**METHODS**

MSCs were cultured from 120 infants enrolled in the Healthy Start study (pMAMR range: 16.5–45.1 kg/m²) (Table 2A). Maternal buffering insulin, HbA1C, and BMI at delivery and during lactation were measured at ≥17.5% and ≤3.5%. Offspring adiposity (NW) was measured in 50% of births at birth and in 4 years. MSCs were cultured from umbilical cord tissue collected at delivery. TC, glycated fatty acids (HbA1C of 300 μM eicosenoic and palmitic acid (12:1, elaeostearic), bound to total serum albumin (BSA) at a ratio of 3:1:1 were measured in multiple different MSCs at ≥17.5% of differentiation. TC, HbA1C, and insulin (TC-HA1C) oxidation of radiolabeled fatty acids was determined. The sum υO2 and CO2-MR measures Total FAO and the ratio of CO2:AO2, represents mitochondrial efficiency for fat oxidation where higher levels indicate less efficiency. We hypothesized that the total FAO and TC-HA1C oxidation of MSCs would be correlated with maternal BMI, offspring adiposity (NW), and adiposity at 4 years of age. Partial correlation coefficients were determined to assess the association between TC-HA1C, CO2:AO2, and insulin (TC-HA1C) oxidation of radiolabeled fatty acids. Adiposity was measured in the full-MSC sample (n=125) and within each subset of maternal BMI to determine differences in association based on BMI category. Significant correlations with Total FAO were further analyzed for association with TC, CO2:AO2, and insulin (TC-HA1C) oxidation of radiolabeled fatty acids. We hypothesized that mitochondrial efficiency and insulin (TC-HA1C) oxidation of radiolabeled fatty acids would be associated with maternal BMI, offspring adiposity, and adiposity at 4 years of age.

**RESULTS**

There were no significant correlations between Total FAO and maternal glucose levels or HbA1C. Maternal total cholesterol was correlated with Total FAO (r=0.3, p=0.001) among all MSC samples, which was driven by NW-MSCs (n=64, p=0.004). In the NW-MSCs, the *p*-values, but not the CO2:AO2 or CO2:AO2 insulin, were significantly associated with insulin (TC-HA1C) oxidation of radiolabeled fatty acids. This was driven by associations with incomplete oxidation of fatty acids (TC-HA1C), which trended toward correlation with insulin adiposity in OB-MSCs (Fig. 3b, Fig. 5c) and was correlated with child adiposity at age 4 years among NW-MSCs (Fig. 5c).

**CONCLUSIONS**

Based on our previous observations of differences in mitochondrial fatty acid oxidation between NW- and OB-MSCs, which appeared to be related to maternal metabolic health markers, we tested the hypothesis that MSC fatty acid metabolism would be correlated with maternal metabolic traits across a range of maternal BMI and regardless of range. While this was true for association of maternal traits with Total FAO and CO2:AO2, we found that maternal insulin was correlated with mitochondrial fatty acid oxidation only among the OB-MSCs. Similar incomplete oxidation and lower mitochondrial efficiency for FAO were positively correlated maternal insulin in OB-MSCs, indicating poorer metabolic health with greater insulin exposure. The incomplete oxidation in MSCs trended toward lower oxidation compared with offspring adiposity at age 4 years, suggesting incomplete oxidation may have a role in obesity, but may have to do with overall elevated insulin in those mothers. Alternatively, these data may suggest a compensating effect of maternal insulin and obesity on MSC mitochondrial metabolism in these mothers; however, these results require our previous findings that mitochondrial fatty acid oxidation of infant MSCs may be an important index of offspring metabolic health that is correlated with maternal metabolic health markers. Such inherent differences in fetal tissue metabolites suggests that metabolic perturbations promote obesity earlier in life may be at birth.

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