

**Supplemental Table 1. Aqueous metabolomic profiling of Spot14 null and control adipose depleted MECs and whole mammary gland.** Aqueous metabolites were quantified using NMR from Spot14 null (S14-/-) and control whole mammary gland and MECs at lactation day 10. No differences were observed in intracellular concentrations of primary carbohydrates lactose and glucose. Aromatic amino acids and TCA cycle intermediates glutamate, pyruvate, and succinate were significantly increased in Spot14 null MECs and trended upward in whole mammary gland. Acetyl-CoA was significantly increased in both MECs and WTL, and Malonyl-CoA trended upward in Spot14 null whole mammary gland. Units are in  $\mu\text{mol}$  per gram.

| Adipose Depleted MECs      |         |     |        |      |             | Whole Mammary Gland |      |        |      |             |
|----------------------------|---------|-----|--------|------|-------------|---------------------|------|--------|------|-------------|
| Sugars                     | Control | sem | S14-/- | sem  | ttest       | Control             | sem  | S14-/- | sem  | ttest       |
| Glucose                    | 1.0     | 0.3 | 0.9    | 0.2  | 0.39        | 1.9                 | 0.4  | 1.3    | 0.4  | 0.21        |
| Lactose                    | 2.7     | 0.3 | 2.4    | 0.5  | 0.30        | 6.7                 | 0.7  | 5.8    | 0.6  | 0.17        |
| Sugars + Polyols           | 51.3    | 4.0 | 45.8   | 11.2 | 0.33        | 145.2               | 6.9  | 99.5   | 24.0 | 0.08        |
| Inositol                   | 0.3     | 0.0 | 7.4    | 6.9  | 0.17        | 1.1                 | 0.0  | 0.6    | 0.1  | <b>0.01</b> |
| Amino Acids + TCA          | Control | sem | S14-/- | sem  | ttest       | Control             | sem  | S14-/- | sem  | ttest       |
| Alanine                    | 0.6     | 0.0 | 0.7    | 0.2  | 0.17        | 2.0                 | 0.3  | 3.1    | 0.3  | <b>0.02</b> |
| Arginine                   | 0.8     | 0.1 | 0.8    | 0.2  | 0.46        | 0.8                 | 0.3  | 2.6    | 0.7  | <b>0.03</b> |
| Aromatic Amino Acids       | 7.9     | 0.3 | 9.1    | 0.6  | <b>0.05</b> | 5.7                 | 0.6  | 6.3    | 0.5  | 0.25        |
| Aspartate                  | 0.1     | 0.0 | 0.1    | 0.0  | 0.11        | 0.4                 | 0.2  | 0.3    | 0.1  | 0.29        |
| Citrate                    | 0.1     | 0.0 | 0.1    | 0.0  | 0.08        | 0.2                 | 0.1  | 0.2    | 0.0  | 0.43        |
| Glutamate                  | 0.3     | 0.0 | 0.9    | 0.3  | <b>0.03</b> | 2.1                 | 0.7  | 3.9    | 0.8  | 0.08        |
| Glutamine                  | 0.3     | 0.0 | 0.3    | 0.1  | 0.39        | 0.4                 | 0.1  | 0.5    | 0.1  | 0.35        |
| Lactate                    | 0.3     | 0.0 | 0.3    | 0.1  | 0.23        | 1.9                 | 0.8  | 0.9    | 0.7  | 0.19        |
| Pyruvate                   | 0.03    | 0.0 | 0.06   | 0.0  | <b>0.05</b> | 0.1                 | 0.0  | 0.2    | 0.1  | 0.14        |
| Succinate                  | 0.16    | 0.0 | 0.27   | 0.1  | <b>0.04</b> | 0.5                 | 0.1  | 0.8    | 0.1  | <b>0.03</b> |
| Val, Leu, Ile              | 2.6     | 0.4 | 2.6    | 0.2  | 0.47        | 3.1                 | 0.9  | 5.0    | 0.8  | 0.09        |
| Oxidative Stress           | Control | sem | S14-/- | sem  | ttest       | Control             | sem  | S14-/- | sem  | ttest       |
| tGlutathione               | 0.19    | 0.0 | 0.23   | 0.0  | <b>0.03</b> | 0.33                | 0.1  | 0.37   | 0.1  | 0.41        |
| rGlutathione               | 0.06    | 0.0 | 0.09   | 0.0  | <b>0.01</b> | 0.26                | 0.0  | 0.20   | 0.1  | 0.24        |
| OH-Butyrate                | 0.16    | 0.0 | 0.58   | 0.2  | 0.06        | 0.14                | 0.0  | 0.21   | 0.0  | 0.14        |
| Cholines                   | Control | sem | S14-/- | sem  | ttest       | Control             | sem  | S14-/- | sem  | ttest       |
| Glycerophosphocholine      | 0.6     | 0.1 | 0.9    | 0.3  | 0.20        | 2.2                 | 0.3  | 1.1    | 0.2  | <b>0.01</b> |
| Phosphocholine             | 0.8     | 0.2 | 1.0    | 0.3  | 0.26        | 1.2                 | 0.3  | 0.7    | 0.4  | 0.18        |
| Cholines                   | 0.2     | 0.1 | 0.1    | 0.0  | 0.21        | 0.2                 | 0.1  | 0.4    | 0.2  | 0.25        |
| Other                      | Control | sem | S14-/- | sem  | ttest       | Control             | sem  | S14-/- | sem  | ttest       |
| Acetate                    | 0.3     | 0.1 | 0.3    | 0.1  | 0.23        | 0.2                 | 0.0  | 0.2    | 0.0  | 0.29        |
| Acetyl-CoA                 | 0.93    | 0.2 | 1.59   | 0.3  | <b>0.04</b> | 0.64                | 0.2  | 1.35   | 0.2  | <b>0.04</b> |
| n-Acetylneuraminic acid    | 0.2     | 0.1 | 0.3    | 0.1  | 0.19        | 0.2                 | 0.0  | 0.2    | 0.0  | 0.26        |
| n-Acetyl-CH <sub>3</sub>   | 1.4     | 0.2 | 1.4    | 0.4  | 0.47        | 1.9                 | 0.7  | 0.7    | 0.5  | 0.11        |
| Adenines                   | 1.6     | 0.5 | 2.0    | 0.3  | 0.27        | 2.5                 | 0.2  | 2.5    | 0.3  | 0.48        |
| Creatine + Phosphocreatine | 0.3     | 0.1 | 0.3    | 0.1  | 0.39        | 0.3                 | 0.1  | 0.2    | 0.1  | 0.37        |
| Dimethyl amines            | 0.1     | 0.0 | 0.0    | 0.0  | 0.15        | 0.2                 | 0.1  | 0.1    | 0.0  | 0.23        |
| Malonyl-CoA                | N/D     |     |        |      |             | 5.9                 | 1.7  | 7.9    | 2.0  | 0.45        |
| Hydroxybutyryl-CoA         |         |     |        |      |             | 120.2               | 45.9 | 83.4   | 21.1 | 0.38        |
| Propionyl-CoA              |         |     |        |      |             | 93.8                | 38.0 | 93.9   | 28.7 | 1.00        |