR.



Identifiction of outliers losi using the program LOSITAN (Antao et al. 2008). Locus highlighted in dark grey *(Fads2)* is candidate for positive selection.



Differences in BMR (mL O_2 h^{-1} g^{-1}) among laboratory mice selected for low (L-BMR) and high (H-BMR) basal metabolic rate for 32 generation (F32) with AA, AG and GG *Fads2* genotypes.



Differences in BMR (mL O_2 h^{-1} g^{-1}) among mice selected for low (L-BMR) and high (H-BMR) BMR and 36 mice from three unselected lines.

Pairwise comparisons of the selected lines of mice, based upon *F*st values at the *Fads2* locus, suggest great and significant genetic differentiation (L-BMR v H-BMR; ***F*st = 0.273**, $P < 0.0001$).

Conclusions

These results for L-BMR and H-BMR lines of mice, as well as for unselected lines of mice, suggest that there may be connection between polymorphism in *Fads2* gene and BMR. However, to fully confirm the membrane pacemaker theory of metabolism it is necessary to:

- amplify and sequence the others desaturases and regulatory protein SREBF-1c;
- analyse of expression of these genes and activity of protein that they are encoding