Circulating MOTS-c levels are decreased in obese male children and adolescents and associated with insulin resistance

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Background and Aims
A novel bioactive peptide, mitochondrial-derived peptide (MOTS-c), has recently attracted attention as a potential prevention or therapeutic option for obesity and type 2 diabetes mellitus (T2DM). MOTS-c profiles have not yet been reported in human obesity and T2DM. We aimed to determine circulating MOTS-c levels in obesity and explore the association between MOTS-c levels and various metabolic parameters.

Methods
In this case-control study, 40 obese children and adolescents (27 males) and 57 controls (40 males) were recruited in the Hubei Province of China in 2017. Circulating MOTS-c levels were measured using ELISA, clinical data (e.g., glucose, insulin and lipid profile) were recorded, and anthropometric measurements were performed. Finally, we investigated correlations between MOTS-c levels and related variables.

Results
- MOTS-c levels were significantly decreased in the obese group compared with the control group (472.81 ± 22.83 ng/mL vs. 561.64 ± 19.19 ng/mL, p < 0.01).
- After classification by sex, MOTS-c levels were significantly decreased in obese male children and adolescents compared to their counterparts (465.26 ± 24.53 ng/mL vs. 584.07 ± 21.18 ng/mL, p < 0.001), while they were comparable between the obese and healthy female subjects (487.89 ± 49.77 ng/mL vs. 508.85 ± 38.76 ng/mL, p > 0.05).
- Further, MOTS-c levels were negatively correlated with body mass index (BMI), HOMA-IR, and HbA1c in the male cohort.

Conclusions
Circulating MOTS-c levels were decreased in obese male children and adolescents and correlated with markers of insulin resistance and obesity. Although the role of MOTS-c as a treatment for obesity and diabetes in humans will require further investigation, it is possible that a decline in MOTS-c might be a biomarker of insulin resistance during childhood obesity.

ACKNOWLEDGEMENTS
This study was supported by grants from Program for Changjiang Scholars and Innovative Research Team in University (PCSIRT1131) and National Nature Science Foundation of China (81670781 and 81400816). The authors confirm that there is no conflict of interests associated with this manuscript.

Fig. 1. Circulating MOTS-c levels were decreased in obese children or adolescents (A, B). Plasma concentrations of MOTS-c in the control group (n=57) and obese group (n=40). Data are shown as mean ± SEM. *p < 0.01.

Fig. 2. Comparison of plasma MOTS-c concentration between sexes: (A) Plasma concentrations of MOTS-c in the all male cohort (n=67) and all female cohort (n=30); (B) Comparison of MOTS-c concentration among male control (n=40), obese male (n=27), control female (n=17), and obese female (n=13) groups. Data are shown as mean ± SEM. *p < 0.01; NS, no significance.

Fig. 3. Circulating MOTS-c levels were significantly decreased in the insulin-resistant obese male group. (A) The comparison of plasma MOTS-c concentrations among the control group (n=67), the non-IR obese group (n=23), and the IR-obese group (n=17). (B) The comparison of plasma MOTS-c concentrations among the control male group (n=40), the non-IR obese male group (n=17), and IR-obese male group (n=10) are shown as mean ± SEM. *p < 0.005, **p < 0.01.

Fig. 4. MOTS-c concentrations were negatively correlated with body mass index (BMI), BMI-SDS, waist circumference (WC), waist-to-hip ratio (WHR), fasting insulin levels, and HOMA-IR of male children and adolescents. (A) BMI, r = -0.521, p < 0.001; (B) BMI-SDS, r = -0.467, p = 0.001; (C) WC, r = -0.559, p = 0.001; (D) WHR, r = -0.314, p = 0.010; (E) fasting insulin levels, r = -0.331, p = 0.006; and (F) HOMA-IR, r = -0.344, p = 0.004.